REVIEW

Practical Dietary Recommendations for the Prevention and Management of Nonalcoholic Fatty Liver Disease in Adults

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ABSTRACT

Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease worldwide. In the absence of effective pharmacotherapies, clinical guidelines focus primarily on weight loss to treat this condition. Established consensus, evidence-based, and clinical dietary recommendations for NAFLD are currently lacking. The aim of this paper is to provide evidence-based practical dietary recommendations for the prevention and management of NAFLD in adults. A literature review focusing on established principles for the development of clinical practice recommendations was employed using the following criteria: based on substantial evidence, ensures risk minimization, is flexible for an individual patient approach, and is open to further modification as evidence emerges. The Practice-based Evidence in Nutrition classification system was used to grade these principles. Five key dietary recommendations were developed: *1*) follow traditional dietary patterns, such as the Mediterranean diet; *2*) limit excess fructose consumption and avoid processed foods and beverages with added fructose; *3*) PUFAs, especially long-chain omega-3 rich foods and MUFAs, should replace SFAs in the diet; *4*) replace processed food, fast food, commercial bakery goods, and sweets with unprocessed foods high in fiber, including whole grains, vegetables, fruits, legumes, nuts, and seeds; and *5*) avoid excess alcohol consumption. Improving diet quality may reduce the incidence and progression of NAFLD and associated risk factors. Many of the benefits are likely to result from the collective effect of dietary patterns. High-quality research—in particular, randomized clinical trials assessing dietary interventions that focus on liver-specific endpoints—are needed as a priority. *Adv Nutr* 2018;9:30–40.

Keywords: nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, diet, dietary recommendations, clinical guidelines

Introduction

Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease worldwide, affecting an estimated 30% of the adult population in many developed countries, including Australia (1). Rates of NAFLD are as high as 90% in obese individuals and 50% in people with diabetes (2, 3). NAFLD encompasses a spectrum of severity, ranging from simple steatosis to the more advanced form, nonalcoholic steatohepatitis (NASH). NASH occurs in ~30% of patients with NAFLD. It significantly increases the risk of cirrhosis, and its complications include portal hypertensive bleeding, hepatocellular carcinoma, and hepatic decompensation (4). It is predicted that NAFLD will become the main risk factor for hepatocellular carcinoma, the most common form of liver cancer (5). Furthermore, NASH cirrhosis has become a common indicator for the need of liver transplantation (1).

Effective pharmacotherapy for NAFLD is limited. Both pioglitazone and vitamin E improve steatohepatitis in nondiabetic patients with biopsy-proven NASH; however, long-term efficacy and safety with both agents are lacking (6). Consequently, lifestyle modifications are the cornerstone of therapy, with the only currently proven treatment for NAFLD being weight loss (7). A reduction in body weight of 3–5% may improve hepatic steatosis, but more significant weight loss (5–10% body weight) is needed to reduce hepatic inflammation (6, 8). Bariatric surgery is not necessarily effective in NAFLD,

ESG was supported by an Australian Government Research Training Program Scholarship.
Author disclosures: ESG, AF, CI, AJN, MR, SS, SKR, and ACT, no conflicts of interest.
Supplemental Table 1 is available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/advances/.
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Abbreviations used: MetS, metabolic syndrome; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; RCT, randomized controlled trial.

as rapid weight loss does not seem to impact fatty liver as it does other metabolic risk factors (6).

Observational studies assessing diet have identified that there are distinct dietary patterns that are likely to prevent the onset of NAFLD (9–11). As such, diet is an important and modifiable risk factor, but despite this there are a lack of practical evidence-based guidelines to support dietary principles that are appropriate and effective for the prevention and management of NAFLD (12).

Recent reviews have demonstrated the vast health benefits associated with particular dietary patterns, such as the Mediterranean diet, in chronic disease management (13). Evidence for the effects of dietary interventions on NAFLD is evolving, although the majority of evidence is derived from observational and large prospective trials (14, 15). Randomized controlled trials (RCT) are few, and need to be repeated with longer duration and focus on functional liver outcomes.

The aims of this paper were to report the current evidence for the effects of dietary intake in adults with NAFLD and translate these dietary recommendations to guidelines for clinical practice. This paper provides practical recommendations for clinicians rather than a comprehensive review (16, 17).

