Comparative review of diets for the metabolic syndrome: implications for nonalcoholic fatty liver disease

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ABSTRACT
Nonalcoholic fatty liver disease (NAFLD) is a significant health problem and affects 70 million adults in the United States (30% of the adult population), and an estimated 20% of these individuals have the most severe form of NAFLD—nonalcoholic steatohepatitis (NASH). The mechanisms underlying disease development and progression are awaiting clarification. Insulin resistance and obesity-related inflammation, among other possible genetic, dietary, and lifestyle factors, are thought to play a key role. A program targeting gradual weight reduction and physical exercise continues to be the gold standard of treatment for all forms of NAFLD. Even though weight loss and dietary and lifestyle changes are recommended as primary treatment for fatty liver, little to no scientific evidence is available on diet and NAFLD. This article reviews the implications of current dietary approaches, including national guidelines and popular weight-loss diets, with a focus on determining the optimal diet to prescribe for NAFLD and NASH patients. The effects of macronutrient content (carbohydrate, fat, and protein ratios) and specific food components, such as soluble fiber, n-3 fatty acids, and fructose, are discussed. The premises, effects, barriers, and issues related to current dietary guidelines and specific diets are discussed, and the question, “Will it work for the pathogenesis of NAFLD and NASH?” is addressed. Am J Clin Nutr 2007;86:285–300.

KEY WORDS Nonalcoholic fatty liver disease, NAFLD, nonalcoholic steatohepatitis, NASH, diet, weight loss

INTRODUCTION
The rising incidence of obesity in today’s environment is associated with many obesity-related health complications (1), including cardiovascular disease, diabetes, hyperlipidemia, hypertension, and nonalcoholic fatty liver disease (NAFLD) (2-5). This constellation is also recognized as the metabolic syndrome and is characterized by underlying insulin resistance. NAFLD is defined as the accumulation of lipid, primarily in the form of triacylglycerols in individuals who do not consume significant amounts of alcohol (<20 g ethanol/d) and in whom other known causes of steatosis, such as certain drugs and toxins, have been excluded (6). The spectrum of NAFLD includes steatosis alone (type 1), steatosis plus inflammation (type 2), steatosis plus hepatocyte injury or ballooning degeneration (type 3), and steatosis plus sinusoidal fibrosis, Mallory bodies (type 4), or both (6-9). NASH is considered to be the most severe form of NAFLD (types 3 and 4) and is associated with an array of adverse clinical outcomes, including cirrhosis (7), hepatocellular carcinoma (10-12), and advanced liver disease, which leads to liver-related death (7, 13).

Given the close relations between obesity, the metabolic syndrome, and the development of NAFLD, it is not surprising that many NAFLD patients have multiple components of the metabolic syndrome, whether or not they are overweight or obese. Insulin resistance is present in and is a significant predictor of NAFLD and NASH in most patients (14), even the ≈10-15% of patients who are not overweight (15, 16). NAFLD is a multifactorial disease that involves a complex interaction of genetics, diet, and lifestyle, all of which combine to form the NAFLD phenotype, as discussed in several recent reviews (17, 18).

A cornerstone of the management strategy in such patients is the use of diet to decrease body weight, and improve glycemic control, dyslipidemia, and cardiovascular risks, as well as to treat fatty liver. There is a bewildering array of diets that have been recommended for the prevention and treatment of all of the components of the metabolic syndrome. Their utility for the treatment of NAFLD remains mostly unknown. It is also important to note that cognitive-behavioral approaches, in addition to dietary modification, are necessary for the long-term success of dietary and lifestyle interventions; however, this is outside the scope of the present review.

In this article, we review the current concepts about the pathogenesis of hepatic steatosis and steatohepatitis and evaluate the existing diets in the context of this knowledge and the available literature. The intent is to enable clinicians to evaluate the diets of NAFLD and NASH patients and make rational decisions based on this perspective—in the absence of controlled trials—to help their patients. Finally, a tailored approach for the dietary...
treatment of NAFLD is offered as a way to optimize the dietary management of this condition.

NAFLD PATHOPHYSIOLOGY AND DIET

The pathophysiology of NASH is not fully understood. The complexities related to disease development and progression are discussed in detail elsewhere (17–21) and will not be reviewed in detail here. The main aspects of NAFLD and NASH pathophysiology as they relate to diet and nutrition are briefly discussed below.

Dietary effects on whole-body metabolism and its regulation via effects on hormones, transcription factors, and lipid metabolic pathways are considered to play a central role in NAFLD. Insulin resistance is currently thought to be a key factor in the development of both NAFLD and NASH (22). Many studies have shown an association of insulin resistance with NAFLD and NASH on the basis of impaired glucose tolerance or impaired fasting glucose (23–29). Despite elevated insulin concentrations, adipose tissue fatty acid flux was not suppressed in NAFLD patients (29), which indicated the presence of peripheral insulin resistance.

In most patients, overnutrition or inappropriate diet are thought to lead to chronically elevated glucose, insulin, and free fatty acid (FFA) concentrations in the blood. Both excessive carbohydrate intake (Figure 1) and excessive fat intake (Figure 2) could play a role in increasing blood glucose, FFA, and insulin concentrations, independently or together. These dietary conditions (Figure 3) contribute to resistance to insulin-stimulated glucose uptake at the level of the adipose tissue and skeletal muscle as well as resistance to the insulin-mediated suppression of TG hydrolysis in adipose tissue (29, 30). Glucose uptake in the liver is not insulin dependent, and increased glucose concentrations in the blood lead to increased glucose uptake by the liver. Insulin-mediated stimulation of de novo lipogenesis (DNL) leads to an increased conversion of glucose to fatty acids (31).

Together, the increased concentrations of both glucose and FFA in the blood contribute to excessive accumulation of neutral lipids in the liver. A recent study by Donnelly et al (32), using a multiple-stable-isotope labeling approach, showed that in NAFLD patients plasma FFAs were the primary contributor to the liver triacylglycerol content in the fasted state (50–70% of total FA) and to the lipoprotein triacylglycerol content in both the fed and the fasted state (50–75% of total FAs). Most of the plasma FFAs were from adipose tissue, which accounted for 70–90% of FAs in the fasted state and 50–70% in the fed state. The de novo synthesis of FAs from glucose, fructose, and amino acids was also dysregulated in NAFLD patients. DNL was elevated in the fasting state—accounting for 25% of liver and VLDL triacylglycerols compared with 5% in healthy individuals (33, 34)—and failed to increase postprandially. Moreover, this study showed that there were likely 2 distinct pools of FAs in the liver, which were handled differently. Plasma FFAs—representing mainly adipose-derived FAs—were thought to be part of a fast-turnover pool that was preferentially incorporated into VLDLs, whereas FAs synthesized de novo were thought to enter a hepatic holding pool. Therefore, especially in the presence of peripheral insulin resistance, in which the flux of FAs from the adipose is not suppressed by insulin and plasma FFAs are persistently high, elevated rates of lipogenesis may be a significant source of accumulated triacylglycerol in the liver.

