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A Review of NAFLD Remission Strategies: From Molecular Mechanisms to Clinical Interventions

Weiyu Chen*

Department of Clinical Medicine, College of Basic Medical Sciences, Naval Medical University, Shanghai 200433, China

**Corresponding author: Weiyu Chen.*

Abstract

Nonalcoholic fatty liver disease (NAFLD) is a liver disease closely associated with insulin resistance and metabolic dysregulation. As a chronic disease for which no curative treatment is currently available, how to alleviate patients' symptoms has become an important research topic. NAFLD affects a broad population worldwide, with a global prevalence exceeding 32.4% and reaching as high as 43.9% in China. To summarize strategies for symptom relief, this review systematically examines the remission approaches for NAFLD and extracts methods from four dimensions based on the existing literature, namely molecular mechanisms, lifestyle interventions, pharmacological therapy, and external therapies of traditional Chinese medicine. The findings indicate that ferroptosis, as a key mechanism in NAFLD progression, regulates lipid peroxidation and iron metabolism through the System xc^-–GSH–GPX4 pathway, providing new insights for targeted therapy. In terms of lifestyle intervention, ≥150 minutes of moderate-intensity aerobic exercise per week combined with resistance training can significantly reduce hepatic fat fraction, while the Mediterranean diet improves hepatic steatosis through antioxidant, anti-inflammatory, and gut microbiota-modulating effects, showing superiority over the ketogenic diet. Regarding pharmacological therapy, GLP-1 receptor agonists (GLP-1RAs) such as semaglutide have demonstrated significant improvement in steatosis in phase III trials, whereas ferroptosis inhibitors, although effective in animal models, still lack sufficient clinical translational data and require further validation. Traditional external therapies of Chinese medicine, such as Baduanjin and acupoint catgut embedding, show unique advantages in improving liver function and metabolic indicators; however, more standardized clinical optimization is required before large-scale promotion. Overall, future research in this field should focus more on multi-omics integrative analysis, the clinical translation of ferroptosis-targeted drugs, and the optimization of integrated traditional Chinese and Western medicine treatment strategies.

Keywords

nonalcoholic fatty liver disease, ferroptosis, lifestyle intervention, GLP-1 receptor agonists, external therapies of traditional Chinese medicine

1. Introduction

Nonalcoholic fatty liver disease (NAFLD) is a chronic liver disease closely associated with insulin resistance and metabolic dysregulation. In this review, the term NAFLD is retained throughout; however, some literature published after 2023 adopts the terms MASLD/MASH (formerly NASH). To ensure terminological accuracy, the original terminology used in the cited references is preserved when discussing those studies. The disease is primarily characterized by excessive lipid accumulation within hepatocytes, and its progression generally proceeds from nonalcoholic fatty liver (NAFL) to nonalcoholic steatohepatitis (NASH). In severe cases, it may further progress to liver fibrosis, cirrhosis, and even hepatocellular carcinoma (HCC) [1]. In recent years, with global changes in lifestyle and dietary patterns, NAFLD has become the most common chronic liver disease. As the liver is a critical metabolic hub in the human body, NAFLD-induced hepatic injury is also closely associated with a variety of metabolic disorders, including type 2 diabetes mellitus, cardiovascular disease, and chronic kidney disease, and substantially increases all-cause mortality in affected patients (approximately 1.3-fold higher than that of healthy individuals) [2].

The pathogenesis of NAFLD is complex and involves metabolic dysregulation at multiple levels. The traditional "two-hit" hypothesis [3] proposes that obesity and insulin resistance constitute the "first hit," leading to intrahepatic triglyceride accumulation. Hepatic steatosis then renders the liver more susceptible to the "second hit," such as inflammatory cytokines, mitochondrial dysfunction, endoplasmic reticulum stress, and oxidative stress, thereby promoting progression to hepatitis and fibrosis. In recent years, the "multiple-hit" hypothesis [4] has further expanded this theory by emphasizing the interplay of multiple pathogenic factors in genetically susceptible individuals. In addition, ferroptosis, an iron-dependent form of programmed cell death, has been confirmed to be closely involved in the occurrence and progression of NAFLD, exacerbating liver injury through lipid peroxidation and iron metabolism dysregulation [5].