Methods

Dietary recommendations were developed based on a formal review of recently published literature on the topic, a standard definition of NAFLD, and acceptable outcome measures to infer a probable benefit in NAFLD patients.

Formal review of recently published literature

A formal review of literature on the topic published within the last 10 y (from January 2006 to May 2017) was conducted using PubMed, Medline, Embase, and Google scholar. Exclusions included papers in languages other than English and studies that were not conducted in adults and animal studies. Search terms included keyword searches: *("NAFLD" OR "nonalcoholic fatty liver" OR "Fatty Liver" OR "NAFL disease" OR "NASH" OR "nonalcoholic steatohepatitis" OR "liver steatosis" OR "liver cirrhosis") AND ("Diet*" OR "Diet* pattern" OR "diet* intervention*" OR "nutri*," OR "nutrition therap*," OR "food*" OR "lifestyle").* The search strategy was developed in PubMed and adapted for the other databases. It was complemented by a comprehensive search for gray literature, including but not limited to government reports, references from cited articles and conference proceedings.

Standard definition of NAFLD

A standard definition of NAFLD encompassing imaging as well as the gold standard, liver biopsy, was included to ensure all key dietary intervention studies were captured. This definition was based on the following criteria: evidence of hepatic steatosis by either imaging [intrahepatic fat content ≥5% as assessed by proton magnetic resonance spectroscopy or determined by ultrasound or computed tomography using standard protocols (18, 19)] or biopsy and no presence of other causes for secondary liver fat accumulation.

Acceptable outcome measures

Studies included were conducted in NAFLD patients. Acceptable outcome measures to infer a probable benefit in NAFLD patients included the following: *1*) liver-specific outcomes assessing markers of liver integrity and function; and *2*) metabolic markers which have a proven association with NAFLD, such as components of metabolic syndrome (MetS).

Consistent with dietary guidelines and recommendations developed for other conditions, including Alzheimer disease and depression (16, 17), 3 philosophies were applied to develop these recommendations: *1*) the recommendations should be based on considerable evidence of benefit, although they may not necessarily be conclusive; *2*) the recommendations when applied should not lead to any risk of harm; and *3*) the recommendations should be modified to reflect future advances in scientific evidence as new literature emerges.

To best characterize the evidence cited and used to support these recommendations, the authors have adopted the classification system used by the Practice-based Evidence in Nutrition (PEN) working group based on published grading principles (20–24). The PEN grading system classification of the strength of recommendations is described in **Supplemental Table 1** (25). The recommendations were graded based on in-depth discussion with 4 of the authors. This was then disseminated to the remaining 4 authors for consultation, before consensus was reached and grades were assigned.

Results

The following 5 recommendations have been developed based on available evidence:

1. ***Follow traditional dietary patterns, such as the Mediterranean diet, which is high in antioxidants and is anti-inflammatory.***

This diet is plant based, high in antioxidants and anti-inflammatory. Evidence suggests that this dietary pattern may be protective against NAFLD and associated risk factors.

While there is a body of literature assessing the effect of the Mediterranean diet on cardiovascular disease, along with cardiac and metabolic risk factors, assessment of liver-specific outcomes are lacking. A meta-analysis conducted on MetS showed that there were significant benefits from adherence to a Mediterranean diet, but as the meta-analysis did not look at liver-specific outcomes, it did not rank highly in terms of generalizability and applicability. The studies analysed included 1 longitudinal trial (9), 1 case-control study (26), and 3 RCTs (27–29), which showed consistent results that were used to determine the evidence grade.

Evidence Grade: B

2. ***Limit excess fructose consumption; avoid processed foods and beverages with added fructose.***

Fructose is prevalent among highly processed foods and offers negligible nutritional value. It has also been linked with increased incidence and severity of NAFLD.

There were 4 cross-sectional studies (30–33) and a systematic literature review encompassing 13 controlled trials, which examined the impact of fructose consumption on NAFLD (34). Despite the large number of trials, there was substantial heterogeneity with regard to duration and fructose concentration, which reduced the nominated evidence grade.