In healthy individuals, elevated lipid concentrations in the liver lead to increased VLDL production and secretion; however, in NAFLD and NASH patients, this increase in fat export via VLDL may be impaired or insufficient to prevent fatty liver (35). Hypertriglyceridemia, low HDL concentrations, and small, dense LDL particles often result from an increase in the concentration, size, or both of circulating VLDL (36), which together...
confer an increased risk of cardiovascular disease (37–44). In NAFLD and NASH patients, blood lipid concentrations may be normal or elevated, and many patients have the atherogenic dyslipidemia associated with the metabolic syndrome, which includes high triacylglycerol, low HDL, and increased small, dense LDL (45).

The original “two-hit hypothesis” of NASH asserts that the accumulation of lipid in the liver (hit one) is followed by a
cascade of prooxidative, hepatotoxic events (hit 2), which are caused by an as yet unknown mechanism (46). Mitochondrial dysfunction has been considered to be such a second hit (21). There are several other mechanisms being investigated also. The increased secretion of tumor necrosis factor-α (TNF-α) and other proinflammatory cytokines by adipocytes and infiltrating macrophages is thought to lead to chronic systemic inflammation (Figure 4) as well as obesity-linked insulin resistance (47). Elevated concentrations of circulating TNF-α have been documented in NAFLD patients (48) and have been implicated in the manifestation of fatty liver disease (49). Small intestinal bacterial overgrowth (50–52) and deficiencies in various nutrients, including essential fatty acids (53), choline (54), and amino acids (55, 56), may also be involved in the development and progression of this disorder; however, limited evidence exists to support these mechanisms.

DIETARY TREATMENT OF NAFLD AND NASH

Because of the strong association of obesity and the metabolic syndrome across the entire spectrum of NAFLD, current recommendations for the treatment of fatty liver disease are aimed at weight loss and dietary modification (28, 57–59). For unknown reasons, sudden or quick weight loss achieved through dietary modification may lead to the progression of liver failure in some NAFLD patients (60). On the other hand, weight reduction through surgical methods, even with quick weight-loss after surgery, has been successful in reducing disease progression (58, 59, 61–63). Despite the fact that weight loss and dietary and lifestyle changes are recommended as primary treatment for fatty liver, no specific guidelines exist pertaining to diet. Very few studies of the effects of different diets on NAFLD have been performed.

The premises, effects, barriers, and issues related to current dietary guidelines and specific popular weight-loss diets as they relate to NAFLD are discussed below.

EFFECT OF INDIVIDUAL DIETARY COMPONENTS ON THE METABOLIC SYNDROME, INSULIN RESISTANCE, HEPATIC LIPID METABOLISM, AND INFLAMMATORY AND FIBROTIC PATHWAYS

Saturated fat

A recent study in a rat model of hepatic steatosis showed that saturated fatty acids (SFAs) promote endoplasmic reticulum stress as well as hepatocyte injury (64). Accumulation of SFAs in the liver due to high-SFA or high-fructose diets led to an increase in markers associated with endoplasmic reticulum stress and liver dysfunction. This, along with ample evidence associating high-SFA intakes with an increased risk of cardiovascular disease (65–67), suggests that the intake of dietary saturated fats should be limited in NAFLD patients. However, what saturated fat intake should be recommended?

A study comparing 25 overweight (BMI < 30; in kg/m²) NASH patients and 25 age- and BMI-matched controls collected 7-d food records and assessed dietary patterns (68). NASH patients had higher intakes of SFA at 14% of total energy, compared with 10% in controls. Insulin resistance, as measured by the insulin sensitivity index, was correlated with SFA intake. Therefore, a SFA intake >10% of total energy may contribute to insulin resistance and may not be suitable for NASH patients.

A randomized, double-blind, crossover study examined the effects of 3 diets in 86 free-living healthy men: a control diet (38% fat with 14% SFAs), the National Cholesterol Education
Program Step I diet (30% fat with 9% SFAs), and the National Cholesterol Education Program Step II diet (25% fat with 6% SFAs) (61). Although both reduced-fat diets decreased LDL, they also decreased HDL and increased plasma triacylglycerol after 6 wk compared with the control diet. In response to the 6%–SFA diet, subjects who were insulin resistant, who had a higher percentage of body fat, and/or who had a higher BMI—characteristics that describe most NAFLD patients—experienced smaller reductions in LDL, larger reductions in HDL, and increases in triacylglycerol compared with subjects who were insulin sensitive. On the basis of this evidence, SFA intakes <7% of total energy may not offer any further improvements in blood lipids in patients with insulin resistance and may even be detrimental.

It is still unclear whether a minimum intake of SFAs in the diet is beneficial or perhaps even required for optimal health (69). On the basis of the clinical evidence discussed above, SFA intakes <7% and >10% of energy may be suboptimal for NAFLD patients.

**Monounsaturated fatty acids**

Monounsaturated fatty acids (MUFAs) are a class of fatty acids that are found in foods such as olive oil, nuts, and avocados. The beneficial effects of MUFAs on cardiovascular disease risk and blood lipid profiles have been extensively studied (65). In particular, dietary MUFAs decrease oxidized LDL (70), LDL cholesterol (66), total cholesterol (TC), and triacylglycerol concentrations, without the concomitant decrease in HDL typically seen with low-fat diets (71–73). Additionally, the replacement of carbohydrate and saturated fat with MUFAs leads to reductions in glucose and blood pressure and to an increase in HDL in patients with diabetes (74). A MUFA-rich diet (40% of energy as fat) also decreased VLDL-cholesterol and VLDL-triacylglycerol more and was more acceptable to patients with non-insulin dependent diabetes mellitus (type 2 diabetes) than was a high-carbohydrate diet (28% of energy as fat) (75). Therefore, an increase in the intake of MUFAs, particularly as a replacement for SFAs and as a higher proportion in the diet in lieu of carbohydrate, may be beneficial for NAFLD patients.

