RESEARCH PAPER

Dietary Strategies for Metabolic Dysfunction-Associated Steatotic Liver Disease: Comparing Mediterranean, Low-Carbohydrate, Ketogenic, and Time-Restricted Eating Approaches.

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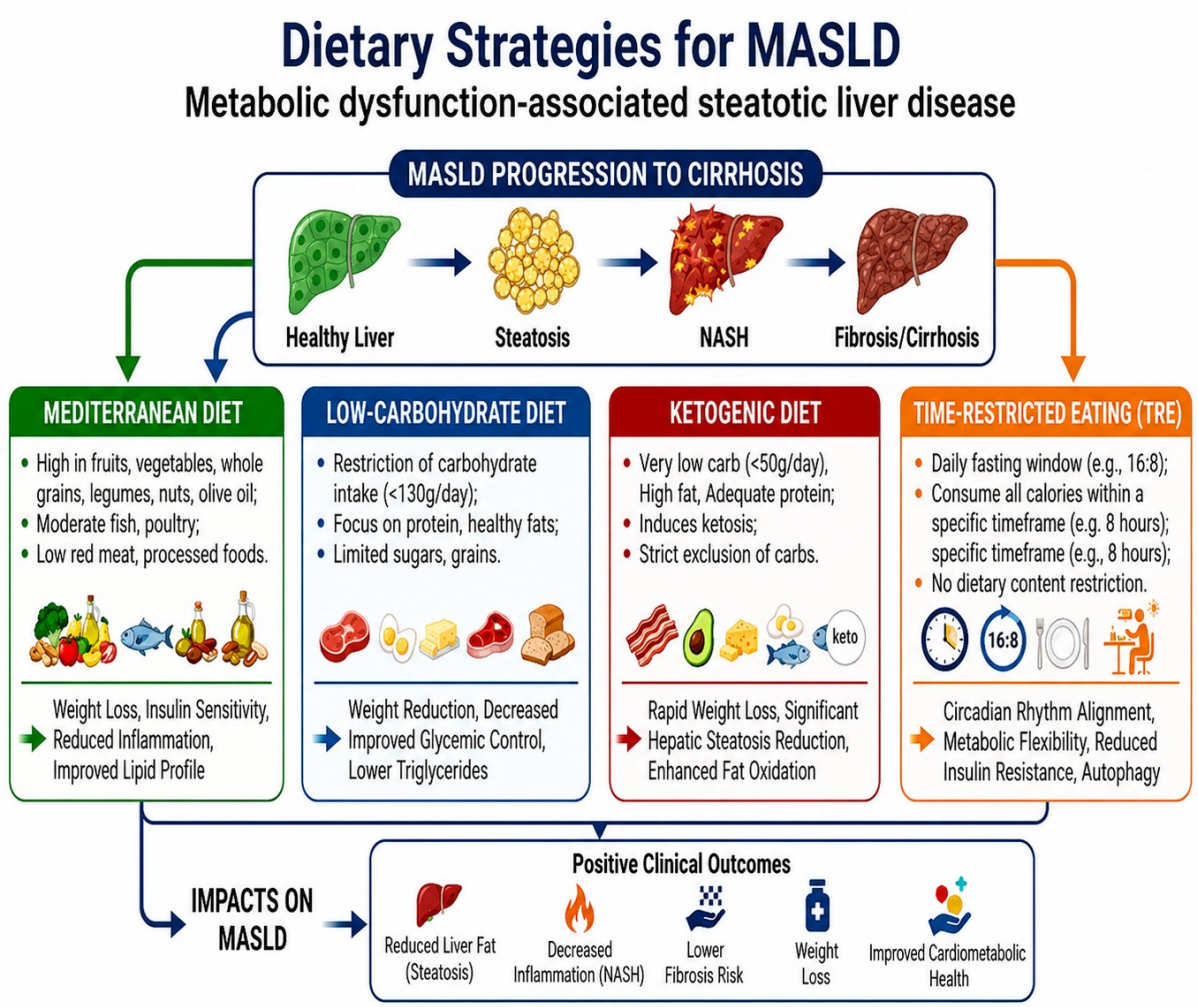
Abstract

Metabolic dysfunction-associated steatotic liver disease (MASLD) is a prevalent metabolic liver disorder closely associated with obesity, insulin resistance, dyslipidemia, and other cardiometabolic risk factors. Lifestyle modification, particularly dietary intervention, remains a cornerstone of MASLD management; however, the optimal dietary strategy for improving hepatic steatosis and metabolic health remains incompletely established. This review examines and compares the evidence supporting four dietary approaches Mediterranean, low-carbohydrate, ketogenic, and time-restricted eating in the management of MASLD. Particular attention is given to their effects on hepatic fat accumulation, body weight, insulin sensitivity, glycemic control, lipid metabolism, and other relevant metabolic and liver-related outcomes. The Mediterranean diet is characterized by a high intake of vegetables, fruits, whole grains, legumes, nuts, and olive oil, and has demonstrated consistent benefits for overall metabolic health and cardiovascular risk, with emerging evidence supporting improvements in hepatic steatosis. Low-carbohydrate and ketogenic diets may promote substantial weight loss and improve glycemic and insulin-related parameters, potentially contributing to reductions in liver fat; however, their long-term efficacy, sustainability, and nutritional adequacy require further consideration. Time-restricted eating represents a potentially practical approach that modifies the timing of food intake rather than prescribing specific macronutrient compositions and may improve metabolic outcomes through weight loss and enhanced circadian metabolic regulation. Across these dietary strategies, improvements in MASLD appear to be influenced substantially by energy restriction, weight reduction, dietary quality, adherence, and individual metabolic characteristics. Current evidence therefore does not support a universally superior dietary pattern for all patients with MASLD. Instead, dietary management should be individualized according to metabolic status, nutritional preferences, comorbidities, lifestyle factors, and the likelihood of long-term adherence. Further well-designed, adequately powered, long-term randomized controlled trials are needed to directly compare these approaches and clarify their independent effects on liver-specific outcomes. Overall, integrating dietary quality, sustainable weight management, and individualized eating patterns may provide the most effective framework for nutritional management of MASLD.

Keywords: Metabolic dysfunction-associated steatotic liver disease (MASLD); Mediterranean diet; low-carbohydrate diet; ketogenic diet; time-restricted eating.

How to cite this article: Manal Almatrafi. Dietary Strategies for Metabolic Dysfunction-Associated Steatotic Liver Disease: Comparing Mediterranean, Low-Carbohydrate, Ketogenic, and Time-Restricted Eating Approaches.. Int J Drug Deliv Technol. 2026;16(80s):507-526. DOI: 10.25258/ijddt.16.80s.62.



Graphic abstract: Dietary Strategies in MASLD: A Comparative Framework of Metabolic and Hepatic Outcomes.

1. Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD) has emerged as one of the most important metabolic and hepatic disorders worldwide, reflecting the rapidly increasing prevalence of obesity, insulin resistance, type 2 diabetes mellitus (T2DM), and other cardiometabolic abnormalities. The term MASLD was introduced to provide a more biologically and clinically relevant framework for steatotic liver disease by identifying the presence of hepatic steatosis together with at least one cardiometabolic risk factor and without the requirement for excessive alcohol consumption. The disease represents a broad clinical spectrum ranging from uncomplicated hepatic steatosis to metabolic dysfunction-associated steatohepatitis (MASH), progressive hepatic fibrosis, cirrhosis, and hepatocellular carcinoma. Importantly, MASLD is not confined to the liver; affected individuals frequently have increased risks of cardiovascular disease, T2DM, chronic kidney disease, and other metabolic complications. Recent evidence indicates that the global burden of steatotic liver disease is substantial, emphasizing the urgent need for effective, sustainable, and scalable preventive and therapeutic strategies. (Rinella et al., 2023). The pathogenesis of MASLD is complex and multifactorial, involving interactions among excessive energy intake, adipose tissue dysfunction, insulin resistance, altered lipid metabolism, hepatic de novo lipogenesis, oxidative stress, mitochondrial dysfunction, inflammation, and disturbances in the gut–liver axis. Insulin resistance plays a particularly important role by promoting increased adipose tissue lipolysis and delivery of free fatty acids to the liver while simultaneously stimulating hepatic lipid synthesis. Excess hepatic lipid accumulation can subsequently contribute to lipotoxicity, oxidative injury, inflammatory signaling, hepatocellular stress, and activation of pathways involved in fibrogenesis. Dietary composition is therefore highly relevant to disease progression because the quality and quantity of dietary carbohydrates, fats, proteins, fiber, and bioactive compounds can influence glucose homeostasis, lipid metabolism, inflammation, oxidative stress, and the intestinal microbiome. Consequently, dietary modification is considered a central component of MASLD management rather than merely an adjunct to pharmacological treatment