Evidence Grade: B

TABLE 1 Key dietary recommendations for practice

Follow traditional dietary patterns (9, 27)	• Consume a diet that is mainly composed of plant-based foods: legumes, vegetables, fruits. • Consume small amounts of meat, especially red meat.
Limit fructose from processed foods and soft drinks (30, 32–34, 45)	• Avoid highly processed foods which contain added fructose, including the ingredients "high fructose corn syrup" and "glucose fructose syrup." • Avoid sweetened beverages.
Increase consumption of ω-3 PUFAs and MUFAs (27, 35–37, 46–48)	• Consume fish 2–3 times/wk, especially oily fish such as salmon, sardines, trout, flathead, gemfish, tuna, mackerel, or herring. • Use extra virgin olive oil as the main added fat, especially for dressing salads and vegetables. • Consume nuts and seeds as snacks daily.
Increase consumption of high-fiber foods (15, 35, 38, 39, 49–54)	• Eat vegetables with all main meals, ensuring they compose the majority of the dish, and choose a variety of colors. • Choose whole grain varieties of breads and cereals. • Have legumes 2–3 times/wk in place of meat. • Have fresh fruit daily. • Consume nuts and seeds as snacks daily.
Limit consumption of highly processed foods (55–57)	• Avoid food that is highly processed or refined. • Avoid foods that contain large amounts of added sugar. • This may include: fast food, commercial bakery goods, and sweets.

3. ***PUFAs, especially long-chain ω-3 rich foods, and MUFAs should replace SFAs in the diet.***

PUFAs (especially ω-3 FAs) and MUFAs are linked with lower incidence and severity of NAFLD and associated risk factors, especially when used as replacements for SFAs.

There is a body of literature assessing replacement of SFAs with PUFAs and/or MUFAs in NAFLD patients that demonstrates benefits on cardiac and metabolic risk factors. Assessment of liver-specific outcomes, however, are lacking. There were 3 cross-sectional studies, 1 focusing on MUFAs and PUFAs as part of the whole diet and 2 specifically assessing ω-3 PUFAs (35–37), and 1 longitudinal trial. ω-3 PUFA was protective (9, 35). One RCT also looked at MUFAs and PUFAs as part of the whole diet (27) and showed that they had consistent benefits with regard to incidence and severity of NAFLD, justifying the evidence grade for this recommendation.

Evidence Grade: B

4. ***Replace processed food, fast food, commercial bakery goods, and sweets (i.e., discretionary foods) with unprocessed foods high in fiber, including whole grains, vegetables, fruits, legumes, nuts, and seeds.***

These plant-based foods are high in fiber and are nutrient dense, so should form the majority of the diet. They are also high in phytochemicals and antioxidants, which are likely to be protective against the oxidative stress that underpins the presence and progression of NAFLD and associated risk factors. Conversely, discretionary foods are nutrient-poor foods that contain excessive amounts of added sugar, refined carbohydrates, SFAs, and *trans* FAs. There is extensive evidence of a negative association between whole grains, vegetables, and fruit intake and the presence of NAFLD and related metabolic risk factors.

Studies in NAFLD patients demonstrated health benefits with increased consumption of high-fiber foods and reduced consumption of refined and/or processed foods. As with the previous recommendations, liver-specific outcomes are lacking, although improvement of associated risk factors, including cardiovascular risk factors, using these dietary improvements are promising. One cross-sectional study (35), 1 case-control study (38), and 1 parallel RCT (39) showing consistent benefits were used to determine the evidence grade for this recommendation. The controlled trials on NAFLD patients cited for recommendations 1 and 3 should also be considered here as participants consumed a plant-based diet high in fiber (26–28, 40).

Evidence Grade: B

5. ***Avoid excess alcohol consumption.***

Excess alcohol consumption is the cause of alcoholic fatty liver disease. In NAFLD, excess consumption of alcohol is likely to increase the risk of more advanced and severe liver outcomes. A systematic review including 18 studies (41), 2 additional cross-sectional studies (42, 43) and 1 longitudinal study (44) demonstrated that the relation between alcohol consumption and liver damage is nonlinear. Much of the inconsistency in the findings was with the impact of alcohol consumption of <40 g/d, regardless of gender. Regular consumption of >40 g/d is consistently reported to be detrimental, as reflected in the evidence grade assigned. In the absence of studies assessing excess alcohol consumption in individuals with NAFLD, this recommendation had reduced weighting for generalizability and applicability.