**Polyunsaturated fatty acids**

Polyunsaturated fatty acids (PUFAs) are a class of fatty acids that include n–6 and n–3 fatty acids. The n–3 fatty acid α-linolenic acid is a precursor for the long-chain products docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). PUFAs have been shown to decrease the risk of heart disease when consumed in lieu of SFAs in both epidemiologic (76, 77) and clinical (78) studies. The ratio of n–6 to n–3 fatty acids seems to be important in determining the effect of PUFAs on various lipid and nonlipid indexes. Replacement of n–6 PUFAs with α-linolenic acid improved peripheral insulin sensitivity and lowered cholesterol concentrations in rats with fructose-induced insulin resistance (79). An approximate dietary intake of 6% n–6 and 1% n–3 fatty acids as percentage of energy has been recommended to maximize the cardiovascular benefits of these essential fatty acids (80).

Several studies have shown a link between essential fatty acid deficiency and the development of steatosis in animal models (51, 53, 55, 81–85), a link that was first observed almost 30 y ago (86). There is also an indication that essential fatty acids may be essential for VLDL secretion (54). In geese overfed with corn, liver steatosis is accompanied by a reduced essential fatty acid content of membrane phospholipids despite an adequate dietary supply of both linoleic and α-linolenic acid (84).

**n–3 Fatty acids**

The effects of n–3 fatty acids on dyslipidemia and insulin resistance have been extensively reviewed (87) and provide convincing evidence that n–3 fatty acids should be an important dietary component in patients with NAFLD and NASH. Specifically, DHA and EPA induce fatty acid catabolism through the activation of peroxisome-proliferator activated receptor (PPAR)–mediated pathways (88) and down-regulate DNL through sterol regulatory element binding protein (SREBP) pathways (89). The effects of dietary fish oil, which is high in DHA and EPA, in animal models of insulin resistance are impressive. The beneficial effects include 1) decreased plasma triacylglycerol, FFAs, glucose, and insulin; 2) prevention of peripheral insulin resistance; 3) decreased triacylglycerol concentrations, VLDL secretion, and lipogenesis in the liver; 4) decreased lipid concentrations and utilization and storage of glucose in skeletal muscle; and 5) decreased adipocyte cell size and visceral fat content and increased insulin-stimulated glucose transport in the adipose tissue (87).

Walnuts, a good source of α-linolenic acid, may also be beneficial. When patients with type 2 diabetes were placed on diets that included 30 g walnuts/d, plasma HDL and the ratio of HDL cholesterol to TC increased, and LDL decreased after 8 wk (90). In another study, hypercholesterolemic men and women who substituted 32% of their MUFA intake with walnuts had significant decreases in TC and LDL and improved endothelial function compared with controls (91).

The first studies to have examined the effects of n–3 fatty acid supplementation in NAFLD patients were recently published. One such study found that 1 g fish oil/d for 12 mo decreased blood triacylglycerol concentrations, liver enzymes, fasting glucose, and steatosis in NAFLD patients (92). Another study also found decreased blood triacylglycerol, liver enzymes, and TNF-α and regression of steatosis as assessed by ultrasonography after 6 mo of supplementation with 2 g fish oil/d (93). These preliminary results, along with the evidence reviewed above, suggest that the consumption of n–3 fatty acids found in fish oils and walnuts is likely to improve blood lipid profiles and to reduce inflammation, steatosis, and liver damage in NAFLD patients.

**Trans Fatty acids**

Trans Fatty acids occur naturally in foods such as dairy products as a result of bacterial metabolism and in foods such as margarines as a result of hydrogenation. Trans Fatty acids consist of multiple isomers that have differential effects on human metabolism (94). The bacterially derived cis-9, trans-11 conjugated linoleic acid and trans-11 oleic acid typically found in dairy products do not have adverse effects on lipoprotein profiles (95). Conversely, intake of trans-10, cis-12 conjugated linoleic acid from hydrogenated oils has been found to increase inflammatory markers (96), induce endothelial dysfunction (97), and unfavorably alter the blood lipid profile by increasing the LDL: HDL and TC: HDL ratios (98).

Effective 1 January 2006, after reviewing available scientific evidence regarding the effect of trans fats on cardiovascular...
health, the Food and Drug Administration ruled that food manufacturers are required to include the content of trans fats on nutrition labels (99). Although the specific mechanisms of action are not yet clear, the recommendation to avoid the intake of trans fatty acids from hydrogenated oils seems well founded for those at risk of dyslipidemia.

**Glycemic index and fiber**

Several trials have shown decreases in TC in response to intake of soluble fiber from sources such as oats (100, 101). This type of evidence has led the Food and Drug Administration to approve a claim of cardiovascular disease risk reduction for the labeling of oat products and foods containing soluble fiber (102). The so-called “second-meal effect” of low-glycemic index (GI) foods or slow-release carbohydrates improves the glycemic response to a subsequent meal and was first described in the early 1980s (103). The effects of high-fiber, low-GI carbohydrates on glycemic response and cholesterol concentrations were reviewed recently in a meta-analysis (104) and provide evidence that these dietary components may be beneficial to individuals with impaired insulin response.

A breakfast containing a high-fiber indigestible and fermentable starch compared with a low-GI starch reduced FFAs in the blood after a subsequent meal (105). Whereas both breakfasts lowered glucose concentrations, only the breakfast containing the low-GI starch decreased insulin concentrations. Although the results of this study cannot be generalized to long-term effects on glycemic control or lipid profiles, it seems reasonable to conclude that the inclusion of carbohydrates that are high in indigestible and fermentable fiber and low in GI can be helpful in maintaining glucose, insulin, and FFA concentrations in individuals with insulin resistance and NASH.

**Sucrose and fructose**

Several studies have shown that high intakes of fructose increase DNL in animal models and in humans (106–108). One study of lean and obese women found that 4 d of overfeeding with either a glucose or sucrose drink increased DNL 2–3-fold (109). The higher the woman’s baseline lipogenesis rate, the higher the increase in DNL in response to the 4 d of overfeeding, with a trend toward a higher increase with sucrose than with glucose. These data suggest that some individuals may be more sensitive to fructose-induced stimulation of DNL.

Studies of the effects of fructose consumption on whole-body energy metabolism were reviewed recently by Havel (110). A feeding study showed that 2 d of a high fructose intake (30% of kcal/d, consumed as a sweetened beverage at every meal) resulted in decreased postprandial glucose concentrations and insulin responses and prolonged alimentary lipemia in women (111). High glucose intakes with meals, on the other hand, resulted in a suppressed postprandial response of the orexigenic hormone ghrelin. These data suggest that a high consumption of fructose and glucose as simple sugars stimulate the de novo synthesis of fatty acids, especially in individuals with insulin resistance and in those who are overweight (32, 109, 113, 114).