The incidence of NAFLD remains high. Although a few agents, such as vitamin E [6] and pioglitazone, have demonstrated certain benefits under specific conditions, the number of drugs that have actually entered clinical use for the treatment of NAFLD remains extremely limited. Therefore, the development of effective remission strategies has become a major focus of current research. This review systematically summarizes the remission strategies for NAFLD from four dimensions: molecular mechanisms, lifestyle interventions, pharmacological therapy, and external therapies of traditional Chinese medicine, with the aim of providing references for clinical practice and future research.

2. Molecular Mechanisms of NAFLD and Ferroptosis

2.1 Molecular Mechanisms of NAFLD

The pathogenesis of NAFLD involves metabolic dysregulation at multiple levels, mainly including the following aspects [7]:

(1) Insulin resistance: Insulin resistance is the common pathological basis for both NAFLD and NASH. It weakens the suppression of hepatic gluconeogenesis, leading to hyperglycemia and hyperinsulinemia, while promoting the persistent chronic excessive delivery of free fatty acids to the liver. Hyperinsulinemia also promotes the expression of fatty acid synthase (FASN) and acetyl-CoA carboxylase (ACC), further aggravating fatty acid synthesis.

(2) Dysregulated lipid metabolism: Imbalance in hepatic lipid synthesis and metabolism is a core pathological feature of NAFLD. Increased hepatic fatty acid uptake, reduced oxidation, and enhanced esterification lead to excessive triglyceride accumulation within hepatocytes and the formation of lipid droplets. Studies have shown that a high-fat diet induces an increase in intrahepatic DKK1, which upregulates CD36 via the ERK–PPARγ axis to enhance fatty acid uptake, while aggravating hepatic insulin antagonism through activation of JNK signaling, representing a key event in the progression of fatty liver disease.

(3) Oxidative stress and inflammatory response: Mitochondrial dysfunction leads to increased production of reactive oxygen species (ROS), while the function of the antioxidant system is simultaneously impaired, resulting in oxidative stress. Oxidative stress activates inflammatory signaling pathways such as NF-κB and the NLRP3 inflammasome, leading to the release of pro-inflammatory factors (e.g., TNF-α and IL-6) and aggravating hepatic inflammation.

(4) Dysregulation of the liver–muscle axis: A bidirectional regulatory liver–muscle axis exists between the liver and skeletal muscle. Dysfunctional skeletal muscle secretes reduced levels of beneficial myokines (such as irisin) and increased levels of pro-inflammatory myokines, thereby weakening its ability to improve hepatic metabolism and exert anti-inflammatory effects. Meanwhile, hepatokines secreted by the steatotic liver (such as fetuin-A and selenoprotein P) further aggravate systemic and muscular insulin resistance, inhibit muscle protein synthesis, and lead to loss of muscle mass (sarcopenia), thereby forming a vicious cycle.

(5) Gut microbiota dysbiosis: The gut microbiota promotes NAFLD through multiple mechanisms, including increased intestinal permeability, release of lipopolysaccharide (LPS) and pro-inflammatory cytokines, and modulation of bile acid metabolism and energy absorption. Metabolites produced by the gut microbiota (such as ethanol and lactate) may also further increase the hepatic burden.

2.2 Association Between Ferroptosis and NAFLD

Ferroptosis is an iron-dependent form of programmed cell death, first proposed in 2012, with iron-dependent lipid peroxidation as its core mechanism. Ferroptosis is closely associated with the occurrence and progression of NAFLD, mainly acting through the following pathways [5].