Evidence Grade: B

Table 1 provides key recommendations for practice based on the 5 key practical recommendations developed.

These recommendations are intended for use by physicians and allied health professionals, and provide evidence-based guidance for dietary changes to prevent and manage NAFLD.

Discussion

The rationale for each of the recommendations is discussed concisely below and a summary of the proposed mechanisms for each of these recommendations is presented in Table 2.

1. ***Follow traditional dietary patterns, such as the Mediterranean diet, which is high in antioxidants and is anti-inflammatory.***

A large body of consistent evidence demonstrates that traditional diets rich in fruit, vegetables, legumes, whole grains, fish, and dairy are associated with a reduced incidence of chronic diseases (77). The Mediterranean diet encompasses these principles, and is both high in antioxidants and anti-inflammatory. The majority of the diet comprises plant-based foods, including plant-based protein sources, especially legumes. The Mediterranean diet also includes moderate amounts of fish and small amounts of red meat and processed food. It is a high-fat diet, with fat comprising 35–45% of the total energy intake, at least half of which should be from MUFAs. Carbohydrates compose 35–40% and protein 15–20% of the energy intake (78). The definition of the Mediterranean diet and the dietary indexes which measure it vary across the literature. Twenty-two indexes that quantify compliance with the definition have been described (79). Consideration of the specific food components included within each of these indexes and the methods used to deduce adherence should be noted when interpreting results. In a study involving almost 350 participants, people with NAFLD consumed 27% more meat than healthy participants (mean intake: 33.3 ± 22.8 compared with 26.2 ± 17.9 g/d, respectively; OR: 1.37; 95% CI: 1.04,1.83; $P < 0.001$) (9). A meta-analysis assessing the Mediterranean diet included 50 studies and 534,906 people, and found that adherence was associated with reduced risk of MetS (log HR: −0.69; 95% CI: −1.24, −1.16) (52).

A small preliminary cross-over study found that a Mediterranean diet intervention significantly reduced intrahepatic lipids compared with a standard low fat diet, by 39% compared with 7%, respectively, over a 6-wk intervention period (27). These results have been supported by 2 subsequent RCTs, which consistently demonstrated benefits in both the risk and the severity of NAFLD (28, 29). One case-control study showed that higher adherence to the Mediterranean diet was not associated with lower incidence of NAFLD. However, there was an association with reduced insulin resistance and less severe liver disease among patients with NAFLD (26). These results need to be replicated in larger participant groups and over a longer period of time.

Of note is the emerging research on the Dietary Approaches to Stop Hypertension (DASH) diet and NAFLD. As additional evidence emerges, this may be considered in revised recommendations (80, 81).

2. ***Limit excess fructose consumption; avoid processed foods and beverages with added fructose.***

Trials that elicit adverse health outcomes predominantly include large quantities of added fructose, which may be excessive (>20% energy consumed or ∼100–220 g/d) compared with average human consumption (34). It is unlikely that these levels of intake can be achieved through unrefined food sources such as fruit. Shifts in food production have seen increased use of high-fructose corn syrup and the addition of fructose as a sweetener. These are predominantly present in highly processed products such as soft drinks, juices, breakfast cereals, and pre-packaged food (82).

Cross-sectional trials have demonstrated that fructose ingestion, particularly through soft drink consumption, is an independent risk factor for the development of NAFLD even in people without pre-existing risk factors for MetS (30–33).

A systematic review of controlled trials assessing fructose consumption on markers of NAFLD was conducted in 260 healthy participants across 13 trials (34). Studies tended to be short in duration (1–10 wk), with small sample sizes (mean $n = 16$), and lacked histopathologic markers of fatty liver. The results showed that isocaloric exchange of fructose for other sources of carbohydrate in the diet did not induce NAFLD. Where fructose provided excess energy at extreme doses, there were increases in intrahepatocellular lipids and alanine aminotransferase—a result that may have resulted from excess energy consumption rather than fructose (34). While more clinical trials with long-term follow-up are required to understand the link between fructose consumption and NAFLD, the current literature suggests that excessive fructose intake (>20% energy consumed or ∼100–220 g/d) may have an adverse impact on both the incidence and the progression of the disease. Processed foods, including soft drinks that are sweetened with fructose, tend to be nutrient poor and are of little nutritional benefit, so they should be avoided. Excessive intake of processed foods sweetened with fructose can lead to weight gain, which in turn increases the risk of developing NAFLD (34).

