Chapter

Perspective Chapter: Lifestyle Interventions for Hepatic Steatosis – Cornerstone of Management in Metabolic Dysfunction-Associated Steatotic Liver Disease

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Abstract

This chapter wang to explore the pivotal role of lifestyle interventions as the first-line therapeutic strategy for managing hepatic steatosis in metabolic dysfunction-associated steatotic liver disease (MASLD). It delves into evidence-based approaches to dietary optimization, physical activity regimens, and sustainable weight loss, emphasizing their direct impact on reducing liver fat, improving metabolic parameters, and halting disease progression. Key topics include macronutrient composition (e.g., Mediterranean diet (MD), low-carbohydrate approaches), exercise modalities (aerobic vs. resistance training), and behavioral strategies to enhance adherence. The chapter also addresses challenges in patient engagement, cultural considerations in lifestyle modification, and the integration of multidisciplinary care teams. Practical clinical tools, such as patient-centered goal-setting frameworks and monitoring protocols, are highlighted to empower healthcare providers in translating research into effective, individualized care plans.

Keywords: hepatic steatosis, MASLD, lifestyle interventions, dietary, exercise, patient adherence

1. Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD), formerly known as nonalcoholic fatty liver disease (NAFLD), is defined as a hepatic steatosis that occurs in the absence of excessive alcohol consumption or other known causes of liver injury, with the presence of at least one cardiometabolic risk factor [1, 2]. As the incidence rates of obesity and type 2 diabetes (T2D) continue to rise globally,

the prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) is also increasing [3]. Currently, 38% of adults and 7–14% of children/adolescents are affected by MASLD. By 2040, the prevalence of MASLD in adults is projected to exceed 55%. The most common cause of mortality among MASLD patients remains cardiovascular disease. Beyond hepatic outcomes (e.g., cirrhosis and hepatocellular carcinoma [HCC]), MASLD is associated with an elevated risk of developing incident type 2 diabetes (T2D), chronic kidney disease, sarcopenia, and extrahepatic malignancies. Furthermore, MASLD correlates with diminished health-related quality of life (HRQoL), reduced work productivity, fatigue, increased healthcare resource utilization, and substantial economic burdens (**Figure 1**) [4].

The hallmark feature of MASLD is excessive hepatic lipid accumulation, which may progress to steatohepatitis and fibrosis, posing significant threats to human health and lifespan [5]. The primary risk factors for MASLD encompass obesity, insulin resistance, hypertension, and hypertriglyceridemia, while its diagnosis concurrently serves to confirm the presence of underlying metabolic risk factors [6]. Current research indicates that MASLD has a multifactorial pathogenesis. Hepatic steatosis triggers oxidative stress, organelle dysfunction, apoptosis, and other pathophysiological alterations, all of which drive disease progression from MASLD to metabolic dysfunction-associated steatohepatitis (MASH) and hepatic fibrosis [7]. As the central hub of lipid metabolism, the liver regulates lipid homeostasis through four primary pathways: (1) uptake of circulating lipids, (2) *de novo* lipogenesis (DNL), (3) fatty acid oxidation (FAO), and (4) lipid export *via* very-low-density lipoprotein (VLDL). These processes are modulated by intricate interactions among hormones, nuclear receptors, and transcription factors, with dysregulation of hepatic lipid homeostasis leading to MASLD development. Similar to other metabolic disorders, lifestyle interventions—such as adopting a healthy diet and increasing physical activity—remain the cornerstone of MASLD management [8]. While no specific therapeutic agents have been unequivocally established for MASLD to date, lifestyle interventions represent a direct and accessible modality. This approach aligns with the multifactorial etiology of metabolic diseases, as lifestyle modifications can simultaneously target multiple pathophysiological pathways contributing to disease progression.

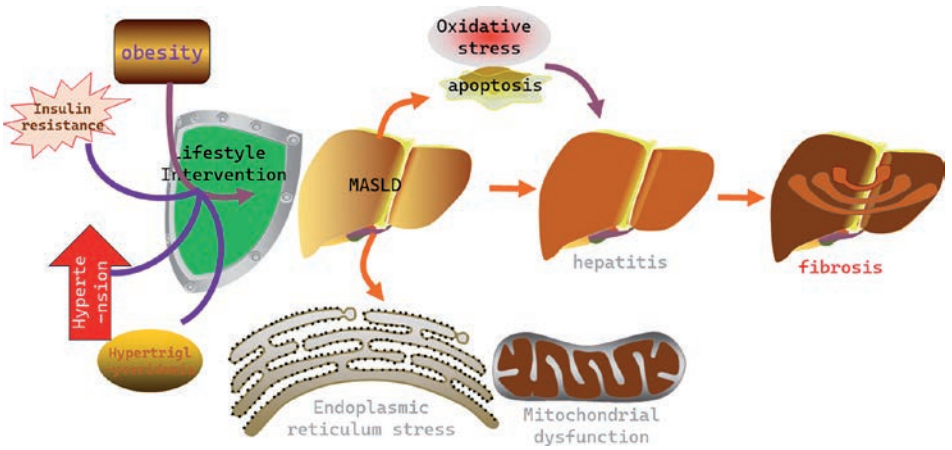

Figure 1.
The inducement and development of MASLD.