(1) System xc^-–GSH–GPX4 pathway. This is the central regulatory axis of ferroptosis. System xc^- consists of two subunits, SLC7A11 and SLC3A2, and is responsible for transporting extracellular cystine into the cell while exporting intracellular glutamate out of the cell. After entering the cell, cystine is reduced to cysteine and subsequently used for the synthesis of glutathione (GSH). GSH serves as a cofactor for glutathione peroxidase 4 (GPX4), which is responsible for eliminating lipid peroxides (L-OOH) and protecting the cell membrane from oxidative damage. In patients with NAFLD, this pathway is functionally impaired, leading to massive accumulation of lipid peroxides and ultimately resulting in cell death.

(2) Iron metabolism axis. Iron overload is commonly present in the livers of patients with NAFLD. Ferritinophagy releases free iron (Fe^{2+}), which catalyzes the conversion of lipid peroxides into lipid radicals through the Fenton reaction, thereby triggering a chain reaction. Studies have shown that the ferroptosis inhibitor Ferrostatin-1 can inhibit the Fenton reaction and reduce ROS burst and lipid peroxidation by lowering the level of the labile iron pool (LIP) and reducing intracellular free Fe^{2+} concentration.

(3) Interaction between the liver–muscle axis and ferroptosis. Ferroptosis plays a key role in NAFLD/NASH. Bioinformatics analyses have identified nine key ferroptosis-related genes in NASH, including ZFP36, ATF3, SOCS1, IL-6, PTGS2, and JUN. Experimental studies confirmed that in free fatty acid (FFA)-treated HepG2 cells, the protein expression levels of c-jun, ZFP36, ATF3, and IL-6 were increased, accompanied by enhanced lipid peroxidation. Inhibition of ferroptosis can almost completely suppress the development of NASH. Ferroptosis also participates in the dysregulation of the liver–muscle axis by regulating the polarization state of hepatic macrophages (Kupffer cells) and influencing inflammatory responses.

2.3 Potential Value of Ferroptosis-Targeted Therapy

Ferroptosis inhibitors such as Ferrostatin-1 and Liproxstatin-1 have shown significant hepatoprotective effects in animal models. Studies have demonstrated that ferroptosis inhibitors can effectively alleviate acute liver injury and reduce hepatocyte death. In mouse models of metabolic dysfunction-associated steatotic liver disease (formerly MASH), Ferrostatin-1 protects against aging-related ferroptotic stress and hepatic senescence, significantly reduces the accumulation of senescent hepatocytes, and improves hepatic metabolism, inflammation, and fibrosis. However, current research on ferroptosis inhibitors in humans is still at an early stage, lacking large-scale clinical trial data, and their long-term safety and efficacy remain to be further validated.

3. Lifestyle Intervention as the Foundational Strategy for NAFLD Remission

3.1 Exercise Intervention

Exercise is a foundational strategy for NAFLD remission and has been confirmed by multiple studies to effectively reduce hepatic fat content, improve insulin sensitivity, and alleviate inflammation.

(1) Aerobic exercise. Aerobic exercise can increase fat oxidation, accelerate fat consumption, and improve insulin resistance, thereby alleviating NAFLD. Studies have shown that ≥150 minutes of moderate-intensity aerobic exercise per week (60%–70% of maximal heart rate) is an effective regimen for improving hepatic steatosis in patients with NAFLD [8]. The 2025 Primary Care Guidelines for the Diagnosis, Treatment, and Management of Metabolic Dysfunction-Associated Fatty Liver Disease clearly state that moderate-intensity aerobic exercise is the cornerstone and principal approach for the treatment of NAFLD [9].

(2) Resistance training. Resistance training improves blood glucose levels and insulin responsiveness to glycemic load by increasing muscle fiber mass and promoting the synthesis and expression of glucose transporter 4 (GLUT4). Studies have shown that resistance training can independently reduce hepatic fat by 13%, and this effect is unrelated to weight loss [10,11]. Therefore, resistance training can serve as a complementary regimen to aerobic exercise, but it cannot completely replace aerobic exercise.