(Bansal et al., 2024). Current clinical recommendations emphasize lifestyle modification, with intentional weight reduction, dietary improvement, regular physical activity, and management of associated metabolic diseases forming the foundation of MASLD treatment. Importantly, the available evidence suggests that the magnitude of weight loss is closely related to improvements in hepatic steatosis and, with greater weight reduction, inflammatory activity and fibrosis. However, focusing exclusively on caloric restriction may underestimate the potential influence of dietary quality and macronutrient composition. Several dietary patterns can produce clinically meaningful metabolic and hepatic improvements, but their relative effectiveness, sustainability, safety, and applicability to different patient phenotypes remain incompletely defined. A recent international multidisciplinary consensus therefore emphasized controlled energy intake and individualized dietary interventions while encouraging greater consumption of whole grains, plant-based proteins, fish, seafood, fruits, vegetables, and unsaturated plant oils and reducing red and processed meat, saturated and trans fats, ultra-processed foods, and added sugars. (EASL–EASD–EASO, 2024). Among the dietary patterns investigated in MASLD, the Mediterranean diet (MD) has received particularly strong scientific attention. This dietary pattern is characterized by high consumption of vegetables, fruits, legumes, whole grains, nuts, seeds, olive oil, and other sources of unsaturated fats, together with moderate consumption of fish and dairy products and relatively low intake of red and processed meat, refined carbohydrates, and highly processed foods. Beyond its potential to facilitate weight management, the Mediterranean dietary pattern may influence MASLD through multiple complementary mechanisms, including improved insulin sensitivity, reduction of oxidative stress and systemic inflammation, favorable modulation of lipid metabolism, and beneficial effects on the gut microbiome. Evidence synthesized in recent reviews supports the use of the Mediterranean diet as a practical dietary strategy for individuals with MASLD, although important questions remain concerning adherence outside Mediterranean populations, the contribution of energy restriction to observed effects, and the extent to which the diet independently influences hepatic fat and fibrosis. (Zeng et al., 2024).

In contrast, low-carbohydrate diets (LCDs) have attracted increasing interest because carbohydrate restriction may improve insulin sensitivity, reduce hepatic de novo lipogenesis, and facilitate reductions in body weight and visceral adiposity. LCDs encompass a heterogeneous group of dietary approaches, ranging from moderate carbohydrate reduction to very-low-carbohydrate regimens, making comparisons between studies challenging. Recent evidence suggests that low-carbohydrate interventions can improve several cardiometabolic parameters in individuals with MASLD, including body weight, triglycerides, glycemic control, and measures of insulin resistance. Nevertheless, the effects of carbohydrate restriction on hepatic outcomes cannot always be separated from the effects of concomitant energy restriction and weight loss. Furthermore, the quality of dietary fat and protein replacing carbohydrate may substantially influence the overall metabolic and cardiovascular profile of an LCD. These considerations highlight the importance of evaluating not simply the quantity of carbohydrate consumed, but also the nutritional quality and overall dietary composition. (Dobbie et al., 2024).

The ketogenic diet (KD) represents a more restrictive form of carbohydrate reduction, typically characterized by very low carbohydrate availability, relatively high fat intake, and moderate protein consumption, resulting in increased hepatic production of ketone bodies. The metabolic effects of nutritional ketosis have generated considerable interest in the context of MASLD because carbohydrate restriction may rapidly alter insulin signaling, fatty-acid utilization, hepatic lipogenesis, and energy metabolism. However, enthusiasm regarding ketogenic diets should be balanced against the relatively limited number of high-quality, long-term clinical trials specifically evaluating MASLD outcomes. A recent randomized controlled trial found that an eight-week ketogenic intervention produced substantially greater weight loss than a DASH-based control intervention, but did not demonstrate a significant between-group difference in liver stiffness or steatosis measurements. These findings illustrate an important issue in interpreting ketogenic-diet research: improvements in body weight and metabolic parameters do not necessarily establish a unique liver-specific benefit of nutritional ketosis. (Yoon et al ., 2025). More recently, time-restricted eating (TRE) has emerged as a distinct nutritional strategy that focuses primarily on when food is consumed rather than prescribing a specific macronutrient composition. TRE typically confines daily energy intake to a consistent eating window, often ranging from approximately 8 to 10 hours, while extending the fasting interval. The proposed mechanisms include improved circadian alignment, enhanced insulin sensitivity, altered substrate utilization, and metabolic switching between fed and fasting states. Importantly, TRE may facilitate spontaneous reductions in energy intake without requiring detailed calorie counting, potentially improving the practical acceptability of dietary intervention for some individuals. Clinical evidence in patients with MASLD is still developing, but randomized trials have reported reductions in hepatic steatosis, body weight, waist circumference, and other metabolic

outcomes following TRE. Recent evidence also suggests that TRE may provide improvements comparable to conventional calorie restriction when energy intake is similarly reduced, raising the important question of whether its principal benefit derives from fasting duration, reduced energy intake, improved meal timing, or a combination of these mechanisms. (Wang et al., 2025). Despite growing evidence supporting several dietary strategies, the optimal dietary approach for MASLD remains unresolved. Differences in study design, carbohydrate and fat thresholds, caloric intake, duration of intervention, patient characteristics, methods used to quantify hepatic steatosis, and adherence make direct comparisons difficult. Moreover, the biological response to dietary interventions may vary according to obesity status, T2DM, insulin resistance, dyslipidemia, genetic background, physical activity, and other metabolic characteristics. Recent clinical research has consequently shifted from asking whether diet is effective toward determining which dietary strategy is most appropriate for which patient, under which circumstances, and for how long This transition from generalized dietary advice toward personalized nutrition may be particularly important in MASLD, where long-term adherence and comprehensive cardiometabolic risk reduction are as important as short-term reductions in liver fat. (Crider et al., 2022). Accordingly, the present review critically examines and compares four increasingly relevant dietary approaches the Mediterranean diet, low-carbohydrate diets, ketogenic diets, and time-restricted eating in the context of MASLD. Particular emphasis is placed on their effects on hepatic steatosis, body weight, insulin resistance, glycemic control, lipid metabolism, liver enzymes, inflammation, oxidative stress, and potential progression toward MASH and fibrosis. The review also considers the biological mechanisms underlying each approach, the quality and limitations of current clinical evidence, dietary adherence and long-term sustainability, and the potential role of personalized nutrition. By integrating conventional dietary-pattern approaches with emerging carbohydrate-restricted and meal-timing strategies, this review aims to clarify the relative strengths, limitations, and clinical applicability of these interventions and to identify priorities for future research in nutritional management of MASLD.

2. Pathophysiological Basis of MASLD and Nutritional Targets

Metabolic dysfunction-associated steatotic liver disease (MASLD) develops through a complex interaction between excess energy availability, adipose tissue dysfunction, insulin resistance, abnormal lipid handling, inflammation, oxidative stress, and disturbances in the gut–liver axis. Hepatic steatosis occurs when the influx and endogenous production of fatty acids exceed the capacity of the liver to oxidize and export lipids. In individuals with metabolic dysfunction, insulin resistance promotes adipose tissue lipolysis and increases the delivery of non-esterified fatty acids to the liver, while persistent hyperinsulinemia and hyperglycemia stimulate hepatic de novo lipogenesis. At the same time, impaired mitochondrial function and altered fatty-acid oxidation may limit the ability of hepatocytes to safely dispose of accumulated lipids. The resulting intracellular lipid overload is not simply a passive storage phenomenon; rather, it can generate lipotoxic intermediates and activate cellular stress pathways that contribute to hepatocellular injury and disease progression. Consequently, dietary interventions capable of modifying energy balance, insulin sensitivity, hepatic lipid synthesis, and substrate utilization represent important therapeutic targets in MASLD. (Rinaldi et al., 2024). A central nutritional target in MASLD is therefore the restoration of a favorable energy balance. Excess caloric intake, particularly when sustained over time, contributes to adiposity and ectopic lipid deposition, while intentional energy restriction can reduce hepatic fat even before substantial changes in other metabolic outcomes become apparent. Importantly, the magnitude of weight reduction appears to influence the degree of hepatic improvement, with modest weight loss generally improving steatosis and greater weight loss being associated with more pronounced improvements in steatohepatitis and, in some patients, fibrosis. Nevertheless, calorie restriction should not be interpreted as the only determinant of dietary efficacy. The source of calories, macronutrient composition, dietary quality, fiber intake, fatty-acid profile, and consumption of ultra-processed foods may independently affect metabolic pathways relevant to MASLD. A recent systematic review and meta-analysis of adults with MASLD and overweight or obesity found that low-calorie dietary interventions reduced body weight and, in selected interventions, intrahepatic lipid content, although considerable heterogeneity existed between studies. (Arita et al., 2025).