3. ***PUFAs, especially long-chain ω-3–rich foods, and MUFAs should replace SFAs in the diet.***

Saturated fat

There is sufficient evidence to suggest that replacing SFAs with PUFAs can improve cardiovascular disease outcomes, including improvements in cardiac event rates, lipid profile, blood pressure, anthropometry, and blood glucose concentrations (69, 83, 84). Given that NAFLD shares many of the same pathophysiologic mechanisms and that there is an increased risk of cardiovascular disease outcome in this patient group, intake of SFAs should be limited (83, 84). Evidence surrounding the positive effects of PUFAs and MUFAs are discussed below. The literature indicates that these fat sources should be preferentially consumed in place of saturated fat (69–71).

Polyunsaturated fat

ω-3 FAs (alpha-linolenic acid, eicosapentaenoic acid and docosahexaenoic acid) and ω-6 FAs (arachidonic acid) are part

TABLE 2 Proposed mechanisms for nutrients, foods and dietary patterns in NAFLD[1]

Dietary components	Association with NAFLD risk	Mechanism of dietary characteristic	Mechanism in NAFLD
Traditional Mediterranean dietary pattern[2]	⇓ Possibly reduces risk and/or disease severity (9, 26–28, 40)	Plant-based diet, mainly vegetables, fruit, and legumes, which are high in antioxidants and anti-inflammatory (58). Legumes have been specifically identified as the most predictive dietary component for longevity (59).	Carotenoids, folic acid, and fiber, may play a fundamental role in the prevention of oxidative stress (60). Vegetables provide an important source of phytosterols, which have been associated with reductions in serum cholesterol concentrations and cardiovascular risk (61).
Dietary fiber	⇓ Possibly reduces risk and/or disease severity (35, 49, 50)	Foods which are unrefined, naturally high fiber may stimulate gut microbiota, leading to increased production of SCFAs, phytochemical composition (vitamins, phenolic acids, betaine) (62).	Increased whole grain, vegetable, legume, and fruit consumption has been shown to reduce the risk of type 2 diabetes mellitus, CVD, and all-cause mortality, and significantly lower concentrations of fasting glucose and total and LDL cholesterol (51, 53). Reduced coronary heart disease rates are associated with increased legume consumption, specifically high plant-based diets providing high antioxidants; vegetables and fruits are the main source of phenolic compounds, and whole grains are an important source of cereal fiber, vitamins, minerals, lignans, and other phytochemicals (54). Animal models demonstrate a possible protective effect of prebiotic fibers, which may modulate the human microbiome to improve health outcomes in individuals with NAFLD (63).
Long-chain ω-3 FAs	⇓ Possibly reduces risk and/or disease severity (35–37, 46, 47)	ω-3 Foods, especially from marine sources, have vascular and anti-inflammatory properties that likely attenuate the oxidative stress that leads to liver apoptosis (64).	Increased ω-6 FAs may increase production of proinflammatory arachidonic acid-derived eicosanoids, impairing the regulation of hepatic and adipose function, which leads to an increased risk of NAFLD (64, 65).
Monounsaturated fats, e.g., olive oil	⇓ Possibly reduces risk and/or disease severity (27, 48)	Olive oil, especially extra virgin olive oil which contains higher amounts of oleic acid, is high in antioxidant phytochemicals. These are likely to attenuate the oxidative stress that leads to liver apoptosis (66).	MUFAs decrease blood triglycerides by increasing fatty acid oxidation through activation of PPARα or by reducing the activation of SREBP and inhibiting lipogenesis (67). Dietary MUFAs activate PPARα and PPARγ, which increase lipid oxidation and decrease insulin resistance, leading to a reduction in hepatic steatosis (67). Oleic acid has been shown to elicit a reduction in LDL cholesterol and TG concentrations without associated reductions in HDL (66, 68).
Saturated fat	⇑ Possibly increases risk and/or disease severity (69–71)	Fatty and processed meats, butter, and commercial bakery goods are high in saturated FAs and pose inflammatory and insulin-antagonizing effects, which contribute to the development of MetS.	SFAs induce endoplasmic reticulum stress and cell death in liver cells (72). Mechanisms responsible include: accumulation of diacylglycerol and ceramide; activation of NF-κB, protein kinase C-θ, and mitogen-activated protein kinases, and thus induction of inflammatory genes in white adipose tissue, immune cells, and myotubes; decreased activation of PPARγ coactivator-1 α/β and production of adiponectin, leading to decreased oxidation of glucose and FAs; and accumulation of immune cells such as macrophages, neutrophils, and bone marrow-derived dendritic cells to white adipose tissue and muscle (73).
Fructose	⇑ Possibly increases risk and/or disease severity (30, 32–34, 45)	Processed foods, especially soft drinks, promote liver fat accumulation through de-novo lipogenesis of fructose in the liver (74).	Liver fat accumulation may be attributed in part to excess dietary sugar consumption, especially from fructose, which increases the levels of enzymes involved in hepatic de-novo lipogenesis, which is already enhanced in individuals with NAFLD (75, 76).