2. Relationship between MASLD and hepatic steatosis

It is well-established that the liver, as the central regulatory organ for lipid homeostasis, orchestrates four tightly regulated metabolic pathways: (1) *de novo* lipogenesis (DNL), (2) fatty acid uptake, (3) very-low-density lipoprotein (VLDL) secretion, and (4) fatty acid β-oxidation (FAO). These pathways collectively maintain a dynamic equilibrium of hepatic lipids [9]. Unhealthy lifestyles such as overeating and physical inactivity create a chronic energy surplus in the body. This disrupts the dynamic regulation of hepatic lipids, leading to excessive fat accumulation and the development of simple hepatic steatosis. Lipid overload in hepatocytes triggers mitochondrial dysfunction, endoplasmic reticulum (ER) stress, and NADPH oxidase activation, resulting in massive intracellular release of reactive oxygen species (ROS) and subsequent oxidative stress [10]. Under the dual assault of lipid metabolic dysregulation and oxidative stress, pattern recognition receptors (PRRs) in hepatocytes—such as nucleotide-binding oligomerization domain (NOD)-like receptors and Toll-like receptors (TLRs)—detect persistently generated pathogen-associated molecular patterns (PAMPs), damage-associated molecular patterns (DAMPs), and lipid metabolites. This activates downstream immune signaling pathways, including MAPK-JNK and NF-κB, ultimately inducing hepatocyte injury and hepatic inflammation. Additionally, when lipotoxicity-driven inflammation and hepatocyte damage occur, hepatic stellate cells (HSCs) are activated and transdifferentiate into proliferative, migratory, and contractile myofibroblasts. These cells enhance the transcription of fibrosis-related genes, secrete excessive collagen, and drive hepatic fibrogenesis [11]. Early-stage simple hepatic steatosis is clinically insidious, with minimal patient symptoms. Compounded by the current lack of effective therapeutic regimens and dynamic biomarkers, patients often miss the reversible therapeutic window. Approximately 20% of cases progress to metabolic dysfunction-associated steatohepatitis (MASH), with nearly 20% of MASH patients already exhibiting F2 fibrosis (≥stage 2) at diagnosis. Once progression reaches advanced stages, the disease may evolve into hepatocellular carcinoma (HCC) or even hepatic failure, leading to drastically reduced survival rates [12]. Impaired mitochondrial fatty acid oxidation (FAO) in hepatocytes leads to lipid accumulation, excessive reactive oxygen species (ROS) production, and oxidative damage, driving the pathogenesis of nonalcoholic fatty liver disease (NAFLD) [13]. Fatty acid translocase (cluster of differentiation 36 [CD36]), a transmembrane protein facilitating long-chain fatty acid (LCFA) uptake, has recently been linked to FAO. The functionality of CD36 is closely associated with its subcellular localization. Palmitoylation, one of the most common lipid modifications, regulates CD36 localization. Studies reveal CD36 localization on hepatocyte mitochondria. Palmitoylation of CD36 is significantly upregulated in NAFLD. Inhibition of CD36 palmitoylation markedly increases its mitochondrial distribution in hepatocytes. Depalmitoylated CD36 on mitochondrial membranes enhances FAO by promoting fatty acid transport into mitochondria. Mitochondria-enriched CD36 interacts with long-chain acyl-CoA synthetase 1 (ACSL1), thereby channeling more LCFAs to ACSL1. This increases long-chain acyl-CoA production, enhancing FAO and alleviating NAFLD [14].

Receptor-interacting protein kinase 3 (RIPK3) mediates NAFLD progression. Research demonstrates that RIPK3 deficiency ameliorates impairments in mitochondrial biogenesis, bioenergetics, and function in hepatocytes. RIPK3 deletion coincides with robust upregulation of antioxidant systems, reducing oxidative stress under lipid overload *in vivo* and *in vitro*. RIPK3-deficient hepatocytes exhibit smaller but

more numerous lipid droplets (LDs) after free fatty acid exposure. RIPK3 deficiency upregulates LD-associated proteins perilipin 1 (PLIN1) and PLIN5 in adipocytes and the liver. PLIN1 overexpression modulates LD structure, mitigates mitochondrial stress during fatty acid overload, and correlates with reduced NAFLD severity in humans. Conversely, pathogenic PLIN1 frameshift variants are linked to NAFLD, fibrosis, and elevated hepatic RIPK3 levels in familial partial lipodystrophy [15].

Vacuole membrane protein 1 (VMP1), an endoplasmic reticulum (ER)-transmembrane protein, regulates autophagosome and lipid droplet formation [16]. Hepatocyte-specific deletion of VMP1 severely impairs very-low-density lipoprotein (VLDL) secretion, leading to massive hepatic steatosis, hepatocyte death, inflammation, and fibrosis—hallmarks of nonalcoholic steatohepatitis (NASH) [17]. Mechanistically, VMP1 deficiency reduces hepatic phosphatidylcholine (PC) and phosphatidylethanolamine (PE) levels and alters phospholipid composition. Experimental findings indicate that VMP1 deletion in the liver also causes neutral lipid accumulation within ER bilayers and impaired mitochondrial β-oxidation. Overexpression of VMP1 ameliorates diet-induced NASH by restoring VLDL secretion. These studies demonstrate that reduced hepatic VMP1 expression correlates with human NAFLD/NASH [16]. Forkhead box A3 (FOXA3), a member of the FOX family, plays a critical role in metabolic homeostasis. Under ER stress conditions, spliced X-box binding protein 1 (XBP1s) specifically induces FOXA3 transcription. FOXA3 exacerbates excessive lipid accumulation triggered by acute ER stressors like tunicamycin (TM), whereas hepatocyte-specific FOXA3 deficiency alleviates this phenotype. Notably, FOXA3 deletion reduces diet-induced chronic ER stress, hepatic steatosis, and insulin resistance. Moreover, FOXA3 inhibition *via* siRNA or adeno-associated virus (AAV) delivery improves fatty liver phenotypes. Mechanistically, FOXA3 directly regulates Period1 (Per1) transcription, which in turn promotes the expression of lipogenic genes, including SREBP1c, thereby enhancing lipid synthesis. Pathophysiologically, hepatic levels of FOXA3, Per1, and SREBP1c are elevated in obese individuals and NAFLD patients [18]. In addition to the conventional understanding that body fat originates from lipid-rich dietary sources, carbohydrates can be converted into fat through *de novo* lipogenesis (DNL)—a process upregulated in fatty liver disease. Biochemically, DNL involves the polymerization and reduction of acetyl-CoA, utilizing NADPH as an electron donor [19]. Studies employing stable isotope tracing demonstrate that adipose tissue DNL is supported by glucose and its catabolism *via* the pentose phosphate pathway to generate NADPH. In contrast, the liver derives acetyl-CoA for lipogenesis from acetate and lactate, while NADPH is sourced from folate-mediated serine catabolism. This NADPH production involves a cytosolic serine pathway in the liver, operating in the reverse direction compared to most tissues and tumors. Here, NADPH is generated through the SHMT1-MTHFD1-ALDH1L1 reaction sequence. Inhibition of serine hydroxymethyltransferase (SHMT) reduces hepatic lipogenesis, indicating that hepatic folate metabolism uniquely supports cytosolic NADPH production and fat synthesis. Critically, while the same enzymatic machinery drives lipogenesis in both liver and adipose tissues, these organs utilize distinct substrate sources. This divergence highlights potential therapeutic targets for intervention [20].

While the U.S. FDA has approved Resmetirom for treating adults with non-cirrhotic steatohepatitis and moderate-to-severe hepatic fibrosis (stages F2–F3), drug development for metabolic dysfunction-associated steatohepatitis (MASH) remains challenging. Although numerous pharmaceutical companies are pursuing MASH therapies, only a few agents—such as semaglutide and lanifibranor—have advanced

smoothly into Phase 3 clinical trials. Metabolic surgery represents another therapeutic avenue for fatty liver disease; however, current evidence lacks high-quality, prospective, randomized controlled studies to validate its safety profile. Most existing studies have not reported postoperative adverse events. Consequently, lifestyle interventions combined with stratified management remain essential for MASLD management [21].