2.1 Insulin Resistance and Hepatic Lipid Accumulation

Insulin resistance represents one of the major metabolic abnormalities linking dietary excess with hepatic steatosis. Under normal physiological conditions, insulin suppresses adipose tissue lipolysis and regulates hepatic glucose and lipid metabolism. In insulin-resistant states, suppression of lipolysis becomes impaired, resulting in increased circulating free fatty acids and greater hepatic fatty-acid delivery. Concurrently, hepatic insulin signaling may remain sufficiently active to stimulate lipogenic pathways despite impaired regulation of glucose metabolism, thereby promoting de novo

lipogenesis. Diets rich in refined carbohydrates and added sugars, particularly when associated with excess energy intake, may further contribute to this metabolic environment. Conversely, dietary strategies that improve insulin sensitivity or reduce excessive carbohydrate availability may decrease hepatic lipid synthesis and facilitate greater utilization of stored energy (Fig. 1).These mechanisms provide a physiological rationale for investigating both Mediterranean-style dietary patterns and carbohydrate-restricted approaches in MASLD. (Dobbie et al., 2024).

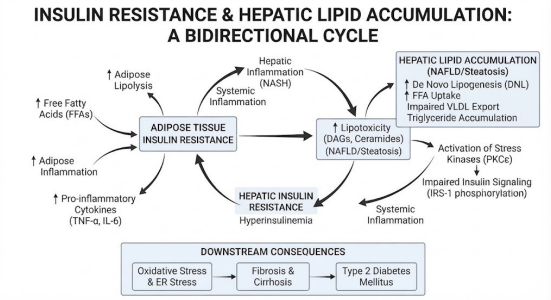


Figure 1. Schematic overview of the bidirectional cycle between adipose tissue insulin resistance and hepatic lipid accumulation, including key molecular pathways and downstream pathological consequences.

2.2 Dietary Fat Quality and Lipotoxicity

The relationship between dietary fat and MASLD is more complex than the total amount of fat consumed. Current nutritional evidence increasingly emphasizes fat quality rather than indiscriminate fat restriction. Diets enriched in monounsaturated and polyunsaturated fatty acids, particularly those derived from olive oil, nuts, seeds, and fish, may exert more favorable metabolic effects than diets dominated by saturated and trans fats. The Mediterranean dietary pattern illustrates this principle by replacing substantial amounts of saturated fat with unsaturated sources while simultaneously increasing plant-based foods and dietary fiber. In contrast, excessive consumption of saturated fats may promote hepatic lipid accumulation, inflammation, and insulin resistance through several metabolic and cellular mechanisms. Accordingly, dietary recommendations for MASLD increasingly favor unsaturated plant oils, fish, nuts, and other nutrient-dense sources while limiting saturated and trans fats rather than simply prescribing a uniformly low-fat diet. (Petersen and Shulman, 2018).

2.3 Carbohydrate Quality, De Novo Lipogenesis, and Metabolic Flexibility

Carbohydrate quantity and quality are also important determinants of metabolic health in MASLD. Excessive consumption of refined carbohydrates and added sugars can increase postprandial glucose and insulin concentrations and may enhance hepatic de novo lipogenesis when energy requirements are exceeded. Fructose is of particular interest because it can be metabolized in the liver and contribute to lipogenic pathways under conditions of excessive intake. However, the clinical interpretation of carbohydrate restriction requires caution because replacing carbohydrates with saturated fat or highly processed protein sources may not necessarily provide equivalent cardiometabolic benefits. Recent expert consensus therefore supports individualized dietary approaches that emphasize whole grains, vegetables, fruits, legumes, and other minimally processed carbohydrate sources while reducing added sugars and ultra-processed foods. This distinction is particularly relevant when comparing Mediterranean, low-carbohydrate, and ketogenic diets because the metabolic consequences of carbohydrate reduction depend substantially on the foods used as replacements. (Silva et al., 2020).

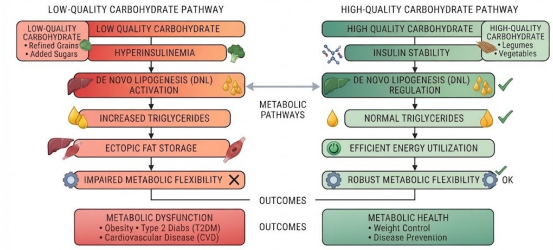


Figure 2. Pathways Linking Carbohydrate Quality, De Novo Lipogenesis (DNL), and Metabolic Flexibility: Comparing Downstream Health Outcomes

2.4 Inflammation, Oxidative Stress, and Progression from Steatosis to MASH

Simple hepatic steatosis does not inevitably progress to steatohepatitis or fibrosis. Progression is influenced by the interaction of metabolic stress, oxidative injury, inflammatory signaling, hepatocyte dysfunction, and individual susceptibility. Excessive lipid accumulation can increase mitochondrial stress and reactive oxygen species generation, while lipid-derived signaling molecules may activate inflammatory pathways and promote cellular injury. Chronic low-grade systemic inflammation associated with visceral adiposity can further amplify hepatic inflammatory responses. Dietary quality may influence these processes through the availability of antioxidant compounds, polyphenols, fiber, unsaturated fatty acids, and other bioactive components. The Mediterranean diet is particularly relevant in this context because its high intake of plant foods, extra-virgin olive oil, nuts, legumes, and fish provides a broad spectrum of potentially anti-inflammatory and antioxidant nutrients. However, evidence linking specific dietary components directly to histological reversal of MASH remains less robust than evidence for improvements in body weight and hepatic steatosis, highlighting the need for longer and better-controlled clinical trials. (Janssen, 2021).

2.5 The Gut–Liver Axis as a Nutritional Target

The gut–liver axis has become an increasingly important component of MASLD pathophysiology. Dietary patterns can influence intestinal microbial composition, microbial metabolites, bile-acid signaling, intestinal barrier integrity, and the transport of microbial products to the liver through the portal circulation. Alterations in these pathways may contribute to hepatic inflammation and metabolic dysfunction, whereas diets rich in fiber and diverse plant foods may support a more favorable microbial environment. Fermentable dietary fibers can increase the production of short-chain fatty acids, which may influence glucose and lipid metabolism, appetite regulation, intestinal integrity, and immune responses. These mechanisms provide another potential explanation for the favorable metabolic effects associated with Mediterranean-style dietary patterns. Nevertheless, the gut microbiome remains highly individualized, and the extent to which microbiota changes mediate clinical improvements in MASLD remains an active area of investigation rather than an established therapeutic endpoint. (Brugts et al., 2010).

2.6 Nutritional Targets for Therapeutic Intervention

The complex pathophysiology of metabolic dysfunction-associated steatotic liver disease (MASLD) indicates that successful dietary interventions must adopt a multi-targeted approach rather than focusing on a single isolated metabolic pathway. Below is an academic overview of the core nutritional targets and clinical recommendations in Table 1)

Table 1. Nutritional targets and clinical recommendations for the therapeutic management of MASLD.

Nutritional Target	Description and Clinical Rationale
Energy Intake and Weight Management	Reducing excessive energy intake and promoting clinically appropriate, gradual, and sustainable weight loss to improve hepatic and metabolic outcomes.
Insulin Sensitivity	Improving systemic insulin sensitivity to address a key component of the metabolic dysfunction underlying MASLD.
Hepatic De Novo Lipogenesis (DNL)	Reducing excessive hepatic de novo lipogenesis to limit intrahepatic fat accumulation and improve hepatic metabolic function.
Dietary Quality and Fat Intake	Improving overall dietary quality by emphasizing unsaturated fats and adopting dietary patterns such as the Mediterranean or DASH diet.
Dietary Fiber and Plant-Based Foods	Increasing the intake of dietary fiber and minimally processed plant-based foods to support metabolic health and overall diet quality.

Nutritional Target	Description and Clinical Rationale
Added Sugars and Ultra-Processed Foods	Limiting added sugars, sugar-sweetened foods and beverages, and ultra-processed foods that may contribute to excess energy intake and metabolic dysfunction.
Cardiometabolic Health	Improving overall cardiometabolic health by addressing body weight, glycemic control, blood lipids, blood pressure, and other metabolic risk factors in accordance with contemporary clinical guidelines.
Individualized Dietary Approaches	Tailoring dietary interventions according to individual metabolic characteristics, nutritional needs, preferences, comorbidities, and the likelihood of long-term adherence, including personalized energy restriction or carbohydrate/protein modification when appropriate.

. (EASL–EASD–EASO, 2024)

2.7 From Pathophysiology to Dietary Strategy Selection

The mechanistic diversity of MASLD explains why no single dietary strategy is likely to be optimal for every patient. A Mediterranean diet primarily modifies dietary quality and overall metabolic health, whereas low-carbohydrate and ketogenic approaches emphasize macronutrient redistribution and reduced carbohydrate availability. Time-restricted eating introduces a different therapeutic dimension by modifying the timing and duration of food intake. These approaches may converge on several common metabolic pathways, including reduced energy intake, improved insulin sensitivity, decreased hepatic lipid availability, and enhanced metabolic flexibility, but they may achieve these effects through different mechanisms and with different degrees of dietary restriction. Therefore, comparison of these strategies should extend beyond changes in body weight and include hepatic fat, liver enzymes, insulin resistance, lipid metabolism, inflammatory markers, adherence, safety, and long-term sustainability. This comparative framework is particularly important because recent evidence suggests that different dietary interventions can produce improvements in MASLD-related outcomes, while the magnitude and consistency of benefit vary according to the intervention and study design. (Palumbo et al., 2026).