**Protein**

There is little information on the effect of protein quantity, quality, and composition on the pathophysiology of NAFLD and NASH. It is known that protein deficiency or malnutrition may cause steatosis (55, 115). Considering that the total protein content and quality are typically high in the average American diet, protein deficiency is highly unlikely in NAFLD patients. Conversely, an excessive intake of protein may cause glomerular sclerosis, intrarenal capillary hypertension, and eventually renal malfunction in certain vulnerable individuals who have underlying renal insufficiency (116–120). Studies of high protein intake and their possible effects on NAFLD are lacking.

**CURRENT DIETARY GUIDELINES**

**US Department of Agriculture Dietary Guidelines for Americans**

The official dietary recommendations for healthy Americans, the Dietary Guidelines for Americans, is published every 5 y as a joint effort of the Department of Health and Human Services, and the US Department of Agriculture (USDA) (121). The guidelines provide advice about dietary habits to promote health and reduce the risk of major chronic diseases. The USDA guidelines are meant for health maintenance and are not guidelines for the treatment of any health condition.

In brief, it is recommended that individuals take in an appropriate amount of calories for body size and activity level. They are encouraged to eat a variety of foods, choose from several food groups, and include predominantly whole grains and their products in the diet. Nine or more daily servings of fruit and vegetables are recommended. Servings of meats, fish, vegetable proteins, dairy, and dairy products are based on energy needs, with fats and sweets to be consumed sparingly as “discretionary calories.” The most recent version of the guidelines, published in 2005, for the first time recognizes and discusses the notion of individual differences and customizes the recommendations, providing sample meal plans, based on height, weight, and activity level estimates.

These basic guidelines do not address the special needs of individuals with various metabolic disorders. NAFLD and NASH patients are typically overweight, with central adiposity (122). As such, their primary nutritional focus must be on weight and body fat reduction rather than on maintenance, for which the USDA Dietary Guidelines are primarily designed. Evidence indicates that NAFLD patients may have increased lipogenesis and that this, in part, contributes to the accumulation of lipid in the liver (32). A higher carbohydrate intake was also associated with a greater odds of inflammation in morbidly obese patients with NAFLD than was a higher fat intake (123). The emphasis of the USDA Dietary Guidelines on the consumption of carbohydrates may therefore be inappropriate for certain patients with NAFLD and NASH.

**American Dietetic Association**

The basic dietary recommendation of the American Dietetic Association for healthy adults is to follow the USDA Dietary
**Guidelines**, as described above. However, the American Dietetic Association also maintains an annually updated *Manual of Nutritional Therapy* for all known metabolic disorders and other diseases that registered dietitians and other nutrition professionals can use to develop diets for their patients. The manual is available by subscription to nutrition professionals (124).

Although there are no specific recommendations in the manual for NAFLD, it does include suggestions for patients with the metabolic syndrome. The first-line therapy for all lipid and non-lipid risk factors associated with the metabolic syndrome is a program incorporating weight loss and exercise. Additional recommendations include a reduction in the intakes of total fat, SFAs, and *trans* fat, and, conversely, an increase in the intakes of PUFAs and MUFAs. There is also a recommendation to include long-chain n−3 fats and plant stanols or sterol esters. The physical activity goal is based on the America on the Move program (125), which specifies a goal of increasing the number of steps per day by 2000 steps above baseline and decreasing energy intake by 100 kcal/d. It is suggested that the caloric goal be reached by opting for regular instead of super-size meals, leaving a few bites on the plate, and drinking water instead of juices and other beverages. Finally, it is stated that the scientific evidence does not support any specific generalized nutritional approach for the metabolic syndrome and, therefore, that interventions must be individualized.

The recommendations regarding fats and plant stanols and sterols are well-founded because of the increased risk of cardiovascular disease in patients with the metabolic syndrome. The specific goals for increasing physical activity and specific suggestions for ways to decrease calorie intake are also prudent and appropriate for NAFLD patients, especially because these approaches are moderate and would likely lead to gradual, long-term, sustained weight loss. The American Dietetic Association recommendations, however, do not address specific approaches for decreasing insulin resistance and do not provide guidance regarding carbohydrate and protein intakes.

**American Heart Association**

Studies have shown associations between fatty liver and hypertension (126) and increased carotid intima-media thickness (127), both of which are indicators of an increased risk of cardiovascular disease in NAFLD patients. Several recent investigations have shown associations between insulin resistance, the metabolic syndrome, and cardiovascular disease (38–40, 42, 128); therefore, NAFLD patients having characteristics of the metabolic syndrome should be treated to reduce their risk of cardiovascular disease (129).

The position of the American Heart Association (AHA) on scientific health habits focuses on the 3 main risk factors associated with heart disease—high blood cholesterol, high blood pressure, and excess body weight (130). The same basic guidelines put forth by the USDA are recommended by the AHA, with several modifications. These include recommendations to eat fish twice a week, avoid *trans* fats, limit SFA intakes to <10% of total calories, and limit cholesterol to <300 mg/d. The AHA/National Heart Lung and Blood Institute (NHLBI) joint scientific statement on the Diagnosis and Management of the Metabolic Syndrome (130) further recommends decreasing SFA intakes to <7% of total daily calories, maintaining a fat intake of 25–35% of total calories, reducing overall calorie intake, avoiding simple sugars, and consuming higher amounts of fruit, vegetables, and whole grains.

The AHA recommendations to decrease SFA, *trans* fat, and cholesterol intakes and to avoid simple sugars, while consuming more low-GI foods and fish, are all reasonable suggestions for NAFLD and NASH patients. An SFA intake of 10% of daily calories, which corresponds with the AHA scientific position statement, rather than the 7% recommendation in the AHA/NHLBI joint statement, is recommended for reasons already outlined above.

**National Heart, Lung, and Blood Institute**

The NHLBI has a set of recommendations that is published on the NHLBI website (131), which recommends the Therapeutic Lifestyle Changes (TLC) diet described below. The Dietary Approaches to Stop Hypertension (DASH) plan, designed for individuals with hypertension, and recommendations specifically pertaining to the dietary management of the metabolic syndrome are also addressed.

**National Cholesterol Education Program**

The National Cholesterol Education Program (NCEP) has been developing guidelines for reducing the incidence of coronary heart disease (CHD) since 1985. The Step I and Step II diets were created by the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults through 2 guidance reports, the Adult Treatment Panel I and II, respectively (132). The Step I diet is a strategy for the prevention of CHD in individuals with LDL concentrations ≥160 mg/dL or in those with a borderline high LDL concentration (130–159 mg/dL) and ≥2 risk factors, including cigarette smoking, hypertension, low HDL, family history of premature CHD, and age (men: 45 y; women: ≥55 y). This diet restricts total fat intake to ≤30% of total daily calories, SFA intake to <10% of total daily calories, and cholesterol to <300 mg/d.