3. Dietary interventions and nutritional optimization

Emerging evidence indicates that dietary patterns in MASLD patients are associated with pro-inflammatory responses and increased risk of severe hepatic steatosis, characterized by excessive intake of added sugars, sugar-sweetened beverages, processed foods, and nonalcoholic baked goods [22]. Chronic high-fat diets (HFDs) induce excessive hepatic lipid deposition, leading to structural and functional liver abnormalities. HFD significantly alters the expression of Hedgehog (Hh) signaling pathway genes, particularly upregulating Sonic Hedgehog (Shh), Indian Hedgehog (Ihh), Hedgehog-interacting protein (Hhip), Patched1 (Ptch1), Smoothened (Smo), and *Glioma-associated oncogene homologs (Gli1/2/3)*. These changes correlate with histopathological features such as inflammatory cell infiltration, sinusoidal dilation, cellular necrosis, and microvesicular steatosis [23]. The hepatotoxic effects of HFD are primarily driven by a "two-hit" mechanism that exacerbates nonalcoholic fatty liver disease (NAFLD) progression: First Hit: Excessive lipid intake (particularly from Western-style diets) overwhelms hepatic metabolic capacity, causing aberrant lipid deposition. This process is tightly linked to insulin resistance, which not only enhances *de novo* lipogenesis (DNL) but also impairs fatty acid transport, aggravating hepatocyte steatosis [24]. Second Hit: Lipid overload triggers mitochondrial dysfunction, endoplasmic reticulum (ER) stress, and oxidative stress, disrupting hepatocyte metabolism and activating inflammatory cascades. These events drive the transition from simple steatosis to nonalcoholic steatohepatitis (NASH) [25]. Long-term HFD synergizes with obesity and dyslipidemia (components of metabolic syndrome) to amplify hepatic lipotoxicity, ultimately increasing risks of cirrhosis and hepatocellular carcinoma (HCC). Notably, even in nonobese individuals, HFD-induced dyslipidemia independently elevates NAFLD risk, underscoring the pivotal role of dietary modulation in liver health [26].

3.1 Clinical manifestations of MASLD caused by improper diet

In the early stage of MASLD, most patients have no obvious symptoms, and liver enzymes are usually found to be elevated by imaging examination (such as abdominal B-ultrasound) or blood examination during a health examination. The following mild symptoms may occur: ① Fatigue: the patient often feels tired and depressed; ② Right epigastric discomfort: slight swelling, pain, or oppression; ③ Dyspepsia: such as abdominal distension and belching. ④ Weight gain or obesity: especially abdominal obesity. When the disease develops to the middle stage, with the progress of the disease, the fatty degeneration of hepatocytes is aggravated, and the following manifestations may appear: ① Abnormal liver function: alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) are increased; ② Insulin resistance: blood sugar rises after meals, and acanthosis nigricans appears on the skin (neck and armpit become black and thick); ③ Hyperlipidemia: the blood lipid (triglyceride, cholesterol) increased; ④ Metabolic syndrome: accompanied by hypertension, hyperglycemia,

obesity, etc. If the dietary disharmony and metabolic problems persist for a long time, what is more serious is that MASLD can progress to metabolic steatohepatitis (MASH) and further develop into liver fibrosis, cirrhosis, and even liver cancer. It may be manifested as obvious fatigue, persistent pain in the right upper abdomen, dull complexion, itchy skin, jaundice (yellow skin and eyeball), ascites, edema of lower limbs, liver palms, and spider nevus.

3.2 Dietary recommendations

To effectively counteract the detrimental effects of carbohydrates in MASLD patients, the ketogenic diet (KD)—a novel low-carbohydrate dietary regimen—has been explored. Initially developed in the 1920s for clinical management of epilepsy, particularly in patients refractory to antiseizure medications [27], KD has garnered significant attention in recent decades for its beneficial roles in metabolic syndrome, neurological disorders, cardiovascular diseases, and cancer. The KD composition typically comprises 3–5% carbohydrates, 20–27% protein, and 70–75% lipids, inducing nutritional ketosis to shift energy metabolism toward fat breakdown. This metabolic state reduces blood glucose levels, enhances insulin sensitivity, and promotes weight loss in overweight/obese individuals [28]. In preclinical studies of HFD-induced MASLD, KD suppresses disease progression by modulating inflammatory pathways. Specifically, KD induces interleukin-6 (IL-6) production, which activates c-Jun N-terminal kinase (JNK). This cascade inhibits aberrant insulin signaling, thereby ameliorating hepatic steatosis and insulin resistance [29]. The Mediterranean diet (MD) is widely recognized for its emphasis on plant-based foods, supplemented by an appropriate amount of olive oil, healthy dairy products, and fish, which together provide patients with anti-inflammatory and antioxidant benefits [30]. In one study, patients followed two plant-based food/cautious diet strategies: the American Heart Association (AHA) diet (55% carbohydrate, 15% protein, 30% lipid) and the MD diet (40–45% carbohydrate, 25% protein, 30–35% lipid). The results showed that both of them could inhibit inflammatory markers, including leptin, adiponectin, M30, and LECT2. The Mediterranean diet (MD) prevents MASLD through various mechanisms. First of all, MD is rich in antioxidant and anti-inflammatory components, such as vitamin E, acids, and carotenoids, which help to reduce oxidative stress and inflammatory reactions, thus protecting the liver from damage. Oxidative stress is an important pathogenic mechanism of MASLD, and antioxidants such as vitamin E can effectively alleviate this process [31]. Secondly, MD's characteristics of low sugar, low fat, and high fiber are helpful in controlling weight and preventing obesity and diabetes. Unsaturated fatty acids in olive oil can improve insulin sensitivity and reduce cholesterol levels, thus promoting metabolic health. In addition, omega-3 fatty acids in fish can reduce inflammatory factors, promote fatty acid oxidation, and reduce liver fat accumulation [32]. MD can also improve intestinal health, promote intestinal peristalsis, maintain healthy intestinal microecology, and reduce the burden on the liver through rich dietary fiber. At the same time, folic acid and vitamins B6 and B12 in MD are helpful to improve cardiovascular health and reduce the risk of cardiovascular diseases [33]. Generally speaking, the Mediterranean diet has become an effective dietary pattern to prevent MASLD by regulating metabolism, reducing inflammatory reaction, protecting the liver, and improving overall health [34].

Next, taking the Mediterranean diet as an example, it introduces the recipe selection and the corresponding mechanism [35, 36].