3. Mediterranean Dietary Pattern

The Mediterranean diet is currently one of the most extensively studied dietary patterns for MASLD and is characterized by a high intake of vegetables, fruits, legumes, whole grains, nuts, seeds, and olive oil; regular consumption of fish and seafood; moderate intake of dairy products and poultry; and relatively low consumption of red and processed meat, refined carbohydrates, and highly processed foods. Rather than representing a rigid macronutrient prescription, the Mediterranean diet is best understood as an overall dietary pattern emphasizing food quality, plant diversity, unsaturated fat, and minimally processed foods. This

characteristic makes it particularly compatible with contemporary MASLD recommendations, which emphasize sustainable dietary quality and cardiometabolic risk reduction in addition to weight management. (Hamamah et al., 2024). The potential benefits of the Mediterranean diet in MASLD are likely to arise from several interacting mechanisms. High intake of monounsaturated fatty acids, particularly from olive oil, together with omega-3-rich foods such as fish, may improve lipid metabolism and reduce the adverse effects associated with saturated-fat-rich dietary patterns. Meanwhile, fruits, vegetables, legumes, whole grains, nuts, and seeds provide fiber, polyphenols, vitamins, minerals, and other bioactive compounds that may influence oxidative stress, inflammation, insulin sensitivity, and the gut microbiome. Thus, the potential hepatic benefit of the Mediterranean diet extends beyond simple calorie restriction and reflects the cumulative metabolic effects of multiple dietary components consumed within a coherent dietary pattern. (Pugliese et al., 2025). Clinical evidence generally supports a favorable effect of the Mediterranean dietary pattern on hepatic and metabolic outcomes, although the magnitude of benefit varies between studies. A 2024 systematic review and meta-analysis of randomized controlled trials comparing Mediterranean and low-fat diets found no significant difference between the two patterns in short-term improvements in liver enzymes or liver fat, suggesting that both may be effective when implemented within an energy-controlled dietary intervention. Importantly, this finding should not be interpreted as evidence that dietary composition is irrelevant; rather, it emphasizes the possibility that multiple healthy dietary patterns can improve MASLD when they successfully reduce energy excess and improve overall diet quality. (Jurek et al., 2025). More recent evidence further supports the Mediterranean diet while highlighting important research gaps. A systematic review and meta-analysis of randomized trials published in 2026 found significant improvements in ALT, liver stiffness, and MRI-derived proton-density fat fraction among participants receiving Mediterranean dietary interventions, although the authors emphasized the need for larger, longer, and more standardized trials. These findings strengthen the rationale for considering the Mediterranean diet as a core dietary strategy for MASLD while also demonstrating why comparisons with alternative dietary approaches are necessary. (2026 systematic review and meta-analysis). A particularly important advantage of the Mediterranean dietary pattern is its potential long-term sustainability. Unlike highly restrictive diets, the Mediterranean approach offers substantial dietary flexibility and can be adapted to different cultural food environments. Nevertheless, adherence outside Mediterranean populations may be challenging because the availability, affordability, cultural acceptance, and habitual consumption of key foods differ considerably across regions. Recent research has specifically emphasized the need to investigate how Mediterranean-style dietary interventions can be culturally adapted in non-Mediterranean countries while retaining their core nutritional characteristics. This issue is highly relevant to the implementation of MASLD dietary therapy at a population level. (Stern
et al., 2024).

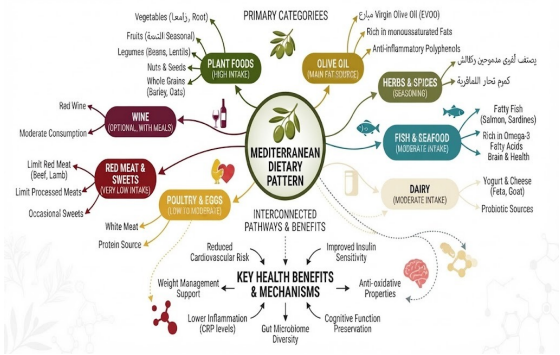


Figure 3. Mediterranean Dietary Pattern, illustrating its key food components, primary categories, and interconnected mechanisms for promoting health benefits.

4. Low-Carbohydrate Dietary Approaches

Low-carbohydrate diets (LCDs) have received increasing attention as a potential nutritional strategy for the management of metabolic dysfunction-associated steatotic liver disease (MASLD). Unlike the Mediterranean diet, which is primarily defined by overall food quality and dietary pattern, low-carbohydrate approaches are principally characterized by a reduction in carbohydrate intake, with the remaining energy supplied predominantly by fat and/or protein. However, the term low-carbohydrate diet encompasses a heterogeneous range of dietary prescriptions, and substantial differences exist among studies regarding the percentage of total energy derived from carbohydrates. This heterogeneity is important because the metabolic effects of a moderately carbohydrate-restricted diet may differ considerably from those of a very-low-carbohydrate or ketogenic regimen. Consequently, the clinical effects of LCDs should be interpreted according to both the degree of carbohydrate restriction and the nutritional quality of the foods used to replace carbohydrate. (Huang et al., 2024).

The rationale for carbohydrate restriction in MASLD is strongly linked to hepatic glucose and lipid metabolism. Reducing the intake of rapidly digestible carbohydrates and added sugars may decrease postprandial glucose and insulin excursions and potentially reduce hepatic de novo lipogenesis. Improved insulin sensitivity may also decrease adipose tissue lipolysis and consequently reduce the delivery of free fatty acids to the liver. In

addition, carbohydrate restriction may promote greater mobilization and oxidation of stored fatty acids, particularly when accompanied by an energy deficit. These mechanisms provide a biological basis for the potential reduction in hepatic fat observed with low-carbohydrate interventions. Nevertheless, the hepatic response is unlikely to depend exclusively on carbohydrate quantity, because the total energy intake, type of dietary fat, protein sources, fiber intake, and degree of weight loss can all influence metabolic outcomes. (Zeng et al., 2025).

Clinical evidence generally indicates that low-carbohydrate dietary interventions can improve several metabolic risk factors in individuals with MASLD. Recent systematic evidence has reported beneficial effects on body weight, glycemic parameters, triglyceride concentrations, and other cardiometabolic outcomes.. An important consideration is whether the apparent hepatic benefit of carbohydrate restriction is independent of weight loss. In many clinical trials, carbohydrate restriction is accompanied by spontaneous reductions in energy intake and body weight, making it difficult to determine whether the improvement in liver fat results specifically from reduced carbohydrate availability or from the resulting negative energy balance. This issue is particularly important when comparing LCDs with Mediterranean or low-fat diets. Current evidence suggests that several nutritionally distinct dietary patterns can improve MASLD when they successfully achieve sustained weight reduction and improve diet quality. Therefore, carbohydrate restriction should not automatically be interpreted as metabolically superior to other approaches simply because it produces rapid changes in body weight or insulin-related parameters. (Miao et al., 2024). The quality of carbohydrate replacement is another critical determinant of the clinical value of an LCD. Replacing refined carbohydrates with vegetables, legumes, nuts, seeds, fish, and unsaturated plant oils may produce a substantially different metabolic profile from replacing carbohydrates with large amounts of saturated fat or processed meat. This distinction is particularly relevant in MASLD because cardiovascular disease represents a major cause of morbidity and mortality in affected individuals. Recent evidence has therefore shifted the focus from carbohydrate quantity alone toward the overall nutritional composition of low-carbohydrate diets. An LCD designed around nutrient-dense foods and unsaturated fats may be more compatible with long-term cardiometabolic health than a carbohydrate-restricted pattern dominated by saturated fat and processed animal products. (Younossi et al., 2023). Recent comparative evidence also highlights the importance of distinguishing between low-carbohydrate diets and ketogenic diets. Although ketogenic diets fall within the broader spectrum of carbohydrate restriction, they impose a substantially greater reduction in carbohydrate availability and are intended to induce nutritional ketosis. Consequently, the metabolic adaptations associated with a ketogenic diet may not be extrapolated directly from evidence obtained using moderate LCDs. This distinction is essential for interpreting the literature and forms an important rationale for evaluating ketogenic diets as a separate dietary strategy in MASLD rather than combining all carbohydrate-restricted approaches into a single category. (Eslam et al., 2020). Overall, low-carbohydrate diets represent a potentially useful option for selected individuals with MASLD, particularly when carbohydrate restriction facilitates sustainable weight loss and improves insulin resistance and metabolic risk factors. However, current evidence does not establish a universally superior carbohydrate threshold or demonstrate that carbohydrate restriction independently provides greater long-term hepatic benefit than other high-quality dietary patterns. Future trials should use standardized carbohydrate definitions, control for energy intake, characterize the quality of replacement nutrients, and employ sensitive measures of hepatic fat and fibrosis. Longer-term studies are also required to determine whether the metabolic improvements associated with LCDs translate into clinically meaningful reductions in MASH progression and fibrosis. (Rinella et al., 2023).