(3) Individualization of exercise prescriptions. On the other hand, exercise prescriptions should also emphasize individualization. Exercise programs should be scientifically and reasonably selected according to the patient's disease condition, physical status, and exercise environment. For patients with mild disease, options such as running, badminton, jump rope, and resistance exercise may be selected. Patients with more severe disease may choose prolonged walking, aerobic dance-based exercise, Tai Chi, and swimming. For patients with particularly severe disease, massage and seated liver-soothing and gallbladder-benefiting exercises may be considered as low-intensity options.

3.2 Dietary Intervention

Dietary intervention is another important strategy for NAFLD remission, and different dietary patterns exert distinct effects on NAFLD.

(1) Mediterranean diet intervention. As one of the most widely recognized healthy dietary patterns worldwide, the Mediterranean diet mainly consists of olive oil, nuts, fruits and vegetables, whole grains, and fish, and is rich in monounsaturated fatty acids (MUFAs), ω-3 polyunsaturated fatty acids (PUFAs), antioxidants, and dietary fiber. Studies have shown that adherence to the Mediterranean diet for 6 months can reduce liver fat content in patients with fatty liver disease by an average of 39%, which is significantly superior to a conventional low-fat diet. Its mechanisms include reducing intrahepatic fat accumulation, improving insulin sensitivity, decreasing hepatic inflammatory responses, alleviating oxidative stress injury, and regulating gut microbiota homeostasis [12].

(2) Low-fat diet. This dietary approach restricts total caloric intake and directly reduces hepatic lipid synthesis. Studies have shown that participants in the low-fat diet group experienced an approximately 17% reduction in hepatic fat content, with $p = 0.02$, indicating statistical significance. A low-fat diet also improved visceral fat content and insulin resistance.

(3) Ketogenic diet (KD). This dietary pattern strictly restricts carbohydrate intake (<50 g/day or <5% of total energy intake) while emphasizing high fat intake (>70% of total energy intake), allowing protein to account for 15%–20% of energy supply. This diet promotes intrahepatic triglyceride breakdown by inducing hepatic fatty acid β-oxidation and ketone body production, thereby mimicking the metabolic characteristics of the fasting state. Clinical studies have shown that 12–24 weeks of short-term ketogenic diet intervention can reduce hepatic fat content in patients with NAFLD by 20%–25%, as assessed by MRI-proton density fat fraction (MRI-PDFF), while body weight decreases by 10%–15% [8,9]. At the same time, serum ALT levels can also be significantly improved [9]. However, current evidence is mostly derived from small-sample short-term studies, and long-term follow-up data are still lacking. In addition, strict carbohydrate restriction may lead to deficiencies in dietary fiber and micronutrients, increase low-density lipoprotein cholesterol (LDL-C) levels, and is associated with poor long-term adherence.

3.3 Comparison of Different Exercise Types

Different exercise modalities exhibit significant differences in their clinical effects and implementation characteristics in improving nonalcoholic fatty liver disease (NAFLD). The relevant conclusions are shown in Table 1.

Table 1: Comparison of intervention effects among different exercise modalities

Exercise type	Intensity	Duration	Frequency	Advantages	Disadvantages	Clinical effects
Aerobic exercise	Moderate intensity (60%–70% of maximal heart rate)	30–120 min/session	≥5 sessions/week	Improves cardiopulmonary function; promotes fat oxidation; improves insulin sensitivity	Requires long-term adherence; may increase joint burden; limited applicability in patients with severe liver disease	Hepatic fat content reduced by 20%–30%; body weight reduced by 5%–8%; liver enzyme levels decreased
Resistance training	Moderate intensity	45–60 min/session	2–3 sessions/week	Increases muscle mass; improves insulin sensitivity; improves hepatic fat independent of weight loss	May increase muscle fatigue; requires professional guidance; limited applicability in patients with severe liver disease	Hepatic fat content reduced by 10%–15%; muscle mass increased by 5%–10%; liver enzyme levels decreased
Combined training (aerobic + resistance)	Mainly moderate intensity	45–60 min/session	≥5 sessions/week	Comprehensively improves hepatic fat and muscle mass; enhances overall metabolic status; improves insulin sensitivity	Requires longer duration; stricter intensity control; limited applicability in patients with severe liver disease	Hepatic fat content reduced by 30%–40%; body weight reduced by 8%–10%; muscle mass increased by 5%–8%