1. The diet is rich in fruits, vegetables, and whole grains. The Mediterranean diet emphasizes the intake of rich, fresh fruits, vegetables, and whole grains. For example, tomatoes are rich in lycopene, which has a strong antioxidant effect and can inhibit cholesterol oxidation, thus reducing the risk of cardiovascular diseases [37]. Whole grains such as wheat, barley, oats, rice, highland barley, and corn are rich in dietary fiber, vitamins, and minerals, which help to maintain cardiovascular health. In the process of food processing and cooking, high temperatures and excessive processing should be minimized to avoid the loss of nutrients.

2. Olive oil is the core of the Mediterranean diet, and it is rich in monounsaturated fatty acids, especially oleic acid, which helps to reduce the level of low-density lipoprotein cholesterol (LDL-C) and maintain the level of high-density lipoprotein cholesterol (HDL-C) [38]. In addition, polyphenols in olive oil have antioxidant and anti-inflammatory effects, which can improve blood rheology and reduce thrombosis, thus reducing the risk of myocardial infarction and other cardiovascular events.

3. Nuts and beans are important sources of high-quality fat, vegetable protein, and soluble fiber. Beans have a low glycemic index, which can release blood sugar smoothly and reduce total cholesterol and triglyceride levels by increasing bile acid excretion and regulating liver lipid metabolism [39]. Eating about 25 grams of soy protein every day, combined with a diet with low cholesterol and saturated fat, can significantly reduce the risk of cardiovascular disease. At the same time, beans also have certain preventive and adjuvant therapeutic effects on some chronic diseases such as cancer, diabetes, and chronic kidney disease.

4. Spices cannot only enhance the flavor of food but also reduce the use of oil and salt in cooking and promote healthy eating habits. Many spices are rich in natural antioxidants, such as allicin and allicin, which have anti-inflammatory, antibacterial, blood pressure, and cholesterol-lowering effects [40]. Studies have shown that long-term consumption of garlic can reduce the risk of hypertension by more than one-third and improve blood viscosity, which has a positive impact on cardiovascular health.

5. Yogurt, cheese, and the Mediterranean diet advocate daily intake of fermented dairy products such as yogurt and cheese. This kind of food is rich in calcium, which is beneficial to bone health and especially suitable for middle-aged and elderly people. In addition, choosing low-fat or skim dairy products can reduce the intake of saturated fat and cardiovascular risk while obtaining nutrition.

6. Fish and seafood are the main sources of protein in the Mediterranean diet, especially deep-sea fish such as tuna, herring, sardine, salmon, and bream, which are rich in ω-3 polyunsaturated fatty acids (such as EPA and DHA). These fatty acids have multiple physiological functions, such as anti-inflammatory, antithrombotic, and heart rate regulation, which can significantly reduce the incidence of cardiovascular diseases [41]. In addition, omega-3 fatty acids can also prevent or alleviate depression, arthritis, and other diseases. When cooking fish, high-temperature frying should be avoided to preserve its nutritional value.

7. Red meat and eggs. It is suggested to limit the intake frequency and quantity of red meat (such as pork, beef, and mutton) in the Mediterranean diet and give priority to lean meat. Comparatively speaking, poultry meat is rich in protein and low in saturated fat, which is more beneficial to cardiovascular health. It is suggested to control the ratio of fat to lean when processing meat; for example, the content of lean meat in meat stuffing should reach above 90%. Eggs are an important source of high-quality protein, especially suitable for vegetarians or people who eat less meat.

8. Adequate water intake has a positive effect on the body's metabolic function and mental state. Although some studies suggest that moderate drinking of red wine may be beneficial to cardiovascular health, most patients are advised to avoid alcohol intake as much as possible.

However, special attention should be paid to patients with gastric ulcers and short bowel syndrome, who should reduce high-fiber food, and children, who need to increase their intake of high-quality protein. The choice of cooking methods should avoid frying and overprocessing and give priority to steaming, boiling, and cold salad.

4. Intervention in sports activities and its strategies

4.1 Mechanism of relieving MASLD by exercise

In addition to dietary intervention, physical exercise is also an effective strategy to treat nonalcoholic fatty liver disease (NAFLD). Exercise intervention can reduce the formation of lipid droplets and liver triglycerides induced by a high-fat diet. Exercise intervention enhances lipid intake by activating the AMPK/ULK1 pathway, respectively. In addition, exercise stimulates the production of FGF21 in muscle, which is then secreted into circulation and promotes lipid uptake in the liver through the AMPK-dependent pathway. It should be noted that fat accumulation will aggravate liver aging, which can be alleviated by exercise and diet intervention [42]. A study on the mechanism of exercise inhibiting the development of nonalcoholic fatty liver disease in mice induced by a high-fat diet (HFD) found that C57BL/6 J mice aged 6 weeks were fed a normal diet or HFD for 12 weeks and then induced to swim or stay sedentary for 8 weeks. NAFLD mice showed obvious steatosis, fibrosis, and liver injury, and the expressions of HMGCS2, Wnt3a/β-catenin, and phosphorylated (p)-AMPK in the liver increased. Exercise significantly reduced these symptoms and lowered the level of Wnt3a/β-catenin in lipotoxic liver tissue. The inhibition of HMGCS2 expression decreased the activation of the Wnt3a/β-catenin pathway and decreased the p-AMPK in HepG2 treated with palmitic acid. That is to say, exercise can prevent NAFLD-related liver injury, steatosis, and fibrosis. Exercise-mediated liver protection is partly achieved by blocking the upregulation of HMGCS2 and weakening the Wnt3a/β-catenin pathway [43]. It is found that swimming can reduce the lipid accumulation in the liver and improve the pathological changes of the liver. In addition, swimming reduced the excessive production of NOX4-derived reactive oxygen species (ROS) and reduced the level of formaldehyde (MDA). At the same time, swimming has an anti-apoptosis effect, which can decrease the expression of apoptosis-related genes (caspase 3, bax) by increasing

the expression of anti-apoptosis factor bcl2. From the mechanism, the swimming intervention activated lipid metabolism and inflammation mediated by the SIRT1/AMPK signal and enhanced the activation of AKT and NRF2 and upregulated the downstream antioxidant genes [44].

However, exercise is not carried out alone, and it often needs to be carried out together with diet intervention. The research shows that compared with the control group, the weight, fat mass, waist circumference, and alanine aminotransferase (ALT) level of the participants in the diet-exercise joint experiment decreased significantly, while the insulin sensitivity increased significantly. Intermittent fasting combined with exercise can effectively reduce hepatic steatosis in patients with NAFLD, but it may not have additional benefits compared with fasting alone [45]. A study to test the combined effects of Time-Restricted Eating (TRE) and resistance exercise training (RT) on obesity and NAFLD in mice fed with a high-fat diet showed that TRF—8 of hours food intake—and RT—including stair climbing three times a week—reduced weight gain, improved blood sugar homeostasis, and reduced lipid accumulation in the liver. TRF combined with radiotherapy improved the respiratory exchange rate, energy consumption, and mitochondrial respiration of the liver. In addition, the analysis of gene expression in the liver showed that in the TRF + RT group, the mRNA expression of lipogenesis and inflammation genes was low, while the mRNA expression of fatty acid oxidation genes was increased. Importantly, TRF + RT has been proven to be more effective in preventing obesity and metabolic disorders. That is to say, compared with the single intervention, TRF and RT play a complementary role, which has a significant impact on the metabolic disorder and NAFLD in mice. When combined with RT, TRF provides additional benefits and is more effective than each intervention alone in increasing energy consumption, preventing weight gain, and regulating blood glucose homeostasis [46].