5. Ketogenic Diet

The ketogenic diet (KD) represents a more restrictive form of carbohydrate reduction and is characterized by very low carbohydrate availability, moderate protein intake, and a relatively high proportion of dietary energy from fat. Severe carbohydrate restriction promotes a metabolic transition from predominantly glucose-based energy utilization toward increased fatty-acid oxidation and hepatic ketogenesis. The resulting ketone bodies including β-hydroxybutyrate, acetoacetate, and acetone serve as alternative energy substrates for extrahepatic tissues. This metabolic transition has generated considerable interest in MASLD because it may influence insulin sensitivity, hepatic lipid metabolism, energy expenditure, and substrate utilization. Nevertheless, the potential advantages of nutritional ketosis must be distinguished from the well-established effects of overall energy restriction and weight loss. (Duell et al., 2023). One proposed mechanism underlying the potential effects of ketogenic diets in MASLD is the rapid reduction in insulin secretion and hepatic carbohydrate availability. Lower insulin signaling may suppress lipogenic pathways, while increased fatty-acid mobilization and oxidation may facilitate the utilization of stored energy. Nutritional ketosis may also alter mitochondrial substrate utilization and

signaling pathways associated with metabolic adaptation. These mechanisms provide a plausible explanation for the rapid reductions in body weight and some metabolic parameters reported in ketogenic-diet studies. However, mechanistic plausibility alone does not establish a disease-modifying effect on MASH or fibrosis, and the available clinical evidence remains considerably less extensive than that supporting general lifestyle modification and Mediterranean-style dietary patterns. (Lee et al ., 2020). Clinical trials evaluating ketogenic diets in MASLD have produced encouraging but heterogeneous findings. Some studies have reported reductions in body weight and hepatic fat following ketogenic interventions, whereas others have shown that improvements in liver outcomes are broadly comparable to those achieved with alternative calorie-restricted diets. Recent evidence is particularly important because it challenges the assumption that nutritional ketosis necessarily produces a liver-specific benefit beyond weight loss. A recent randomized controlled trial comparing a ketogenic intervention with a DASH-based approach demonstrated substantially greater weight reduction in the ketogenic group but did not establish a significant between-group advantage in liver stiffness or steatosis. These findings indicate that rapid weight loss should not be equated automatically with superior hepatic efficacy. (Chirapongsathorn et al., 2025). A further issue concerns the long-term nutritional quality and safety of ketogenic diets. Because carbohydrate-containing foods are substantially restricted, individuals may consume fewer whole grains, legumes, fruits, and certain vegetables unless the diet is carefully formulated. Conversely, poorly designed ketogenic diets may contain excessive saturated fat and processed meat, potentially creating an unfavorable cardiovascular risk profile. This consideration is especially important in MASLD because cardiovascular disease is a major component of overall disease burden. Therefore, if ketogenic diets are used clinically, emphasis should be placed on nutrient density and the selection of unsaturated fat sources rather than simply maximizing dietary fat intake. (Holmer et al., 2021). Adherence represents another major determinant of ketogenic-diet effectiveness. The substantial restriction of bread, grains, many fruits, legumes, and other carbohydrate-containing foods can make long-term adherence challenging for some individuals. In contrast, individuals who prefer clearly defined dietary rules may find carbohydrate restriction easier to follow than calorie counting. Thus, adherence is likely to be highly individualized and may depend on food preferences, cultural dietary practices, socioeconomic factors, metabolic phenotype, and the availability of appropriate dietary counseling. The most appropriate dietary intervention should therefore be selected according to both metabolic objectives and the individual's ability to sustain the dietary pattern over time. (Gepner et al., 2019). Overall, ketogenic diets should be regarded as a potentially effective but more restrictive dietary option, rather than a universally preferred treatment for MASLD. Their strongest potential may lie in facilitating substantial weight loss and improving insulin resistance in selected individuals, while the evidence for independent effects on liver inflammation and fibrosis remains insufficient. Future randomized trials should directly compare ketogenic diets with Mediterranean and other carbohydrate-restricted diets under isocaloric conditions and should include MRI-based hepatic fat measurements, elastography, metabolic biomarkers, adverse events, and long-term adherence. (Cunha et al.,2020).

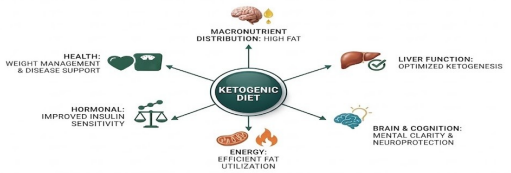


Figure 4. Overview of the Ketogenic Diet's metabolic pathways and health impacts, illustrating its effects on macronutrient distribution, liver function, energy utilization, brain health, hormonal balance, and overall health support.

6. Time-Restricted Eating

Time-restricted eating (TRE) represents a fundamentally different nutritional strategy because it modifies the timing of food consumption rather than prescribing a specific macronutrient composition. TRE typically confines daily caloric intake to a consistent eating window while extending the fasting period, commonly involving an eating window of approximately 6–10 hours. Unlike alternate-day fasting or periodic prolonged fasting, TRE is generally practiced every day and does not necessarily require substantial restriction of specific food groups. Its increasing popularity in metabolic disease has stimulated interest in whether manipulation of meal timing can provide additional benefits beyond conventional calorie restriction. (Rosenbaum et al., 2019). The biological rationale for TRE extends beyond simple caloric restriction. Prolonged daily fasting may increase the time spent in a relatively low-insulin metabolic state and promote a transition from nutrient storage toward mobilization and oxidation of endogenous energy substrates. Meal timing may also interact with circadian rhythms that regulate glucose metabolism, insulin sensitivity, lipid metabolism, hepatic clock-gene activity, and energy expenditure. Early TRE, in which the eating window is shifted toward earlier hours of the day, may therefore have different metabolic effects from late TRE despite similar fasting durations. Recent network meta-analytic evidence involving 41 randomized trials suggests

that both the timing and duration of the eating window may influence metabolic outcomes, supporting the concept that "when" food is consumed may be relevant to metabolic health. (Younossi et al ., 2016). Evidence specifically addressing TRE in fatty liver disease is promising but remains less mature than the evidence for Mediterranean dietary patterns. A systematic review of randomized controlled trials in patients with NAFLD identified four trials involving 443 participants, with interventions generally using an 8-hour eating window for periods ranging from four weeks to 12 months. The available evidence suggested improvements in several metabolic and liver-related outcomes, including intrahepatic triglyceride content and liver stiffness. However, substantial variation in study populations, intervention duration, and outcome assessment limits definitive conclusions. The authors therefore considered TRE promising but concluded that the evidence was not yet sufficient to recommend it as a standard dietary treatment for fatty liver disease. (Hagstrom et al., 2017).

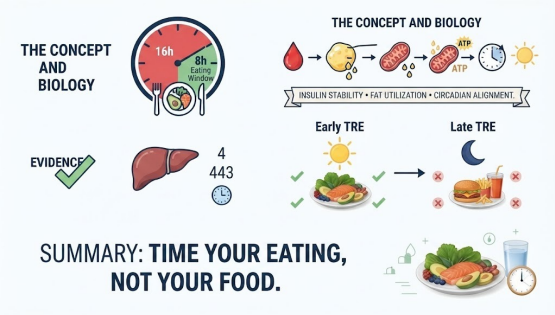


Figure 5. Time-Restricted Eating (TRE): Mechanisms, Clinical Evidence, and Practical Guidelines.

A major question is whether TRE provides benefits beyond those attributable to reduced energy intake. This issue is critical because restricting the daily eating window may naturally reduce the number of eating occasions and consequently decrease total energy consumption. A systematic review of randomized trials comparing calorie restriction plus TRE with calorie restriction alone found mixed results: some trials demonstrated greater weight loss or metabolic benefits with TRE, whereas others did not identify meaningful additional effects. These findings suggest that TRE may be particularly useful as a behavioral framework for facilitating adherence to energy restriction, but they do not yet establish that fasting duration itself produces a consistent liver-specific effect independent of calorie reduction. (Luci et al., 2020).

More recent evidence provides additional support for fasting-based approaches in MASLD while simultaneously emphasizing their limitations. A 2026 systematic review and meta-analysis of randomized controlled trials reported that fasting interventions were associated with reductions in ALT and liver stiffness compared with control interventions. However, the same synthesis found that low-carbohydrate/ketogenic diets did not significantly alter ALT, whereas Mediterranean dietary interventions produced significant improvements in ALT, liver stiffness, and MRI-derived hepatic fat fraction. These findings are particularly relevant to the present review because they suggest that fasting and Mediterranean strategies may influence hepatic biomarkers through somewhat different pathways.