[1] CVD, cardiovascular disease; MetS, metabolic syndrome; NAFLD, nonalcoholic fatty liver disease; SREBP, sterol regulatory element binding protein.
[2] Mechanisms listed for all other dietary components are also applicable to the Mediterranean dietary pattern which encompasses these components.

of the PUFAs group. Traditional diets have an ω-6–to–ω-3 FA ratio close to 2:1, whereas Western diets report a ratio closer to 20:1 (58). Evidence demonstrates that in the westernized regions of Australia, Europe, and North America consumption of ω-3 FAs is estimated to be 0.19, 0.15, and 0.25 g/d, respectively (85). These values are below the recommended adequate intake of 0.25–2 g/d (86, 87).

There is a lack of trials evaluating the impact of ω-3 FAs consumed as a part of a whole diet, which may be more protective than supplementation (88). Cross-sectional studies demonstrate higher rates of NAFLD with lower intakes of oily fish rich in long-chain ω-3 FAs (9, 35–37) and higher intakes of meat containing saturated fat (9, 35).

It is likely that an increase in dietary marine ω-3 FAs would be beneficial given the benefits seen from supplement trials, which indicate overall that an increased dose is associated with reduced hepatic steatosis (47). More research is required to assess the metabolic and liver-specific benefits of increasing dietary ω-3 FAs.

Monounsaturated fat

Meta-analyses including evidence from observational trials and RCTs show that MUFAs, particularly when consumed as a part of a Mediterranean diet, reduce risk factors associated with MetS (89–92). Evidence from a number of epidemiologic and human clinical trials have demonstrated that MUFAs promote improved lipid profile, blood pressure, insulin sensitivity, and glycemic control (93–96). These findings were seen in a crossover study in which hepatic steatosis and associated risk factors were improved in patients with NAFLD who consumed a high-MUFA diet containing extra virgin olive oil, which is likely to have benefits attributable to polyphenols as well as the MUFA content (27, 48). Due to the apparent benefits of MUFAs, and in the absence of any adverse effects, they pose an appropriate alternative to saturated fats. MUFAs are likely to prevent and manage risk factors associated with NAFLD and possibly liver-specific outcomes. RCTs in humans with confirmed NAFLD would help strengthen this recommendation.

Extra virgin olive oil

Olive oil is predominantly composed of MUFAs; the most abundant of the FAs is oleic acid. Other oils that have a high MUFA composition, such as canola, peanut, sunflower, corn, and soybean oils, have not shown the same benefits on chronic disease risk factors (97, 98). Some of the proposed mechanisms are outlined in Table 2. The additional health benefits present especially in extra virgin olive oil may be attributed to the high amounts of antioxidants, α-tocopherol, and phytochemicals. Extra virgin olive oil also contains higher concentrations of phenolic antioxidants than refined olive oil and seed oils (69).

MUFA from olive oil may play an important role in the prevention of NAFLD by managing coexisting risk factors. Further research is required to assess the impact on liver-specific outcomes in order to substantiate effects on liver function.

4. ***Replace discretionary foods with unprocessed foods high in fiber, including whole grains, vegetables, fruits, legumes, nuts, and seeds.***

Whole grains are an important source of fiber, vitamins, minerals, and other food components that contribute to maintaining health (99). A cross-sectional study in 73 adult patients who were diagnosed with NAFLD demonstrated a negative correlation between whole grain consumption and the presence of MetS: increasing whole grain consumption by 1 serving/wk was associated with 8% lower odds of MetS compared with an increase of 1 serving/wk of refined grain consumption, which was associated with 2% higher odds of MetS (35).