4.2 Lack of sports to promote the mechanism of MASLD

When there is a lack of physical exercise, the first thing that bears the brunt is excess energy, which in turn leads to fat deposition in the liver. If the dietary calorie intake is unchanged or increased, it will further make the calorie surplus, and the excess energy will accumulate in the liver cells in the form of triglycerides, which will lead to fatty degeneration of the liver and form MASLD. Exercise can improve the sensitivity of muscles to insulin, while lack of exercise can lead to increased insulin resistance, especially in skeletal muscle, adipose tissue, and liver. If insulin resistance occurs, it will lead to ① the increase of lipolysis, which leads to the release of free fatty acids (FFA) into the blood; ② the intake of FFA in the liver increases, and then the triglyceride synthesized in the liver increases; and ③ insulin resistance will also inhibit the output of liver fat, which will eventually show more and more liver fat. Lack of exercise will also lead to hypertrophy of adipose tissue and sustained release of inflammatory factors (such as TNF-α and IL-6), which will destroy the structure of liver cells, induce apoptosis and fibrosis of liver cells, and finally promote the development of MASLD steatohepatitis. Intestinal flora is also a link that cannot be ignored. Lack of exercise is related to the imbalance of intestinal flora. Healthy exercise can promote the growth of probiotics and maintain the intestinal barrier function. When intestinal permeability increases, endotoxin (LPS) may enter the blood, induce a hepatic inflammatory reaction, and aggravate hepatic steatosis. Exercise can strengthen the antioxidant enzyme system (such as SOD and GSH), while a lack of exercise will increase the level of oxidative stress in the body, damage

the hepatocyte membrane, promote lipid peroxidation, and aggravate liver inflammation and fibrosis.

4.3 Suggested exercise mode

When adopting corresponding exercises, the first exercise is aerobic exercise and resistance exercise. Aerobic exercise can activate metabolism and liver fat consumption, including types of exercise like brisk walking, jogging, swimming, cycling, elliptical machine, and so on. Recommended five times a week, 30–45 minutes each time, moderate intensity (heart rate reaches 60–70% of the maximum heart rate, that is, "can talk but cannot sing"). Further, intermittent high-intensity interval training (HIIT) can be added, such as 30-second sprint +1-minute jogging alternately, twice a week. Aerobic exercise activates the AMPK pathway, enhances mitochondrial function, and accelerates fat decomposition and energy supply in the liver and muscle. Studies have shown that regular aerobic exercise can reduce liver fat content by 6–10% (which is independently related to weight loss). In addition, aerobic exercise increased the expression of the GLUT4 transporter in skeletal muscle, decreased the fasting insulin level, and inhibited the *de novo* synthesis of liver fat (DNL). It can also reduce pro-inflammatory factors (such as TNF-α and IL-6), upregulate antioxidant enzymes (SOD and glutathione), and reduce oxidative stress damage to the liver [47–49]. Resistance exercise can reconstruct muscle metabolism and protect the liver. Its forms include dumbbell/barbell training, elastic belt training, and self-weight training (squats, push-ups). It is recommended to do 8–10 movements 2–3 times a week, 8–12 times in each group (reaching 70–80% of exhaustion). And give priority to training large muscle groups (legs, back, chest), taking into account the core muscle groups (flat support). Resistance exercise stimulates muscle protein synthesis, improves basal metabolic rate (about 50–70 kcal per day for every 1 kg of muscle), and indirectly reduces liver fat accumulation. On the other hand, muscle, as a "metabolic buffer pool," can reduce the fluctuation of blood sugar and liver lipid regeneration by increasing glucose intake and glycogen storage. Studies have proved that resistance training can reduce the liver fat content of patients with MASLD by 5–8%. This may be achieved by promoting the release of muscle factors such as IL-15, inhibiting the inflammation of adipose tissue, and blocking the vicious circle of "liver-adipose tissue" [50, 51].

However, the combined effect of the two is better than that of a single exercise. Aerobic exercise directly consumes fat, while resistance exercise increases muscle metabolic capacity and improves insulin resistance and adiponectin levels together. However, the selection of different groups of people should be adjusted accordingly. For example, obese MASLD patients should mainly take low-impact aerobic exercise (swimming and cycling) in the early stage to avoid joint injury and gradually join resistance training with weight loss. The elderly or sarcopenia patients should focus on low-intensity resistance (elastic belt, sitting training) and balance training (Tai Chi) to prevent falls and maintain muscle function. People with diabetes need to pay attention to avoid fasting exercise and monitor blood sugar before and after exercise; resistance training is arranged 1 hour after meals to reduce the risk of hypoglycemia. During the exercise intervention, attention should be paid to gradual progress. At the same time, liver function (ALT, GGT), liver fat content (controlled attenuation parameter (CAP) value), and body composition (muscle/fat ratio) should be detected every three months. If the liver cirrhosis is decompensated, high-intensity exercise should be avoided, and training should be suspended in acute hepatitis.