Time-restricted eating may also offer practical advantages because it does not necessarily require patients to eliminate specific foods. This flexibility can make the strategy attractive to individuals who find macronutrient restriction difficult to sustain. Nevertheless, the feasibility of maintaining a consistent eating window may be influenced by work schedules, social meals, family routines, sleep patterns, and cultural practices. Early eating windows may theoretically offer greater circadian alignment, but they may also be socially difficult for some patients. Consequently, successful implementation of TRE requires consideration of both metabolic timing and real-world lifestyle constraints. (Abuelazm et al., 2024). Overall, TRE should currently be considered a promising behavioral and metabolic strategy rather than an established stand-alone treatment for MASLD. The available evidence supports potential reductions in body weight and selected hepatic and metabolic biomarkers, but the extent to which these effects are independent of calorie reduction remains uncertain. Future trials should compare early, mid-day, and late eating windows; standardize fasting duration; control for energy and macronutrient intake; and incorporate objective measures of liver fat and fibrosis. Such studies will be essential to determine whether meal timing represents an independent therapeutic target or primarily an alternative method for achieving sustainable energy restriction. (Rinella et al., 2023).

7. Comparative Perspective: Four Dietary Strategies and Their Potential Roles in MASLD

Table 2 summarizes the main dietary strategies currently considered in the management of metabolic dysfunction-associated steatotic liver disease (MASLD). The Mediterranean diet primarily targets overall dietary quality and cardiometabolic health and is supported by evidence for improving hepatic steatosis and metabolic parameters. Low-carbohydrate diets may benefit body weight, glycemic control, triglyceride levels, and hepatic fat, particularly in patients with obesity or insulin resistance, although effects on liver enzymes remain inconsistent. Ketogenic diets may promote weight loss and reductions in hepatic fat through nutritional ketosis; however, their long-term efficacy and sustainability require further investigation. Time-restricted eating focuses on

meal timing and fasting duration and may improve body weight, metabolic health, and selected liver-related outcomes. Overall, as shown in **Table 2**, dietary selection should be individualized according to metabolic characteristics, preferences, and the likelihood of long-term adherence(Kord et al ., 2023).

Table 2. Comparison of Dietary Strategies for the Management of Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD)

Dietary Strategy	Primary Target	Key Evidence	Clinical Application
Mediterranean Diet	Dietary quality and cardiometabolic health	Improves hepatic steatosis, metabolic parameters, and liver-related outcomes.	Preferred for comprehensive, sustainable long-term management.
Low-Carbohydrate Diet	Carbohydrate restriction and metabolic control	May improve weight, glycemic control, triglycerides, and hepatic fat; effects on ALT are inconsistent.	Useful for selected patients with obesity, insulin resistance, or dysglycemia.
Ketogenic Diet	Nutritional ketosis and weight reduction	May reduce body weight and hepatic fat, but long-term evidence remains limited.	Consider for selected patients able to maintain strict carbohydrate restriction.
Time-Restric	Meal timing and	May improve	Suitable for patients

Dietary Strategy	Primary Target	Key Evidence	Clinical Application
ted Eating	fasting duration	weight, metabolic health, and selected liver outcomes.	who prefer modifying meal timing rather than food composition.
Dietary Strategy	**Primary Target**	**Key Evidence**	**Clinical Application**

MASLD, metabolic dysfunction–associated steatotic liver disease. Dietary interventions should be individualized according to patient characteristics, metabolic comorbidities, nutritional status, treatment goals, and long-term adherence. The strength of evidence and long-term effects vary among dietary strategies.

Discussion

Managing metabolic dysfunction-associated steatotic liver disease (MASLD) requires a comprehensive understanding of the complex metabolic mechanisms underlying hepatic fat accumulation and disease progression. Although lifestyle modification and weight reduction remain the cornerstone of MASLD management, the metabolic effects of different dietary patterns may extend beyond their influence on total energy intake. Dietary composition can modify hepatic substrate availability, insulin signaling, de novo lipogenesis (DNL), fatty acid oxidation, adipose tissue lipolysis, and systemic inflammatory pathways. Consequently, the clinical effects of dietary interventions should be interpreted not only in terms of weight loss but also in relation to the quality and metabolic characteristics of the diet.

Hepatic steatosis develops when the influx and synthesis of fatty acids within the liver exceed the capacity for fatty acid oxidation and triglyceride export. Insulin resistance plays a central role in this process by increasing adipose tissue lipolysis and the delivery of non-esterified fatty acids to the liver, while hyperinsulinemia and increased carbohydrate availability can stimulate hepatic DNL. Experimental and clinical evidence indicates that DNL contributes substantially to hepatic triglyceride accumulation in individuals with fatty liver disease. Therefore, interventions capable of improving insulin sensitivity, reducing excessive free-sugar intake, and modifying hepatic substrate flux may theoretically exert beneficial effects on hepatic steatosis independently of, or in addition to, weight reduction.

The importance of dietary carbohydrate quality is particularly relevant in this context. Excessive consumption of free sugars, especially rapidly absorbable carbohydrates, may promote hepatic lipogenesis through increased substrate availability and insulin-mediated activation of lipogenic pathways. In a randomized controlled trial involving adolescent boys with fatty liver disease, restriction of dietary free sugars for eight weeks significantly reduced hepatic DNL and hepatic fat content (Dalibalta et al., 2021). The reduction in DNL was accompanied by improvements in hepatic steatosis, supporting the biological plausibility of reducing excessive free-sugar intake as part of nutritional management. However, these findings should not be interpreted as evidence that all carbohydrates are detrimental, because the metabolic effects of carbohydrates vary substantially according to their source, fiber content, degree of processing, and glycemic characteristics.

Accordingly, the physiological rationale for dietary treatment of MASLD should move beyond a simple dichotomy between "high-carbohydrate" and "low-carbohydrate" diets. A more clinically meaningful distinction is between dietary patterns characterized by high consumption of refined carbohydrates, free sugars, saturated fats, and ultra-processed foods and patterns emphasizing minimally processed foods, fiber, unsaturated fatty acids, vegetables, fruits, legumes, whole grains, nuts, and fish. This distinction is consistent with contemporary clinical guidelines, which emphasize overall dietary quality and sustainability rather than prescribing a single macronutrient distribution for all patients with MASLD (Eshraghian et al., 2017).

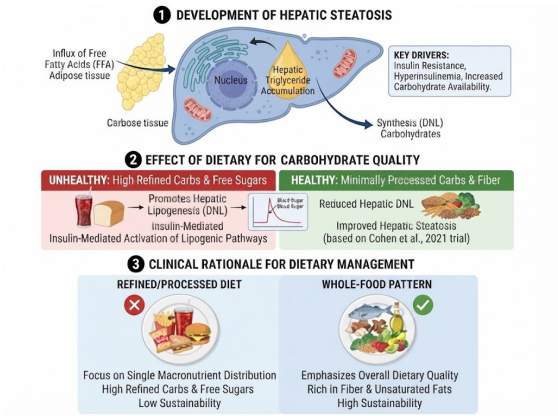


Figure 6. Physiological mechanisms of hepatic steatosis development, the impact of dietary carbohydrate quality and de novo lipogenesis, and the clinical rationale for whole-food dietary patterns in the management of MASLD.

Among the dietary patterns investigated in MASLD, the Mediterranean diet has received considerable attention because of its favorable effects on metabolic and cardiovascular health in addition to its potential hepatic benefits. The Mediterranean dietary pattern is characterized by a high intake of vegetables, fruits, legumes, whole grains, nuts, seeds, fish, and olive oil, together with relatively low consumption of processed foods, refined carbohydrates, processed meat, and foods rich in saturated fat.

The potential hepatic benefits of the Mediterranean diet are biologically plausible because several of its components may simultaneously influence multiple pathways involved in MASLD. The predominance of monounsaturated and polyunsaturated fatty acids, particularly from olive oil, nuts, seeds, and fish, may favor a more metabolically favorable lipid profile than diets characterized by high saturated-fat intake. Furthermore, dietary fiber and plant-derived bioactive compounds may influence insulin sensitivity, oxidative stress, inflammatory signaling, and the gut–liver axis. These mechanisms provide a plausible explanation for why the Mediterranean diet may improve metabolic health even when weight reduction is relatively modest.

Clinical evidence generally supports these observations. A systematic review and meta-analysis of six randomized controlled trials involving 250 participants found that Mediterranean dietary interventions significantly reduced the fatty liver index and improved HOMA-IR compared with control diets, without significant differences in body mass index or waist circumference between groups (Sarwar et al., 2018). These findings suggest that at least part of the metabolic benefit of the Mediterranean diet may not be explained solely by changes in body weight.

Similarly, a systematic review and meta-analysis of dietary interventions reported that Mediterranean dietary interventions without deliberate energy restriction were associated with significant reductions in intrahepatic lipid content, although effects on liver enzymes were less consistent (Younossi et al., 2016). This distinction is important because hepatic fat accumulation is only one component of MASLD, and reductions in steatosis do not necessarily translate into equivalent improvements in steatohepatitis or fibrosis. The limited availability of adequately powered studies assessing histological endpoints remains an important limitation in the current evidence base.