The Step II diet was created to address the need for further risk reduction in persons with established CHD and in those who are already at Step I goals and with a high-risk TC concentration of ≥240 mg/dL. This diet restricts SFA intake further to <7% of total calories and cholesterol to <200 mg/d. The terms Step I and Step II are no longer used in the new literature; however, the Step I diet is still recommended for the general public, whereas the Step II diet has been updated and renamed the TLC diet.

**Therapeutic lifestyle changes**

The Adult Treatment Panel III was published in 2001 and describes the updated TLC diet (131). The TLC recommends lowering LDL cholesterol with plant sterols and stanols (2 g/d) and viscous and soluble fiber (20–30 g/d), weight reduction, and increased physical activity. The TLC diet guidelines recommend a decrease in SFA to 7% of daily calories, a reduction in total fat intake to 25–35% of daily calories, <200 mg cholesterol/d, <2400 mg Na/d, PUFAs up to 10% of daily calories, MUFA up to 20% of total calories, carbohydrate intake of 50–60% of calories, protein at ≈15% of calories, and calorie intakes that lead to the achievement and maintenance of a healthy weight (133).

As discussed above, the severe restriction of SFA to <10% of daily calories recommended by the Step II and TLC diets had less benefit in terms of LDL reduction, yet was accompanied by a
further decrease in the HDL:TC ratio, than did a more moderate 9–10% SFA intake in individuals with insulin resistance (134). This may be particularly true for patients with fatty liver disease, especially if the fat calories are replaced with simple carbohydrates, which are known to increase DNL. The TLC diet recommends a saturated fat intake that may not be suitable for NAFLD patients with a high BMI and low insulin sensitivity but that may be appropriate for patients with established CHD or for those with LDL concentrations >160 mg/dL and multiple CHD risk factors.

**Dietary Approaches to Stop Hypertension**

The DASH eating plan is recommended for lowering blood pressure and has been found to lower blood cholesterol (135). DASH is a modification of the USDA Dietary Guidelines, with specifications related to sodium intake. Studies have shown that reducing sodium intake to <1500 mg/d as part of the DASH diet, alone or in conjunction with medication in more severe cases, effectively lowers blood pressure in prehypertensive patients (136).

Hypertension is associated with NAFLD (14, 23). African Americans appear to be especially sensitive to the blood pressure–lowering benefits of low-sodium diets that incorporate reductions in salt intake and increases in potassium intake (136). One study found particularly favorable results for African Americans and hypertensive patients with high adherence rates (≈90%) in the 11-wk period of the clinical study (137). Little to nothing is known about the pathogenesis of NAFLD in the African American population.

The DASH diet plan, however, is not particularly palatable to many individuals, the menu is rather limiting, and adherence is low in the long term. Outpatient studies that more closely mimic free-living conditions, compared with inpatient clinical trials, have much lower adherence rates (138). Because of its effects in lowering blood pressure, the DASH diet may be a reasonable and preferable solution in some NASH patients, particularly in those who are African American, those who have increased salt sensitivity and high blood pressure, and those who are able to maintain this diet in the long term despite lower palatability.

**American Diabetes Association**

The American Diabetes Association has developed its own food pyramid, which uses the same basic layout of the USDA Food Guide Pyramid, to illustrate the dietary recommendations for patients with diabetes. This food pyramid can be found on the official American Diabetes Association website, along with other information pertaining to nutrition, including recommendations on eating out, holiday meal planning, recipes, and exchange lists (139). The American Diabetes Association pyramid groups foods on the basis of their carbohydrate and protein contents rather than on their classifications as foods. For example, starchy vegetables such as potatoes are placed in the “breads, grains and other starches” category rather than the “vegetables” category because of their high starch content. Serving sizes for foods containing high amounts of carbohydrate are smaller in the American Diabetes Association pyramid than in the USDA pyramid.

The American Diabetes Association position statement on evidence-based nutritional recommendations for diabetic patients (140) presents specific goals and recommendations based on A-, B-, and C-level evidence, depending on the quality and quantity of scientific evidence collected through clinical trials and evaluated using the American Diabetes Association evidence grading system. The goals of nutritional therapy for both type 1 and type 2 diabetes, as outlined in this position statement, are to attain normal glucose concentrations, improve health through nutrition and physical activity, and prevent and treat obesity, dyslipidemia, cardiovascular disease, hypertension, and nephropathy.

Although the basic nutritional recommendations of the American Diabetes Association are similar to those of the USDA Dietary Guidelines, the American Diabetes Association recommendations further discuss carbohydrates by subdividing them into the 3 categories of sugars, starch, and fiber. Specifically, the benefits of low-GI diets and the inclusion of fiber and resistant starch are discussed. According to the American Diabetes Association, clinical trials show no significant differences between sources or types of carbohydrates on glycemic response if the total amount of carbohydrate is the same. The American Diabetes Association also concludes that there are no consistent long-term benefits with low-GI diets compared with high-GI diets, that the intake of fiber shows no metabolic benefit unless it is consumed in very high amounts likely to produce gastrointestinal side effects and that dietary sucrose does not induce hyperglycemia more than do equal caloric amounts of starch.

The conclusions of the American Diabetes Association are surprising in light of trials showing decreases in serum cholesterol concentrations in response to the intake of soluble fiber (100, 101) and of the Food and Drug Administration’s approved claim of cardiovascular disease risk reduction for the labeling of oat products and foods containing soluble fiber (102). The conclusion of the American Diabetes Association that the intake of simple sugars, such as sucrose, has no adverse effect on patients with type 2 diabetes is particularly surprising given the evidence discussed above, which points to the effects of simple sugars, specifically fructose, on DN, and the resulting increases in circulating FFAs (32, 113) and plasma triacylglycerol (32, 107, 113, 114). The exchange lists, recipes, and other support materials provided on the American Diabetes Association website (139) are valuable. However, the lack of recommendation to limit the intake of simple carbohydrates, especially fructose, and to include low-GI carbohydrates and fiber in the diet are at odds with other evidence discussed previously.

**WEIGHT-LOSS DIETS, POPULAR DIETS, AND FAD DIETS**

**Mediterranean dietary pattern**

The Seven Countries Study, an epidemiologic survey of dietary patterns and incidence of CHD published in 1970, first identified a lower risk of CHD in Mediterranean countries where the consumption of fruit, vegetables, grains, nuts, legumes, dairy, olive oil, and small amounts of poultry, fish, red meat, and red wine were emphasized (140). Since then, clinical trials have repeatedly shown this Mediterranean dietary pattern to be beneficial. Several recent reviews concluded that adherence to the Mediterranean dietary pattern leads to improvements in lipoprotein indexes, insulin sensitivity, endothelial function, and cardiovascular mortality (141–145).
It is unclear which specific features of the Mediterranean dietary pattern are responsible for the observed beneficial effects. It has been difficult to define the Mediterranean Diet because the Mediterranean region represents a large diversity of cultures and lifestyles. Nonetheless, diets that are higher in MUFAs, have a lower GI, and are higher in fiber than the average American diet, which are characteristics of the Mediterranean dietary pattern, tend to have beneficial effects on insulin sensitivity (146).