5. Weight management and psychological intervention

5.1 Weight management

Obesity is a complex chronic disease and a global public health challenge. Obesity is characterized by excessive accumulation of body fat, which greatly increases the risk of many diseases, including nonalcoholic fatty liver disease, and is related to shortened life expectancy. Although lifestyle intervention (diet and exercise) has a significant effect on weight management, it is extremely challenging to achieve long-term successful weight loss, and the prevalence of obesity continues to rise around the world. In the past decades, the pathophysiology of obesity has been widely studied, and more and more signal transduction pathways are related to obesity, which makes it possible to fight obesity in a more effective and accurate way [52]. It is found that the same percentage of weight loss can be achieved at slow or fast speed (range: 0.2–3.2 kg/week) through dietary calorie restriction, exercise, and weight loss surgery. Compared with the slow weight loss rate, the faster weight loss rate may lead to more fat-free mass and less fat mass loss in the dynamic stage of weight loss and, at the same time, reduce the resting energy consumption to a greater extent. However, after 2–4 weeks of stabilization at a new low weight, these differences are weakened, and the rate and amount of weight recovery after 9–33 months are not affected (nor does it affect the tissue composition of weight recovery). Waist circumference, visceral fat and liver fat content, resting blood pressure, fasting blood lipid profile, insulin, and fat factor concentration show little difference under different weight loss rates. After rapid weight loss of 6–11%, the decrease of fasting blood glucose concentration and the improvement of insulin sensitivity are greater than those after gradual weight loss, but there is no difference after weight loss of 18–20%. After losing the same weight at different rates, the changes in body composition and metabolism are similar to a great extent, and occasional differences may have no clinical significance for the long-term management of obesity and cardiac metabolic diseases [53]. The research shows that compared with the control group, exercise training subjects are more likely to achieve a relative reduction of liver fat measured by MRI of ≥30% (odds ratio 3.51, 95% confidence interval 1.49–8.23, P = 0.004). A task of minutes/week with an exercise dose of ≥750 metabolic equivalents (for example, a brisk walk of 150 minutes/week) leads to a significant therapeutic response (MRI response odds ratio is 3.73, 95% confidence interval is 1.34–10.41, P = 0.010), but a small dose of exercise does not. Treatment response is independent of clinically significant weight loss (> 5%) [54]. It should be noted that weight loss is not once and for all. After successful weight loss, it is necessary to adhere to a healthy lifestyle to prevent recurrence.

5.2 Psychological intervention and compliance improvement

Lifestyle intervention requires high compliance from patients, which is also a difficulty in implementation. There may be the following reasons for poor patient compliance: (1) lack of motivation and vague goals, which show that patients lack internal motivation (such as "no sense of urgency in asymptomatic period") or the goal setting is too general (such as "eat less and move more"); (2) limited time and resources, which show that it is difficult for busy people to exercise regularly, and those with limited economic conditions cannot afford healthy food or gym fees; (3) lack of knowledge and cognitive bias, manifested as misunderstanding of dietary

principles (such as "sugar-free food can be eaten at will") or underestimating the risk of disease ("fatty liver is not a serious illness"); (4) lack of social support, manifested as uncooperative family members (such as continuing to cook high-fat meals) and interference from bad habits in social circles (drinking and gathering); (5) psychological and emotional disorders, which show that patients with anxiety or depression give up their diet plan because of emotional eating, and perfectionists give up completely after occasionally violating the rules; (6) physical discomfort and frustration, manifested as muscle aches after initial exercise and gastrointestinal discomfort caused by dietary changes (such as abdominal distension caused by a high-fiber diet).

Compliance may be improved in the following ways:

1. Clarify the motivation and goal: First, wake up the intrinsic motivation by understanding the benefits of lifestyle intervention to the body; Then gradually start from the specific goal: transform "losing weight" into "walking fast for 30 minutes three times a week and adding one vegetable to dinner" [55].

2. Reasonable planning: A single long-term training can be replaced by fragmented exercise (such as short-term stretching exercise). Eggs are used instead of salmon, and family weight training is used instead of gym training [56].

3. Timely positive feedback and understanding: During this period, if we face up to clinical data such as liver ultrasound images, we can show the changes of fatty liver by contrast and strengthen the disease cognition. At the same time, it positively guides patients to treat them positively, such as dispelling patients' view that failure once equals failure [57].

4. Family support: Patients' families can participate in a low-fat diet together, organize family exercise days with patients, and improve patients' compliance [58].

5. Psychological intervention: Guide patients to pay attention to the hunger-satiety signal and reduce emotional eating, especially the depression caused by insufficient positive feedback in the process, which should be noticed and intervened in in time [59].

6. Gradual adjustment and adaptation: starting with increasing one cup of water and reducing one spoon of oil every day, gradually transition to comprehensive diet adjustment; Adopt low-intensity exercise at the beginning, gradually increase the resistance ratio, and persist for a long time [60].

With the development of information technology, smart wearable devices can be used for long-term feedback, using an app to record diet/exercise (such as MyFitnessPal), and setting up an automatic reminder and achievement reward mechanism. Wearable devices (smartwatches) monitor heart rate and steps in real time and provide immediate feedback. For example, research has found that wearable devices can help patients easily track body data and promote a healthier and more active life [61]. It should be noted that being sedentary is also the main inducement of MASLD [62]. In modern society, most people are sedentary in their work and life, and smart devices can detect their sitting time and remind them.

6. Consideration of cultural factors and individual differences

6.1 Effects of dietary habits and cultural background on intervention effects

Lifestyle interventions are the cornerstone of MASLD management. Besides, the dietary modification is the most effective strategy [58]. However, the success of dietary interventions in the population is not consistent. An often underappreciated but critical factor influencing therapeutic outcomes is the patient's dietary habits and cultural background.

Dietary habits are deeply influenced by cultural, regional, and religious traditions. On the one hand, the Mediterranean diet, which is rich in fruits, vegetables, legumes, whole grains, and olive oil, is considered highly beneficial for the prevention and management of MASLD [35]. The southern European people naturally adhere to such a pattern, which is congruent with the recommended dietary approach for MASLD patients [59]. On the other hand, traditional East Asian diets, characterized by high consumption of rice, vegetables, fermented foods, and fish, generally exhibit a lower fat content and high fiber intake, which may also exert protective effects against hepatic steatosis [60, 61]. However, the rapid pace of urbanization and globalization has led to a nutrition transition in many regions [62]. Western dietary patterns—characterized by high intake of processed foods, added sugars, saturated fats, and red meats—have increasingly infiltrated regions with previously healthier eating traditions [63]. This nutritional transition has been a major driver of the increasing incidence of MASLD in non-Western countries, often coexisting with persistent cultural food preferences that may either conflict with or support modern dietary interventions [64].

Cultural perceptions of food are significantly influenced by dietary recommendations. For instance, in some Middle Eastern and South Asian cultures, abundant food and a larger body size are historically associated with wealth and health, potentially reducing motivation to adopt calorie-restricted diets [65]. Conversely, certain cultures emphasize communal meals and shared dishes, which can make individual dietary control more challenging. Furthermore, religious practices such as fasting (e.g., Ramadan in Islam, Lent in Christianity, or fasting in Buddhism) influence not only meal timing but also food choices [66]. These practices may interact with metabolic processes and, depending on their implementation, either benefit or exacerbate MASLD. For example, time-restricted feeding during fasting periods has been shown in some studies to improve metabolic markers; however, excessive caloric intake during non-fasting hours may negate such benefits [67]. Understanding and respecting these cultural dynamics are essential when designing patient-centered dietary interventions. Culturally tailored counseling and meal planning that integrates traditional foods and preparation methods can enhance patient engagement and compliance [68]. Another critical element influencing dietary intervention outcomes is nutritional literacy, which varies significantly across cultural and socioeconomic contexts [69]. Individuals with limited understanding of nutrition may misinterpret or be unaware of the health implications of their diet. Additionally, some cultures may lack equivalent terms for medical concepts like "insulin resistance" or "fatty liver," complicating education and communication efforts [70].