Aerobic exercise, centered on moderate intensity (60%–70% of maximal heart rate), with 30–120 minutes per session and ≥5 sessions per week, can improve cardiopulmonary function, promote fat oxidation, and enhance insulin sensitivity, thereby reducing hepatic fat content by 20%–30%, decreasing body weight by 5%–8%, and improving liver enzyme levels. It is suitable for patients with good adherence and without severe joint disease, although it requires long-term persistence and has limited applicability in patients with advanced liver disease.

Resistance training, also mainly performed at moderate intensity, with 45–60 minutes per session and 2–3 sessions per week, primarily improves insulin sensitivity by increasing muscle mass. It can reduce hepatic fat content by 10%–15%, increase muscle mass by 5%–10%, and simultaneously achieve mild weight reduction. It is suitable for patients wishing to preserve muscle mass, but it may easily induce muscle fatigue and requires professional guidance. Its use is likewise limited in patients with severe liver disease.

Combined training (aerobic + resistance) integrates the advantages of both exercise types. Conducted at moderate intensity for 45–60 minutes per session and ≥5 sessions per week, it can comprehensively improve hepatic fat, muscle mass, and overall metabolic status. Its clinical effects are more pronounced, reducing hepatic fat content by 30%–40%, decreasing body weight by 8%–10%, and increasing muscle mass. It is suitable for patients with stable disease and good tolerance, although it requires stricter control of exercise duration and intensity, and caution is still warranted in patients with severe liver disease.

In summary, all three exercise modalities can effectively improve NAFLD-related indicators. In clinical practice, personalized exercise intervention plans should be selected according to the patient's disease status, physical tolerance, and adherence in order to achieve optimal intervention outcomes.

4. Clinical Evidence and Limitations of Different Remission Strategies

4.1 Clinical Evidence and Limitations of Lifestyle Intervention

Lifestyle intervention is the first-line strategy for NAFLD remission and is supported by solid clinical evidence.

(1) Relevant clinical evidence

- The 2025 Primary Care Guidelines for the Diagnosis, Treatment, and Management of Metabolic Dysfunction-Associated Fatty Liver Disease clearly state that lifestyle intervention is the cornerstone and primary approach for the treatment of NAFLD.
- Studies have shown that ≥150 minutes of moderate-intensity aerobic exercise per week or ≥75 minutes of vigorous physical activity per week can significantly reduce hepatic fat content and improve liver function.
- Both the Mediterranean diet and low-fat diet can effectively improve hepatic fat content and insulin resistance in patients with NAFLD, while the low-fat diet shows a more pronounced effect in reducing intrahepatic fat content.

(2) Limitations

- Lifestyle intervention requires long-term adherence, and patient compliance may be insufficient.
- In patients with severe NAFLD, lifestyle intervention alone may have limited efficacy.
- There is still a lack of individualized intervention protocols for patients with different levels of disease severity.

4.2 Clinical Evidence and Limitations of Pharmacological Therapy

When lifestyle intervention yields unsatisfactory outcomes, pharmacological therapy becomes an important adjunctive and supportive strategy.

(1) GLP-1 receptor agonists (GLP-1RAs). These agents are widely recognized as effective classical drugs related to the remission of steatohepatitis [15]. Clinically, after 72 weeks of semaglutide treatment in patients with NAFLD (formerly MASH), 36.8% of patients were observed to have fibrosis improvement, and 62.9% achieved steatohepatitis remission [15].

- Long-term use may lead to gastrointestinal adverse reactions (such as nausea and vomiting); may increase cardiovascular risk; relatively high cost; requires professional monitoring.

(2) SGLT2 inhibitors. Also referred to as ipragliflozin, these agents can improve liver enzyme levels, fasting blood glucose, liver fibrosis, and obesity in patients with type 2 diabetes mellitus (T2DM) complicated with NAFLD. They can likewise alleviate various episodes of hepatitis [16].