A randomized study comparing the effects of a Mediterranean dietary pattern with a “prudent diet,” consisting of 50–60% carbohydrates, 15–20% protein, and total fat <30%, found that at 2 y of follow-up, a higher proportion of patients in the Mediterranean dietary pattern group (50/90) than in the prudent diet group (129/90) no longer had features of the metabolic syndrome (147). In this study of 180 patients, the Mediterranean dietary pattern was more effective than a low-fat diet at reducing body weight, BMI, waist circumference, inflammatory markers, glucose, TC, triacylglycerol, and insulin resistance, as well as improving endothelial function and increasing HDL concentrations. Patients also had a lower ratio of plasma n-6 to n-3 fatty acids after the Mediterranean dietary intervention (147).

The Mediterranean dietary pattern emphasizes the inclusion of particular foods rather than the limitation of particular macronutrients. Because of this, it may be easier for individuals to understand and follow the diet. It is also a highly palatable diet that is well-liked and may lead to a higher adherence among dieters in the long term. The effectiveness of this diet on multiple factors of the metabolic syndrome in the 2-y randomized trial discussed above provides convincing evidence that the combination of high MUFA and high fiber intakes, a low GI, and the emphasis on lean protein sources may be a good option for NAFLD patients.

**Ornish Diet**

The Ornish Diet was developed as a preventive lifestyle approach for the treatment and management of CHD (148). The program consists of intensive lifestyle changes incorporating moderate fat-burning exercise, relaxation and stress-relief techniques, and a low-fat, high-fiber vegetarian diet. The diet allows the unlimited consumption of fruit, vegetables, grains, beans, and legumes and suggests moderate consumption of nonfat dairy products and nonfat or very-low-fat commercially available products, such as nonfat frozen yogurt bars. The diet restricts the intake of all meats (including fish), oils and fats, nuts, avocados, dairy products, sugar and simple carbohydrates, alcohol, and commercially prepared foods that have >2 g fat per serving.

Several studies have shown the effectiveness of the Ornish Diet in preventing and even reversing CHD in patients who had moderate-to-severe artery disease as assessed by coronary angiography (149–151). In fact, in one study, patients following the low-fat, vegetarian, Ornish Diet experienced more regression of atherosclerosis after 5 y than after 1 y, whereas the control group following a usual care diet experienced progression of atherosclerosis at both 1 and 5 y of follow-up (151).

One of the main criticisms of the Ornish Diet for NASH is the severe restriction of all fats, including n-3 fats and MUFAs. As mentioned above, these fats have been associated with improvements in metabolic measures related to NAFLD, including insulin resistance, inflammation, and blood lipids. Furthermore, many low-fat and non-fat commercially prepared foods contain high levels of simple sugars and are high-GI foods, which would tend to exacerbate insulin resistance. Finally, although it is reasonable to suggest higher intakes of fruit, vegetables, legumes, and whole grains, a vegetarian diet may be too drastic and too limiting for most patients in the long term. The effects of different vegetarian diets on NAFLD patients have not been studied. It is also possible that, with such low fat intakes, phospholipid production would be impaired, which would decrease the ability to synthesize lipoproteins. The Ornish Diet may be an option for a highly motivated NAFLD patient who has already developed concomitant CHD and who needs a drastic change to reverse the progression of atherosclerosis. However, this diet is likely to be too drastic for most NAFLD patients.

**Atkins Diet**

The Atkins Diet focuses on high-protein and high-fat intakes and drastically low-carbohydrate intakes (152). The premise is to eat as much as one needs to “feel satisfied.” The dieter should limit carbohydrates and focus on protein, leafy vegetables, and healthy oils. Specifically, during the 2-wk phase one of the diet, carbohydrate intake is limited to 20 g/d and should come primarily from salad and other nonstarchy vegetables. During phase 2, the carbohydrate intake is gradually increased by 5 g/wk until the desired weight is achieved or the dieter stops losing weight. At this point, the dieter has found their “carbohydrate equilibrium” (ranging from 25 to 90 g carbohydrate/d) and should use this carbohydrate intake for the maintenance of weight in the long term. The diet accounts for increases in carbohydrate intake beyond 90 g/d for those who exercise regularly (vigorous exercise 5 d/wk for 45 min).

A recent trial showed that obese men and women lost more weight with the Atkins Diet than with the conventional low-fat diet at 3 and 6 mo, but the difference was not significant at 12 mo (153). Individuals consuming the Atkins Diet had lower triacylglycerol and higher LDL and HDL concentrations throughout the study than did those consuming the low-fat diet, who experienced the opposite effect. Both diets significantly decreased blood pressure and the insulin response to an oral glucose load. Another study in obese, insulin-resistant women found that those consuming the Atkins Diet had significantly greater reductions in triacylglycerol, body weight, and waist circumference than did women consuming either the high-carbohydrate or the high-protein Zone diet after 24 wk (154). However, 25% of the women consuming the Atkins Diet experienced a >10% increase in LDL.

The long-term effects of the Atkins Diet and other high-fat, high-protein diets are still controversial, especially with regard to increasing the risk of CHD and possible effects on renal function. The consistent increases in LDL and TC, high intakes of SFAs, and low intakes of fiber associated with the Atkins Diet are contraindicated for NAFLD patients because of their proven effects in increasing CHD risk. The Atkins Diet tends to induce sudden weight loss and ketosis, especially in the first 3 mo, which may also be deleterious in NAFLD patients. This diet is unlikely to be suitable for most NAFLD patients.

**Zone Diet**

The Zone Diet is designed to modulate macronutrient balance at each meal for improved glycemic control (155). The dieter is allowed to eat as much as desired at each meal. The emphasis is on eating smaller meals throughout the day, preferably 3 meals...
with 2 snacks in between. The proportions of carbohydrate, fat, and protein are to be kept constant at 40%, 30%, and 30%, respectively. The Zone Diet also emphasizes supplementation with a high-dose of fish oil (4 g/d).