The Mediterranean diet may therefore be particularly attractive clinically because it combines potential liver-specific benefits with established benefits for cardiovascular risk factors. This is relevant because cardiovascular disease represents a major cause of morbidity and mortality among individuals with MASLD. Consequently, a dietary pattern should not be evaluated solely according to its ability to reduce hepatic fat but also according to its effects on obesity, insulin resistance, dyslipidemia, hypertension, and overall cardiovascular risk.

Nevertheless, it would be inappropriate to conclude that the Mediterranean diet has a universally superior effect compared with all alternative dietary approaches. A recent meta-analysis comparing Mediterranean and low-fat dietary interventions found broadly similar short-term effects on liver enzymes and liver fat, suggesting that several nutritionally appropriate dietary patterns may be effective when they successfully improve overall dietary quality and energy balance (2024). Thus, the principal advantage of the Mediterranean diet may lie not in a unique macronutrient composition but in its combination of dietary quality, nutritional adequacy, metabolic benefits, and relatively high potential for long-term adherence.

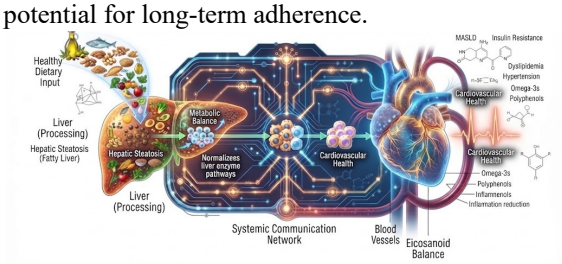


Figure 7 The metabolic intersection of the Mediterranean diet, linking potential liver-specific benefits with established cardiovascular risk reduction in individuals with MASLD.

Weight reduction remains the most consistently demonstrated nutritional determinant of improvement in MASLD. Importantly, the relationship between weight loss and hepatic outcomes appears to be dose-dependent. Evidence from histological studies demonstrates that greater weight loss is associated with greater improvements in steatosis, lobular inflammation, hepatocellular ballooning, and, in some patients, fibrosis.

In a prospective study of 293 patients with biopsy-proven NASH, (Kudaravalli and John, 2023)

demonstrated a clear association between the magnitude of weight loss and histological improvement. Among participants who achieved at least 10% weight loss, 90% experienced resolution of NASH and 45% demonstrated fibrosis regression. Even more modest weight loss was associated with clinically meaningful improvements, supporting the concept that weight reduction is a central therapeutic target rather than simply a secondary outcome of dietary intervention.

These findings are consistent with randomized lifestyle-intervention studies. Promrat et al. (2010) reported that an intensive lifestyle intervention targeting 7–10% weight reduction resulted in substantially greater improvement in histological disease activity than structured education alone. Participants who achieved the prescribed weight-loss target demonstrated improvements in steatosis, inflammation, hepatocellular ballooning, and overall NAFLD activity score (Kord et al., 2022).

An important question, however, is whether macronutrient composition provides additional hepatic benefits when weight loss is similar. Low-carbohydrate and ketogenic diets have attracted considerable attention because carbohydrate restriction can reduce insulin secretion, increase fatty acid oxidation, and reduce the availability of substrates for DNL. These mechanisms may produce relatively rapid reductions in hepatic glycogen and triglyceride stores. Clinical studies provide some support for these metabolic effects but do not establish consistent superiority over other calorie-restricted dietary patterns. In a randomized controlled trial, (Xiao et al. 2022) found that both a low-carbohydrate high-fat diet and intermittent calorie restriction reduced hepatic steatosis more effectively than standard lifestyle advice. However, both interventions also produced substantial weight loss, making it difficult to determine whether the observed hepatic benefits resulted specifically from macronutrient composition or primarily from energy restriction and associated weight reduction.

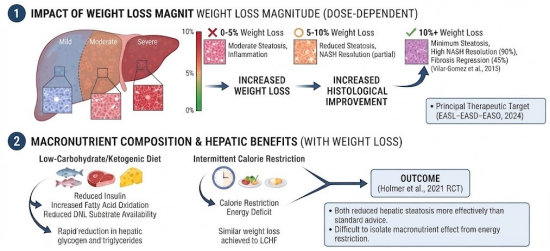


Figure 8 The dose-dependent impact of weight reduction on histological improvement in MASLD alongside the comparative effects of macronutrient composition and energy restriction.

Similarly, a controlled feeding study comparing a hypocaloric ketogenic diet with an energy-matched low-fat diet found that liver fat decreased significantly following the intervention, but there was no significant difference between the dietary groups despite similar weight loss (Wei et al., 2023). These findings argue against the assumption that nutritional ketosis necessarily provides an additional liver-specific benefit when caloric intake and weight loss are comparable.

Therefore, the available evidence supports a more cautious interpretation. Carbohydrate restriction may be an effective dietary strategy for selected patients, particularly when it facilitates reduction in energy intake, improves glycemic control, or reduces consumption of refined carbohydrates and free sugars. However, the current evidence does not establish ketogenic diets as universally superior to Mediterranean or other nutritionally balanced approaches.

Time-restricted eating (TRE) represents a different nutritional strategy because it modifies the timing of food intake rather than primarily altering macronutrient composition. The potential metabolic rationale for TRE is based on the interaction between feeding behavior and circadian biology. Meal timing can influence daily patterns of glucose tolerance, insulin secretion, substrate oxidation, and energy metabolism. Restricting food intake to a defined daily window may also reduce opportunities for excessive caloric intake and prolong the physiological fasting period.

The theoretical metabolic benefits of TRE are therefore potentially mediated through both behavioral and biological mechanisms. From a behavioral perspective, shortening the eating window may spontaneously reduce caloric intake. From a physiological perspective, aligning food intake with circadian rhythms may influence glucose and lipid metabolism. However, distinguishing the independent effect of meal timing from the effect of reduced energy intake remains challenging. The TREATY-FLD randomized clinical trial provides important evidence in this regard. (Chaix et al. 2019) compared an 8-hour time-restricted eating regimen with daily calorie restriction in adults with obesity and NAFLD over 12 months. Both interventions were designed to provide a similar caloric target, and the investigators found that TRE did not produce a significant additional reduction in intrahepatic triglyceride content compared with conventional daily calorie restriction. These findings suggest that, when caloric restriction is already achieved, restricting the timing of food intake may not confer a substantial additional reduction in hepatic fat. Nevertheless, TRE should not be regarded as ineffective. Its principal clinical value may be behavioral rather than pharmacological. Some individuals may find it easier to follow a defined eating window than to continuously count calories or calculate macronutrient intake. Therefore, TRE may serve as an alternative strategy for facilitating energy restriction in patients who prefer meal-timing interventions. Future studies should determine whether the timing of the eating window itself

particularly earlier versus later eating has independent effects on hepatic insulin sensitivity and liver fat.

An increasingly important consideration in MASLD is that macronutrient quantity alone does not adequately describe dietary quality. Two diets containing an identical proportion of carbohydrates may produce substantially different metabolic effects depending on whether carbohydrates are derived predominantly from whole grains, legumes, vegetables, and fruits or from sugar-sweetened beverages, refined grains, confectionery, and other ultra-processed foods.

This distinction is particularly relevant to hepatic DNL. (Abuelazm et al. 2024) demonstrated that restricting free sugars in adolescents with fatty liver disease resulted in a marked reduction in hepatic DNL and hepatic fat within only eight weeks. Although the study population was relatively young and predominantly male, the findings provide mechanistic evidence supporting the reduction of excessive free-sugar intake as a relevant component of dietary management.

Accordingly, nutritional recommendations for MASLD should emphasize reducing sugar-sweetened beverages, foods high in added sugars, refined carbohydrates, and ultra-processed foods rather than simply prescribing a low-carbohydrate diet. This approach allows patients to retain nutrient-dense carbohydrate sources while reducing the dietary components most strongly associated with adverse metabolic outcomes.

The Mediterranean diet naturally incorporates many of these principles and may therefore represent a practical framework for improving dietary quality. However, similar principles can also be incorporated into other dietary patterns. Thus, the therapeutic objective should be to establish a nutritionally adequate and sustainable dietary pattern characterized by high consumption of minimally processed foods, adequate dietary fiber, predominantly unsaturated fats, and limited intake of free sugars and ultra-processed foods.

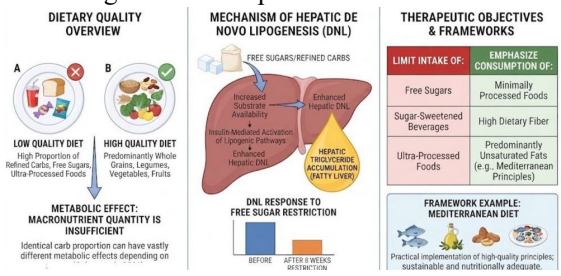


Figure 9 Dietary quality overview, mechanisms of hepatic de novo lipogenesis (DNL) in response to free-sugar restriction, and therapeutic objectives emphasizing whole-food dietary patterns in the management of MASLD.