- Long-term use may cause hypoglycemia and hypotension; may increase the risk of genitourinary infections; the direct mechanisms of action on liver disease remain incompletely understood.

(3) Ferroptosis inhibitors. Ferrostatin-1 has demonstrated significant hepatoprotective effects in animal models and can alleviate hepatic steatosis, inflammation, and fibrosis.

- Although ferroptosis inhibitors are considered highly promising novel agents that have attracted considerable attention for alleviating steatohepatitis-related symptoms, human trial data remain limited. They may also interfere with normal systemic iron metabolic balance; their long-term safety remains unknown, and standardized treatment regimens are lacking.

4.3 Clinical Evidence and Limitations of External Traditional Chinese Medicine Therapies

External traditional Chinese medicine (TCM) therapies, as complementary strategies for NAFLD remission, possess unique theoretical foundations and practical value.

(1) Acupuncture therapy:

Clinically, electroacupuncture stimulation at acupoints such as Zhongwan (CV12), Quchi (LI11), Shuifen (CV9), Huaroumen (ST24), Daheng (SP15), and Guanyuan (CV4) can effectively improve insulin resistance and liver function in patients with NAFLD [17].

However, current practice still suffers from insufficient standardization, lack of unified efficacy evaluation criteria, and inadequate mechanistic research.

(2) Baduanjin exercise

A 24-week Baduanjin exercise prescription intervention can effectively improve lipid metabolism, hepatic functional status, and blood glucose levels in patients with mild, moderate, and severe NAFLD.

However, as a form of exercise therapy, the intensity and frequency of Baduanjin vary greatly among individuals, and there is a lack of individualized protocols for patients with different severity levels. Research on its mechanisms of action also remains insufficiently detailed [18].

(3) Acupoint catgut embedding

- Clinical evidence: The *Practice Guidelines of Traditional Chinese Medicine for Acupoint Catgut Embedding in the Treatment of Nonalcoholic Fatty Liver Disease* provide clear operational standards. Acupoints including Zhongwan (CV12), Tianshu (ST25), Daimai (GB26), Huaroumen (ST24), Guanyuan (CV4), and Qihai (CV6) are selected, which can effectively reduce serum liver function indicators and blood lipid levels, increase plasma adiponectin and PPAR-α levels, and improve hepatic fat deposition [19,20].

The treatment cycle is relatively long (usually 4–8 weeks), local discomfort may occur, and efficacy evaluation still lacks unified standards.

5. Future Research Directions and Recommendations

5.1 Multi-omics Integrative Analysis

Future research should place greater emphasis on the integrative analysis of multi-omics data, including genomics, transcriptomics, proteomics, and metabolomics, in order to comprehensively elucidate the molecular mechanisms of NAFLD and the therapeutic targets of remission strategies. For example, by integrating transcriptomic and proteomic data, key regulators of ferroptosis-related pathways can be identified more accurately; through metabolomic analysis, the effects of different dietary patterns on hepatic metabolism can be understood more deeply.

5.2 Clinical Translation of Ferroptosis-Targeted Drugs

Ferroptosis-targeted drugs represent a frontier direction and major research hotspot in the treatment of NAFLD. Future studies should focus on the following aspects:

(1) Development of novel ferroptosis inhibitors, such as specific inhibitors targeting ACSL4, which may selectively inhibit hepatic ferroptosis without affecting other tissues.

(2) Optimization of the clinical trial design of ferroptosis inhibitors. Future clinical trials should pay greater attention to the direct effects of ferroptosis inhibitors on liver histopathology, rather than relying solely on metabolic indicators.

(3) In-depth exploration of the interactions between ferroptosis and other cell death pathways. This requires further investigation into the crosstalk between ferroptosis and other cell death pathways, such as apoptosis, necrosis, and autophagy, in order to optimize pharmacological treatment strategies.