A recent study in obese women following a diet that had nutrient ratios similar to those recommended in the Zone Diet (46% carbohydrate, 20% fat, and 34% protein) compared with a higher carbohydrate diet (64% carbohydrate, 20% fat, and 17% protein) found that triacylglycerol decreased more in women following the Zone-like diet, although weight loss, LDL, HDL, glucose, insulin, FFAs, and C–reactive protein decreased equally in both groups and were correlated with the extent of weight loss (156). Women who had higher baseline triacylglycerol concentrations lost more fat mass and had greater decreases in triacylglycerol with the higher-protein Zone-like diet than with the higher-carbohydrate diet.

Another study in obese adults compared a diet of 40% carbohydrates, 30% fat, and 30% protein, which was termed the nonketogenic diet, with an Atkins-like higher-fat diet consisting of 10% carbohydrates, 60% fat, and 30% protein, which was termed the ketogenic diet (157). The 6-wk trial showed that blood concentrations of β-hydroxybutyrate in the ketogenic diet group were almost 4 times those in the nonketogenic diet group and that LDL was directly correlated with β-hydroxybutyrate concentrations. Insulin sensitivity and energy expenditure increased in both diet groups.

The Zone Diet may be an option for reducing weight, controlling insulin resistance, and reducing the risk of CHD in some NASH patients. The emphasis on MUFAs in lieu of saturated fats, high-dose fish-oil supplements, fruit, vegetables, and high-fiber, low-GI carbohydrates are all especially relevant for NASH patients. However, the high protein intakes associated with this diet may not be appropriate for patients with underlying kidney dysfunction (116–120). Type 2 diabetes is associated with higher morbidity and mortality rates linked to kidney dysfunction, especially in youth-onset compared with adult-onset diabetes (158). Overall, the Zone Diet has favorable elements for most NASH patients, but may be inappropriate for those patients at risk of renal dysfunction.

**South Beach Diet**

The South Beach Diet is based on the GI and entails an induction phase in which very little carbohydrate is consumed. This phase is followed by the gradual addition of “the right” carbohydrates in the second phase and a maintenance phase (159). Three daily meals and 2 snacks in between are “mandatory.” The theory is that eating these snacks, even when not hungry, will keep the dieter from overeating at the next meal. The dieter chooses foods from the allowable list for each phase and avoids foods that are on the “avoid list.” The emphasis is on foods that have a low GI and are high in MUFAs throughout the diet phases. In the first phase, all fruit, bread, rice, potatoes, pasta, sugar, alcohol, and baked goods are eliminated from the diet, whereas meat, chicken, turkey, fish, eggs, shellfish, vegetables, cheese, nuts, and salad vegetables are to be eaten at each meal until full. In phase 2, the dieter gradually re-introduces carbohydrates by adding one serving of a low-GI, high-fiber carbohydrate to one meal per day for 1 wk and then another serving and so on. Supplemental fiber in the form of psyllium husks added to water is recommended before lunch and dinner to help the dieter reach a point of satiety more quickly.

One study compared the effects of the South Beach Diet, which has been described as a modified carbohydrate diet, with those of the NCEP Step II diet in 60 overweight adults (160). Individuals in the South Beach group lost more weight, had a greater decrease in waist-to-hip ratio, and experienced decreases in triacylglycerol, whereas those following the NCEP diet experienced decreases in LDL and HDL. In both groups, weight and TC decreased significantly, whereas there were no changes in glucose, insulin, or inflammatory markers after 12 wk. However, exercise and total calorie intake were not monitored in this trial; therefore, it is impossible to discern whether the observed effects were due to differences in the effectiveness of the diets, exercise, or weight loss in and of itself.

The South Beach Diet incorporates some of the main issues pertinent to NAFLD patients that have already been discussed above, including a focus on the consumption of low-GI foods, fiber, and MUFAs. However, sudden weight loss is often a result of phase 1 of this diet, and this is not advisable in NAFLD patients, as mentioned above. The fat content of this diet throughout the 3 phases is high, ranging from 40% to 60%, which can lead to an increased risk of CHD. Studies of the long-term effect of high protein and fat intakes in NAFLD patients are lacking.

**Weight Watchers Diet**

The Weight Watchers Diet provides 2 options, both of which focus on reduced calorie consumption within an intensive support community (161). In one plan, the dieter consumes foods throughout the day and monitors total intake by making sure not to exceed a certain number of allowable points. Foods with a higher nutrient density, such as fruit and vegetables, are worth fewer points, whereas foods that have a low nutrient density “cost” more and, therefore, are to be consumed in smaller amounts or not at all. With the second plan, instead of counting points, the dieter focuses on the consumption of “wholesome” foods that are higher in nutrient density and avoids empty calories, with the exception of an occasional treat consumed in small amounts.

The true advantage of the Weight Watchers Diet is the built-in support structure that accompanies the diet. The diet itself does not go beyond a simple recommendation to eat less to lose weight and basically adheres to the USDA Dietary Guidelines. Weight Watchers is known for its strong community support network and high success rates because dieters attend motivational meetings regularly. This support strategy may be critical because adherence to modified-calorie diets in the long term is very poor (138, 153, 162–166).

**SPECIFIC RECOMMENDATIONS AND FUTURE DIRECTIONS**

Taking into account the evidence discussed in this article, the authors recommend a highly individualized approach for the dietary treatment of NAFLD and NASH based on a thorough assessment of individual metabolic, physiologic, and nutritional status and personal goals and preferences. The effects of each diet discussed in this article on specific health indexes, such as blood triacylglycerol concentration and insulin sensitivity, are shown in Table 1 and are based on a review of the references included in this article. The composition and the relative macronutrient content of each diet are shown in Table 2. Most NAFLD patients would benefit from the guidelines given below.
an oral fat load compared with controls, despite normal fasting response and an increased production of large VLDL detected by needed (60).

Further studies are needed to elucidate the effects of specific exercise strategies in the NAFLD and NASH populations.

NASH patients have a higher postprandial triacylglycerol response and an increased production of large VLDL detected by an oral fat load compared with controls, despite normal fasting blood lipid concentrations, which suggests that the metabolism of dietary fat is impaired in these individuals (37). Decreased total fat consumption could lead to a decrease in postprandial lipemia and the associated disruptions in lipid metabolism. Further studies are needed to ascertain whether the consumption of smaller meals that are lower in total fat may be helpful in NAFLD patients.

Regular, moderate exercise is independently associated with a 25–35% decrease in CHD risk over a 20-y period (167), regardless of diet and other risk factors. An exercise strategy of walking a distance of 2 miles, 3 d/wk, at a target heart rate of 60% of heart rate reserve (as measured by peak oxygen uptake) resulted in increases in HDL and fitness equivalent to a more rigorous exercise program of walking 3 miles, 3 d/wk, at 80% of heart rate reserve (168). Further studies are needed to elucidate the effects of specific exercise strategies in the NAFLD and NASH populations.