Dietary habits and cultural background play a crucial role in the effectiveness of lifestyle interventions in MASLD. A nuanced understanding of these factors enables healthcare professionals to deliver more effective, sustainable, and culturally resonant

care. As the global burden of MASLD grows, so too must our capacity to individualize treatment strategies in a way that respects and integrates the lived experiences of patients from all cultural backgrounds [71].

6.2 Differences in health beliefs and acceptance among different groups of people

Differences in cultural values, socioeconomic conditions, education level, and exposure to health information all contribute to how individuals assess the seriousness of MASLD, their perceived vulnerability to the disease, and the perceived benefits of lifestyle modification or pharmacological therapy.

Cultural perceptions also shape treatment acceptance. In some communities, where obesity is not culturally stigmatized or recognized as a health risk, the early stages of MASLD are underrecognized until complications arise [72]. Gender roles may further influence how individuals engage with healthcare systems—men in certain societies may be less likely to seek preventive care, while women may encounter social or familial constraints that limit their ability to adopt personalized dietary and activity plans [73]. These context-specific factors underscore the importance of culturally sensitive educational approaches in MASLD management. Treatment outcomes can be significantly improved when healthcare professionals align their communication with the patient's belief systems. Approaches such as motivational interviewing, community-driven health education, and the integration of culturally resonant practices have demonstrated efficacy in enhancing treatment uptake and long-term adherence [74]. Ultimately, aligning clinical recommendations with patients' values and perceptions is vital for achieving sustainable improvements in MASLD outcomes.

7. Multidisciplinary team cooperation and clinical integration

7.1 Collaborative model of nutrition, exercise, psychology, and medicine

MASLD is a lifestyle-related condition that demands a multidisciplinary approach for optimal management. Traditional models relying solely on pharmacological treatment or physician-led counseling often fail to produce sustainable outcomes [75]. Recent evidence suggests that collaborative care models—incorporating nutritionists, exercise specialists, psychological counselors, and clinicians—can significantly improve both adherence and long-term effectiveness of MASLD interventions [76].

Nutritionists play a foundational role by offering personalized dietary plans that align with the patient's metabolic profile, comorbidities, and cultural eating habits. Their guidance helps patients adopt sustainable changes in calorie intake, macronutrient balance, and meal timing—factors crucial for reducing hepatic fat accumulation [77]. Exercise specialists, on the other hand, tailor physical activity programs to individual fitness levels and preferences. Structured aerobic and resistance training not only facilitates weight loss but also improves insulin sensitivity and liver enzyme profiles [78]. Psychological counselors help manage frequently overlooked factors such as emotional eating, low motivation, and mental health disorders, including depression and anxiety, which frequently co-occur with MASLD. Cognitive-behavioral strategies, motivational interviewing, and stress management techniques can enhance

patients' readiness for change and long-term adherence to lifestyle interventions. Clinicians serve as coordinators, integrating diagnostic insight, pharmacotherapy when needed, and continuous medical monitoring to guide the overall care plan [79]. The synergy among these professionals allows for a patient-centered, holistic approach that goes beyond isolated interventions. Regular interdisciplinary meetings, shared electronic health records, and aligned treatment objectives ensure continuity of care and reduce conflicting advice. Evidence indicates that such integrated models lead to greater reductions in hepatic steatosis, improved cardiometabolic markers, and higher patient satisfaction rates compared to standard care [80].

In conclusion, a collaborative care framework that actively involves nutrition, physical activity, mental health, and clinical medicine offers a promising path for enhancing MASLD treatment outcomes. Future healthcare systems should prioritize integrated delivery models to address the complex behavioral and metabolic dimensions of MASLD.

7.2 The outpatient intervention pathway is linked to community resources

Effective management of MASLD demands a shift from episodic clinical care; it necessitates a structured, continuous intervention model that extends beyond the clinic. Outpatient-based intervention pathways, when linked effectively with community health resources, have demonstrated improved adherence, metabolic outcomes, and patient engagement in MASLD care [81]. In the outpatient setting, early risk stratification and personalized treatment plans form the foundation of intervention. These typically encompass lifestyle counseling, regular biomarker assessment, and the initiation of pharmacologic therapies when indicated [82]. However, without continuity of support, especially in lifestyle modification, patient dropout rates remain elevated. To address this gap, integrating outpatient care with community-based resources—such as local dietitians, exercise programs, mental health services, and digital health platforms—has emerged as a promising strategy [83, 84]. Community resource linkage enhances the scalability and sustainability of MASLD interventions. For example, referral systems connecting patients to local fitness centers or subsidized nutrition workshops help ensure that patients can act on clinical advice in their daily environments. Furthermore, collaboration with community health workers or peer support groups offers culturally relevant education and motivation, particularly in underserved populations. These linkages not only reinforce behavior change but also foster a sense of accountability and shared progress [85].

Digital tools also serve as an extension of outpatient care, enabling remote monitoring, virtual coaching, and real-time feedback. When aligned with community services and clinical oversight, these platforms help bridge logistical barriers and maintain patient engagement between clinic visits. The integration of outpatient pathways with community resources leads to a more comprehensive, ecosystem-based approach to MASLD management. Studies have shown that such coordinated care models can improve liver enzyme profiles, reduce hepatic fat content, and enhance patient satisfaction. Importantly, they also help address social determinants of health that are often barriers to successful MASLD treatment [86].

In conclusion, linking structured outpatient interventions with accessible, community-level resources plays a critical role in improving MASLD outcomes [87]. Healthcare systems should prioritize this integration to deliver more equitable, sustainable, and effective long-term care.

8. Clinical application tools and practice guidelines

8.1 Goal setting and individualized plan development

MASLD requires a patient-centered approach that emphasizes realistic and individualized goal setting [88]. Given the chronic and behavior-dependent nature of MASLD, traditional generic advice—such as "eat healthier" or "exercise more"—is often insufficient. Instead, structured frameworks such as SMART goals (Specific, Measurable, Achievable, Relevant, and Time-bound) are essential for creating clear, actionable, and sustainable treatment plans [89].

The initial phase of goal setting should be based on a comprehensive assessment of the patient's metabolic profile, comorbidities, psychosocial context, readiness to change, and available resources. Clinicians, together with patients, can co-develop personalized objectives that are both medically relevant and practically feasible. For example, rather than broadly recommending weight loss, a SMART goal might be: "Lose 5% of current body weight over the next 3 months through walking 30 minutes five times a week and reducing daily caloric intake by 500 kcal [90]." Importantly, goals should be revisited and adjusted regularly to reflect patient progress and evolving clinical needs. Continuous monitoring of anthropometric data, liver enzymes, and patient-reported outcomes helps in refining interventions and maintaining motivation. This iterative process encourages accountability while avoiding the discouragement that can result from overly ambitious targets [91].