A case-control study carried out on 200 adults showed that consumption of whole grains (described as coarse cereals), potatoes, vegetables, and fruit was significantly lower in people diagnosed with NAFLD compared with healthy controls (15.4 compared with 23.4 g/d, 21.0 compared with 25.6 g/d, 435.5 compared with 479.9 g/d, and 89.4 compared with 109.3 g/d, respectively, $P < 0.05$) (38). In a parallel RCT, individuals with NAFLD had poorer-quality diets compared with healthy controls and consumed larger quantities of overall energy, carbohydrate, and fat and less antioxidant vitamins, calcium, and vitamin D (39).

5. ***Avoid excess alcohol consumption.***

NAFLD is diagnosed on the presumption that the subject does not have a history of significant alcohol consumption. While the cutoffs for alcohol ingestion vary globally, the guidelines in Australia recommend $\leq$20 g/d in both genders (100). There is controversy surrounding the consumption of alcohol in NAFLD, stemming from the stigma associated with alcoholic fatty liver disease. There is a comprehensive body of evidence to support the risk of heavy alcohol consumption which suggests that $\leq$40 g of alcohol should be consumed on a single occasion (100, 101).

A systematic literature review of 18 articles including 25,662 cases of hepatic steatosis reported that the association between alcohol consumption and the risk of hepatic steatosis was complex and nonlinear, and demonstrated differences by ethnicity. At moderate alcohol intake ($\leq$20 g/d), studies from Japan showed a favorable reduction in hepatic steatosis (RR for <20 g pure alcohol/d: 0.75; 95% CI: 0.71, 0.79; $I^2 = 0\%$), whereas studies from other areas, including China, Europe, and North America, found no overall association (RR: 1.05; 95% CI: 0.86, 1.30; $I^2 = 84\%$) (41).

A study assessing light to moderate alcohol consumption in 132 participants identified no difference in the severity or stage of liver disease between participants who were grouped as nondrinkers, moderate drinkers (>20g/d) or light drinkers (<20 g/d). This study did, however, demonstrate that the presence of insulin resistance (determined by a homeostatic model of assessment) was similar in moderate and no alcohol consumption (81.3% and 78.7%, respectively) but significantly less in the light consumption group (54%, $P < 0.05$) (42). Heavy and erratic consumption of al-

cohol should be avoided, as a study assessing biopsy-proven NAFLD patients confirmed that heavy episodic drinking (>60 g ethanol/d in men and >48 g/d in women consumed on 1 occasion) ≥1 time/mo was independently associated with significant fibrosis progression ($P < 0.001$) (43). Patients with cirrhosis should avoid alcohol consumption, which was shown to be an independent risk factor for the development of hepatocellular carcinoma in a 5-y follow-up study in which patients reporting any alcohol consumption were at greater risk of hepatocellular carcinoma than those who never drank (HR: 3.8, 95% CI: 1.6, 8.9; $P = 0.002$) (44).

In summary, there is a lack of clinical studies with convincing evidence about the benefits or otherwise of alcohol consumption; however, light or modest alcohol intake (≤20 g/d) does not appear to have adverse health outcomes with regard to NAFLD. In NASH-cirrhosis, avoiding alcohol is recommended owing to the potentially elevated risk of developing hepatocellular carcinoma.