### TABLE 1
Effects of diets on selected indexes important to patients with nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH)1

<table>
<thead>
<tr>
<th>Diet</th>
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<th>Steatosis</th>
<th>Insulin sensitivity2</th>
<th>DNL</th>
<th>Inflammation3</th>
<th>TC</th>
<th>TG</th>
<th>HDL</th>
<th>LDL</th>
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</tr>
</tbody>
</table>

1 An “up” arrow indicates a likely increase, and a “down” arrow indicates a likely decrease in the index based on studies reviewed in this article. A blank space indicates that there is not enough evidence to predict outcomes. DNL, de novo lipogenesis; TC, total cholesterol; TG, triacylglycerol; USDA, US Department of Agriculture; AHA, American Heart Association; NCEP, National Cholesterol Education Program; DASH, Dietary Approaches to Stop Hypertension; TLC, Therapeutic Lifestyle Changes.

2 Based on the insulin sensitivity index.

3 Determined on the basis of plasma cytokine and C-reactive protein concentrations.

4 This diet may cause rapid or sudden weight loss in the induction period, which may be deleterious in patients with NAFLD and NASH.

5 This diet may be deleterious in patients with hyperuricemia or kidney dysfunction because of its high protein content.

### TABLE 2
Relative amounts of selected nutrients typical of each diet1

<table>
<thead>
<tr>
<th>Diet</th>
<th>Carbohydrate</th>
<th>Fat</th>
<th>Protein</th>
<th>SFA</th>
<th>MUFA</th>
<th>PUFA</th>
<th>Cholesterol</th>
<th>Fiber</th>
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<tr>
<td></td>
<td>% of daily energy</td>
<td>% of daily energy</td>
<td>% of daily energy</td>
<td>% of daily energy</td>
<td>% of daily energy</td>
<td>% of daily energy</td>
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<td>g/dl</td>
<td>mg/dl</td>
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<td>&lt;300</td>
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<td>&lt;300</td>
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<td>Weight Watchers</td>
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<td>&lt;300</td>
<td>20–30</td>
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</table>

1 SFA, saturated fatty acids; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; USDA, US Department of Agriculture; AHA, American Heart Association; NCEP, National Cholesterol Education Program; DASH, Dietary Approaches to Stop Hypertension; TLC, Therapeutic Lifestyle Changes.
n-3 Fatty acid intake—specifically DHA and EPA—has been shown to improve CHD risk by affecting metabolic variables such as blood triacylglycerol concentrations (80, 169–171) and through independent mechanisms related to antiarrhythmic effects (172–177). α-Linolenic acid from walnuts also improves blood lipid profiles (79, 91, 178). Furthermore, n-3 fatty acids have been found to decrease steatosis in both preliminary trials in humans (92, 93) and in animal models (85, 87). More studies are needed to clarify the specific dosages, formulations, and effects of n-3 fatty acids in individuals with NAFLD.

Beneficial effects on both insulin sensitivity and lipid markers have been found in response to low-GI carbohydrates and high-fiber intakes from fresh fruit, vegetables, legumes, and grains (33, 68, 100, 101, 103–105, 146, 147, 171, 179–182). A reduction in the amount of total carbohydrates, especially simple sugars, would reduce the total pool of acetyl CoA in the liver and, therefore, reduce the flux through the DNL pathway. The reduction in fatty acid synthesis would also result in reduced triacylglycerol synthesis and prevent the excess accumulation of total fat in the liver. A reduction in the rate at which glucose enters the bloodstream, via the consumption of lower-GI carbohydrates and higher amounts of fiber, would also reduce the subsequent exaggerated insulin excursions and thereby reduce insulin resistance. However, nutritional studies of the specific effects of modulating carbohydrate type and quantity on insulin resistance and disease progression in NAFLD patients are needed.

The intake of diets that are lower in carbohydrate, lower in saturated fat, but higher in protein than the average American diet—which consists of 47% carbohydrate, 38% fat (20% SFA), and 15% protein—tend to be beneficial for ameliorating features of the metabolic syndrome, including effects on insulin sensitivity and blood lipids (85, 115, 123, 134, 140, 141, 153, 154, 156, 160, 183, 184). Certain individuals may be susceptible to renal malfunction associated with high protein intakes (116); therefore, an increase in total protein intake may not be appropriate in these patients. Studies are needed to examine the effects of modifying the protein content in NAFLD patients.

An emphasis on MUFAs from foods such as olive oil, in favor of high-SFA foods such as fatty meats and full-fat dairy products, is advisable because SFAAs have deleterious effects on liver function (185) and raise blood LDL concentrations (68, 134, 186–189), whereas MUFAs are beneficial in reducing the risk of CHD and type 2 diabetes through effects on blood lipids, endothelial function, and insulin sensitivity (74, 75, 104, 144, 146, 147, 184, 186, 190, 191).

The recommendation to avoid the intake of sodas and other sweetened drinks is substantiated by observations that high fructose intakes, high sucrose intakes, or both can induce DNL, which leads to higher blood triacylglycerol concentrations and lower insulin sensitivity (33, 106–108, 114). Soda consumption contributes a substantial proportion of the calorie intake in many overweight and obese individuals (112, 192). A reduction in the consumption of simple sugars, especially in the form of sweetened beverages, which provide sugar in a very accessible and easily absorbable form, would help to reduce the exaggerated glucose and insulin excursions that are associated with insulin resistance. In addition, a reduction in the consumption of sweetened beverages would lead to a reduction in total calories consumed, which would facilitate weight loss.

Poor adherence in weight loss and lifestyle modification is a crucial issue in overweight and obese individuals (138, 153, 162, 163, 193–196). Weight loss through diet and exercise tends to be successful in the first 6 mo, but in the long-term, most individuals are unable to maintain this weight loss (167). Strategies to improve adherence and long-term behavioral modification are therefore imperative for the successful treatment of NAFLD through dietary approaches.

SUMMARY

There is no consensus as to what diet or lifestyle approach is the right one for NAFLD and NASH patients, largely because of a lack of scientific evidence. It is likely that there will be no one correct approach for all NAFLD patients, and diets will therefore need to be tailored to individual needs. The inclusion of n-3 fatty acids, high-MUFA foods, fruit, vegetables, and low-GI, high-fiber foods and reduced intakes of saturated fats, simple carbohydrates, and sweetened drinks may be universally recommended to NAFLD patients. More studies are needed to clarify the specific effects of different diets and dietary components on the health of NAFLD patients. The general recommendations described in this review may be a useful guide for determining the appropriate diet for individual patients now, while evidence-based recommendations from future clinical trials are assembled.

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