The effectiveness of any dietary intervention in MASLD ultimately depends on long-term adherence. A dietary pattern that produces substantial short-term metabolic improvements but is difficult to maintain may have limited real-world effectiveness. This issue is particularly important because MASLD is a chronic metabolic condition that requires sustained behavioral modification rather than a short-term intervention. The Mediterranean diet may have an advantage in this regard because it does not require complete exclusion of major food groups and can be adapted to different cultural and culinary environments. Low-carbohydrate and ketogenic diets may also be successful in selected individuals, particularly when carbohydrate restriction improves appetite control or glycemic regulation. However, their long-term sustainability and nutritional adequacy require individualized assessment (Cai et al ., 2019)

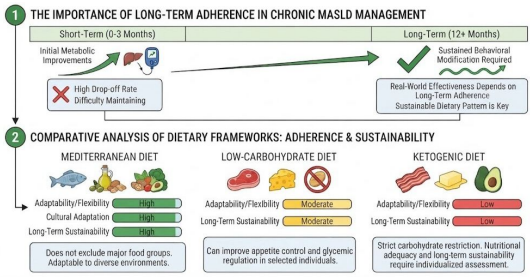


Figure 10. Behavioral adherence, flexibility, and long-term sustainability of the Mediterranean diet compared with low-carbohydrate and ketogenic dietary frameworks in chronic MASLD management.

Similarly, TRE may improve adherence among individuals who prefer a structured meal schedule. However, its feasibility may be influenced by occupational schedules, social activities, family eating patterns, cultural practices, and medication requirements. Consequently, adherence should be regarded as a core determinant of dietary effectiveness rather than a secondary consideration.

This concept supports the current clinical approach of individualized nutritional counseling. The EASL–EASD–EASO guidelines emphasize lifestyle modification as a central component of MASLD management and support dietary interventions that can be sustained over time while addressing obesity and associated metabolic comorbidities (Holmer et al , 2021).

Personalized Nutrition in MASLD

The heterogeneity of MASLD provides a strong rationale for individualized dietary management. Patients may differ substantially in obesity severity, insulin resistance, type 2 diabetes, dyslipidemia, hypertension, dietary preferences, socioeconomic circumstances, and stage of liver disease. Consequently, a universal dietary prescription is unlikely to provide optimal outcomes for every patient. For example, a Mediterranean-style diet may be particularly appropriate for individuals with multiple cardiovascular risk factors because of its favorable overall dietary composition. A lower-carbohydrate strategy may be considered for patients

with substantial intake of refined carbohydrates or difficulty controlling glycemia, provided that carbohydrate restriction does not result in excessive consumption of saturated fat or nutritionally poor foods. TRE may be considered for individuals who find meal scheduling more sustainable than continuous calorie counting. Importantly, dietary treatment should be integrated into a broader multidisciplinary approach. Management of MASLD should address physical activity, body weight, type 2 diabetes, dyslipidemia, hypertension, and other cardiometabolic risk factors. Current guidelines recommend lifestyle modification, including dietary change and physical activity, as a fundamental component of management (Johari et al ., 2021). This personalized approach is particularly important when MASLD progresses from isolated steatosis to MASH and clinically significant fibrosis. In patients with advanced fibrosis, dietary intervention remains important but should be incorporated into specialist hepatology care and appropriate fibrosis risk stratification. Therefore, nutritional management should be viewed as part of a comprehensive disease-management strategy rather than as an isolated treatment.

Limitations of the Current Evidence

- Despite the growing literature on dietary treatment of MASLD, several limitations should be considered when interpreting the current evidence. First, many dietary trials have relatively short follow-up periods and include small sample sizes. This limits the ability to assess long-term adherence and clinically important outcomes such as progression to cirrhosis, hepatocellular carcinoma, liver-related mortality, and cardiovascular events.
- Second, a substantial proportion of studies evaluate hepatic steatosis using imaging or biochemical markers rather than paired liver biopsies. Although magnetic resonance-based measurements of liver fat provide valuable non-invasive information, a reduction in hepatic steatosis does not necessarily indicate resolution of MASH or regression of fibrosis. Consequently, dietary interventions should not be considered equivalent simply because they produce similar short-term reductions in liver fat.
- Third, disentangling the effects of diet composition from the effects of weight loss remains a major methodological challenge. Many dietary interventions produce simultaneous reductions in energy intake, body weight, visceral adiposity, and carbohydrate or fat intake. As a result, an observed improvement cannot always be attributed to one nutritional component.
- Fourth, adherence varies substantially between studies and individuals. Self-reported dietary intake may introduce measurement error, while differences in counseling intensity and behavioral support may influence outcomes independently of the assigned dietary pattern. Future randomized trials should therefore incorporate objective measures of dietary adherence whenever possible and provide standardized behavioral support across intervention groups.

Finally, relatively few large-scale trials have directly compared multiple dietary strategies while achieving equivalent weight loss and controlling for physical activity. Such studies are necessary to determine whether specific dietary compositions exert clinically meaningful effects independent of energy restriction.

Future Research Directions

Future research should prioritize adequately powered, long-duration randomized controlled trials comparing Mediterranean, low-carbohydrate, ketogenic, and time-restricted eating approaches under carefully controlled energy conditions. Such studies should distinguish between the effects of dietary composition, meal timing, and weight loss rather than evaluating these factors simultaneously. Mechanistic studies should also incorporate direct assessment of hepatic DNL, insulin sensitivity, fatty acid oxidation, adipose tissue lipolysis, and circulating inflammatory markers. In addition, the interaction between dietary interventions and the gut microbiome, genetic susceptibility, sex, age, and baseline metabolic phenotype warrants further investigation.

Importantly, future trials should include clinically meaningful liver outcomes. Where ethically and practically appropriate, paired histological assessment should be incorporated to determine whether dietary interventions can induce resolution of MASH or regression of fibrosis rather than simply reducing hepatic fat. Non-invasive markers of fibrosis, including elastography and validated fibrosis scores, should also be systematically incorporated.

Another important research priority is the identification of patient characteristics that predict response to individual dietary strategies. Rather than asking whether one diet is universally superior, future research should aim to determine which dietary pattern is most effective for a particular metabolic phenotype. This approach could ultimately facilitate the development of precision nutrition algorithms for MASLD.

8. Conclusion and Future Directions

Metabolic dysfunction-associated steatotic liver disease represents a complex, multi-system disorder whose management relies heavily on targeted nutritional and lifestyle modifications. As

demonstrated through the comparative evaluation of the Mediterranean diet, low-carbohydrate regimens, ketogenic approaches, and time-restricted eating, no single dietary strategy exhibits universal superiority across all clinical phenotypes. While Mediterranean-style eating offers robust long-term cardiovascular and metabolic benefits, carbohydrate-restricted and time-restricted frameworks provide rapid improvements in glycemic control and insulin sensitivity, often mediated by reductions in energy intake and body weight. However, differences in study durations, patient adherence, and individual metabolic flexibility highlight the limitations of applying generalized dietary prescriptions to a heterogeneous patient population. Future clinical research must prioritize large-scale, long-term randomized controlled trials that directly compare these dietary patterns while utilizing standardized, non-invasive or histological assessments of hepatic steatosis, inflammation, and fibrosis. Investigating the independent mechanisms of meal timing versus macronutrient composition will further refine therapeutic precision. Ultimately, effective clinical management of MASLD requires a paradigm shift from rigid, short-term dietary restrictions toward personalized nutrition plans. By integrating dietary quality, sustainable weight management, and patient-specific preferences and comorbidities, clinicians can optimize long-term adherence and improve comprehensive liver-related and cardiometabolic outcomes.

9. Recommendations

- **Adopt Individualized Dietary Frameworks:** Clinicians should avoid a one-size-fits-all prescription for metabolic dysfunction-associated steatotic liver disease (MASLD). Dietary interventions must be tailored to each patient's metabolic profile, baseline insulin resistance, body mass index, personal preferences, and long-term adherence capacity.
- **Prioritize Dietary Quality over Single Macronutrients:** Nutritional guidance should focus on whole, nutrient-dense foods such as extra-virgin olive oil, fresh vegetables, fruits, whole grains, legumes, and omega-3-rich fish while systematically minimizing ultra-processed items, added sugars, and refined carbohydrates, regardless of the chosen dietary pattern.
- **Integrate Sustainable Energy Balance and Weight Management:** Because weight reduction is a potent driver of hepatic fat loss and histological improvement, clinical strategies should emphasize gradual, sustainable caloric restriction rather than aggressive, short-term diets that carry a high risk of weight regain.
- **Combine Meal Timing and Macronutrient Strategies Carefully:** Healthcare providers can consider time-restricted eating as a practical, complementary tool to help patients spontaneously regulate energy intake and improve circadian metabolic alignment, provided it aligns with the patient's lifestyle and medication regimen (especially for those with type 2 diabetes).
- **Establish Multidisciplinary and Long-Term Monitoring:** Nutritional counseling for MASLD should be delivered within an ongoing multidisciplinary care model that utilizes non-invasive liver assessments (such as elastography or validated serum biomarkers) to track longitudinal changes in hepatic steatosis, metabolic health, and fibrosis progression.

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