5.3 Optimization of Integrated Traditional Chinese and Western Medicine Treatment Strategies

As an important direction for the effective remission of NAFLD, future research on the integration of traditional Chinese medicine (TCM) approaches with Western medical treatment courses may focus on the following aspects:

(1) Promotion of the standardization of external TCM therapies. According to reports, in 2026, the National Administration of Traditional Chinese Medicine of China will launch the compilation of new national standards and their English editions, including *Technical Operation Standards of Traditional Chinese Medicine: Common External Therapies*. Future research should place greater emphasis on the clinical validation and dissemination of standardized procedures.

(2) Investigation into the mechanisms of integrated Chinese and Western medicine treatment. This requires in-depth exploration of the synergistic mechanisms between external TCM therapies and modern pharmacological treatments, thereby providing a theoretical basis for individualized therapy.

(3) Improvement of the efficacy evaluation system for integrated Chinese and Western medicine treatment. A unified evaluation system should be established, including hepatic fat content, liver function indicators, inflammatory biomarkers, and quality of life, in order to improve the comparability and reliability of research findings.

5.4 Individualized Protocols for Lifestyle Intervention

Lifestyle intervention is the foundational strategy for NAFLD remission, and future research should place greater emphasis on the development and optimization of individualized protocols.

(1) Development of personalized lifestyle intervention strategies for patients with different genotypes, such as PNPLA3, TM6SF2, and SREBF.

(2) Design of targeted exercise prescriptions based on the functional status of the liver–muscle axis, in order to improve intervention efficacy.

(3) Gut microbiota-based dietary intervention: by analyzing the composition of the patient's gut microbiota, individualized dietary intervention protocols can be designed to optimize therapeutic outcomes.

6. Conclusion and Perspectives

Nonalcoholic fatty liver disease (NAFLD) is a chronic liver disease closely associated with insulin resistance and metabolic dysregulation. Its incidence continues to rise and it has become one of the most common chronic liver diseases worldwide. This review systematically summarizes the remission strategies for NAFLD and provides a comprehensive analysis from four dimensions: molecular mechanisms, lifestyle intervention, pharmacological therapy, and external traditional Chinese medicine therapies. The findings indicate that ferroptosis, as a key mechanism in NAFLD progression, provides new insights for targeted therapy; lifestyle intervention, particularly aerobic exercise and the Mediterranean diet, constitutes the foundational strategy for NAFLD remission; pharmacological therapy, such as GLP-1 receptor agonists, has demonstrated favorable efficacy in specific patient populations; and external TCM therapies, including acupuncture, Baduanjin, and acupoint catgut embedding, show unique advantages in improving liver function and metabolic indicators.

Despite the availability of multiple remission strategies, many challenges still remain. The clinical translation of ferroptosis-targeted drugs requires further validation; the adherence to and personalization of lifestyle interventions need further optimization; the long-term safety of pharmacological therapy and its direct effects on liver fibrosis require additional investigation; and the standardization of external TCM procedures and efficacy evaluation systems still need improvement.

Future studies should focus on multi-omics integrative analysis, the clinical translation of ferroptosis-targeted drugs, and the optimization of integrated Chinese and Western medicine treatment strategies. Through these efforts, it is expected that more precise and safer remission strategies for NAFLD can be developed, thereby improving patients' quality of life and prognosis.

In clinical practice, individualized remission strategies should be selected according to the patient's specific conditions, such as disease severity, comorbidities, and genotype. Lifestyle intervention should be prioritized, while pharmacological therapy and external TCM therapies may be combined when necessary to form a multidimensional and systematic comprehensive treatment regimen. At the same time, patient

education and follow-up management should be strengthened to improve adherence and long-term therapeutic outcomes.

With the deepening understanding of the molecular mechanisms of NAFLD and advances in therapeutic technologies, it is expected that in the coming years more highly effective drugs specifically targeting NAFLD will be approved, along with the establishment of more precise and personalized comprehensive treatment strategies. This will bring new hope to the hundreds of millions of patients with NAFLD worldwide, significantly improving their quality of life and prolonging survival.

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