Further Dietary Considerations

Coffee consumption

The impact of coffee consumption on liver disease is a growing area of research. Animal models have indicated that coffee may reduce inflammatory cytokines, alter adipose tissue gene expression, protect against the development of any metabolic risk factors, and reduce liver fat and collagen deposition (102–105), thereby protecting against MetS as well as the development of NAFLD (106). In human trials conducted specifically in those with NAFLD, early evidence from 1902 Japanese people demonstrated by multivariate analysis after adjusting for confounding factors that, except for HDL cholesterol, all components of MetS were significantly ($P < 0.01$) and inversely related to coffee consumption. The frequency of MetS decreased as coffee consumption increased (107). This has been supported by a number of trials carried out across the globe (108–112). A case-control study showed that graded fatty liver involvement, using the bright liver score determined by ultrasound, was significantly lower in all coffee drinkers (>3 cups/d) ($\chi^2 = 15.986$; $P = 0.003$) (109). A subsequent cross-sectional study with almost 350 participants reported no association between coffee consumption and the onset of NAFLD. It did, however, show that coffee consumption may have a prohibitive effect on fibrosis progression in patients with NAFLD when fibrosis was assessed using the FibroTest (based on fasting biochemical markers) (113). A systematic review reported that coffee consumption was inversely related to the severity of steatohepatitis in patients with NAFLD (114). This review also found that there was a decreased risk of progression to cirrhosis, a lowered mortality rate in cirrhosis patients, and a lowered rate of hepatocellular carcinoma development (114). While the findings from this review seem promising, it is worth noting that all of the evidence, with the exception of one trial, was from observational epidemiologic studies, so cause and effect could not be determined. The trials assessing coffee consumption were also heterogeneous, and the quantity as well the potential protective effect of coffee need to be confirmed by clinical trials.

A review of coffee consumption concluded that doses of ≤400 mg/d (up to ~4 cups) were not associated with any adverse effects (115, 116). In the absence of interventional research, routine prescription of coffee is not recommended, although consumption within the aforementioned parameters should not be discouraged.

Additional Comments

Current research into chronic diseases that share pathophysiologic mechanisms with NAFLD demonstrate consistent associations between improved dietary intake and reduced incidence of adverse metabolic outcomes, and these associations are evident across a range of countries, ethnicities, and age groups (117, 118). These outcomes are also consistent with a comprehensive pathophysiologic rationale, and are in line with recommendations to prevent and manage associated comorbidities and chronic diseases (119). Diet can improve multiple chronic conditions and associated risk factors, and is a cost-effective (120), noninvasive, and low-risk intervention that does not cause adverse outcomes. In addition to these dietary recommendations, which are suggested to provide benefits to the hepatic and cardiometabolic risk factors for NAFLD patients, weight loss has been proven to improve liver-specific outcomes (6, 8). These dietary recommendations have been developed to achieve health benefits in the absence of weight loss, which is not easy to achieve or maintain. Nonetheless, provision of these recommendations in conjunction with weight loss will have the most substantial benefit on health outcomes in patients with NAFLD.

Future Considerations

Distinct dietary patterns appear to have favorable effects on NAFLD. This has been affirmed in a number of trials, including cross-sectional trials and a small number of RCTs (26–28, 40). Larger RCTs assessing dietary interventions are needed to confirm cause and effect, and should include measures of functional liver outcomes and longer follow-up to determine sustainability of dietary outcomes. Dietary interventions should be designed and conducted well, and report dietary prescription and adherence to enable translation into future research and clinical practice. Additional research focusing on the impact of the Mediterranean diet on NAFLD is currently underway and may provide more insight into causality (121).

To ensure that future clinical trials in this area are robust and account for probable individual predispositions, the inclusion of genetic analysis in the form of gene expression and/or metabolomics to describe and substantiate responders and nonresponders to various dietary patterns should be considered. The impact of dietary interventions on NAFLD patients with a genetic cause, such as PNPLA3, which confers susceptibility to NAFLD, should also be considered in future research (122). In combination with high-quality dietary interventions, research findings may lead to a better under-

standing of plausible strategies for personalized nutrition to prevention and treat NAFLD patients (123).

There is also emerging evidence of the association between the gut microbiota and liver outcome. NAFLD forms part of a large, complicated array of metabolic diseases, which are likely to be the product of numerous perturbations resulting from a cascade of factors, including gut microbiota, which is largely influenced by diet (124). Therefore, modulation of the gut microbiome through diet may be an important consideration for future research targeting the prevention and treatment of NAFLD and associated risk factors (123).

Conclusions

Dietary patterns captured within these recommendations are likely to reduce the onset and progression of NAFLD. Following these recommendations is also likely to have a positive effect on other associated chronic diseases, such as type 2 diabetes and cardiovascular disease. There is a need for additional high-quality research assessing diet and NAFLD, in particular with direct measures of liver function and disease severity in NAFLD patients. These recommendations should be revised in the light of emerging evidence to ensure they remain best practice.

Acknowledgments

All authors read and approved the final manuscript.

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