Personalized planning also involves prioritizing the patient's preferences and cultural norms. A flexible approach might integrate dietary changes aligned with regional food habits or recommend physical activities that are enjoyable and accessible. In patients with psychological or socioeconomic barriers, including a mental health professional or social worker in the care team can help address nonmedical factors that hinder adherence [92].

Ultimately, SMART goals not only enhance communication between patients and providers but also increase the likelihood of long-term behavioral change—an essential element in reversing hepatic steatosis and improving metabolic outcomes. When paired with regular feedback and multidisciplinary support, individualized goal setting transforms MASLD care from a reactive model into a proactive, empowering process.

8.2 Monitoring metrics and follow-up recommendations

MASLD requires structured and evidence-based monitoring to assess disease progression, treatment response, and associated metabolic risk. Given the heterogeneity of MASLD—from simple steatosis to advanced fibrosis—the selection of appropriate monitoring parameters and timely follow-up is critical in preventing complications such as cirrhosis or hepatocellular carcinoma.

Key monitoring indicators include body weight, serum alanine aminotransferase (ALT), and liver imaging findings. Weight is a primary, modifiable risk factor and surrogate marker for therapeutic response [93]. A sustained weight loss of ≥5–10% is associated with histological improvement in steatosis and inflammation, and possibly fibrosis regression. Regular measurement of body mass index (BMI) and waist circumference at each follow-up visit offers insight into visceral adiposity, a key driver of hepatic lipid accumulation [94].

ALT and other liver enzymes (e.g., AST, GGT) are routinely used to monitor hepatic inflammation, though they lack specificity and may not accurately reflect histological changes in all patients. Nonetheless, downward trends in ALT—particularly when correlated with lifestyle modification—can indicate treatment efficacy [95]. For patients with persistently elevated transaminases or signs of liver dysfunction, further diagnostic evaluation is warranted.

Noninvasive liver imaging, such as ultrasound, transient elastography (FibroScan), or magnetic resonance imaging-proton density fat fraction (MRI-PDFF), plays an important role in both diagnosis and monitoring. Ultrasound is cost-effective for initial screening, while transient elastography provides a quantitative assessment of hepatic stiffness and steatosis, helping to detect fibrosis progression [96]. MRI-PDFF, though less accessible, offers a highly sensitive method to quantify liver fat and track longitudinal changes.

Follow-up intervals should be individualized based on disease severity, comorbidities (e.g., type 2 diabetes, cardiovascular disease), and treatment modality. For patients with early-stage MASLD and no advanced fibrosis, 6–12-month intervals may suffice [97]. Those with increased fibrosis risk or high ALT levels may require more frequent monitoring (every 3–6 months), particularly during initiation of therapeutic interventions [98].

A multidisciplinary follow-up plan—including input from hepatologists, primary care, dietitians, and physical activity specialists—is essential for ensuring adherence, tracking progress, and adjusting therapy [99]. Continuous monitoring using validated parameters helps clinicians detect early signs of disease progression and reinforces patient engagement in long-term care.

8.3 Clinical assessment tools and risk stratification

Effective clinical management of MASLD hinges on accurate assessment and risk stratification. Given the disease's broad clinical spectrum—from benign steatosis to progressive nonalcoholic steatohepatitis (NASH) and advanced fibrosis—early identification of high-risk individuals is essential to guide monitoring intensity and therapeutic interventions [100].

Initial evaluation of MASLD should begin with a comprehensive clinical history, including assessment of metabolic comorbidities such as obesity, type 2 diabetes mellitus (T2DM), hypertension, and dyslipidemia. Routine laboratory testing includes liver function tests (ALT, AST), fasting glucose, HbA1c, and lipid profile [101]. While elevated ALT is commonly used as a surrogate marker, many patients with advanced fibrosis may present with normal transaminase levels, underscoring the need for more sensitive tools [102].

Noninvasive fibrosis scoring systems are central to MASLD risk stratification. The Fibrosis-4 (FIB-4) Index and the NAFLD Fibrosis Score (NFS) are among the most widely used tools in both primary and specialty care. These scores incorporate age, liver enzymes, platelet count, and metabolic markers to estimate the likelihood of advanced fibrosis. Patients with low-risk scores can typically be managed in primary care, while those with indeterminate or high-risk scores may require referral for further evaluation [103].

Transient elastography (FibroScan) offers additional value by directly measuring liver stiffness and steatosis through controlled attenuation parameter (CAP). It is a noninvasive, reproducible tool that helps differentiate fibrosis stages and guide

clinical decisions [104]. In some settings, magnetic resonance elastography (MRE) provides superior accuracy, particularly in obese patients, but is less accessible due to cost and availability [105].

Emerging tools, including serum biomarkers (e.g., PRO-C3, ELF test) and genetic risk scores, are being explored for enhanced prediction of disease progression, particularly in individuals with intermediate risk based on traditional algorithms [106]. Risk stratification is not static; it must be revisited regularly as the patient's metabolic profile, lifestyle, or treatment response evolves. A tiered approach—starting with simple scoring systems and escalating to advanced imaging or biopsy when indicated—maximizes resource efficiency while ensuring high-risk patients receive timely intervention [107].

Ultimately, integrating clinical assessment tools with a personalized, risk-based management plan is key to preventing MASLD-related complications and optimizing long-term outcomes.

9. Conclusions

As the cornerstone of the management of fatty liver disease (MASLD) associated with metabolic dysfunction, lifestyle intervention shows significant clinical value by directly targeting hepatic fat deposition and metabolic disorders. Based on the existing evidence, this chapter shows that the intervention strategy centered on diet optimization (such as the Mediterranean diet) and a personalized exercise program (combining aerobic and resistance training) cannot only effectively reduce the liver fat content and improve insulin sensitivity but also delay or even reverse the disease progress through moderate weight loss (5–10%). However, insufficient patient compliance and cultural background differences are still the main obstacles to long-term intervention. Therefore, integrating multidisciplinary team resources, adopting a patient-centered dynamic goal-setting framework, and combining with digital monitoring tools can enhance the feasibility and sustainability of intervention. In the future, it is necessary to further explore precise intervention models, such as nutrition stratification based on metabolic phenotype or exercise prescription optimization, and at the same time pay attention to the deep influence of socioeconomic factors on lifestyle changes so as to promote the transformation of MASLD management from "one size fits all" to an individualized and full-cycle care model.

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Conflict of interest

The authors declare no conflict of interest.

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