

## Diet and non-alcoholic fatty liver disease, a short narrative review

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### Abstract

The growing importance of non-alcoholic fatty liver disease (NAFLD), the biggest non-communicable liver disease, inherently leads to an increased attention to lifestyle and diet that are closely intertwined with NAFLD. Elements of the Western diet such as saturated fats and carbohydrates and thus soft drinks, red meat and ultra-processed foods are linked to NAFLD. Contrarily, diets rich in nuts, fruits, vegetables and unsaturated fats as seen in the Mediterranean diet are linked to less prevalent and less severe NAFLD. In the absence of approved medical therapy for NAFLD, therapy mostly focusses on lifestyle and diet. This short review tries to provide a succinct overview of the current knowledge on the influence of certain diets or individual nutrients on NAFLD and discusses different dietary approaches. It ends with a short list of recommendations that can be used in daily practice. (*Acta gastroenterol. belg.*, 2023, 86, 306-310).

**Keywords:** NAFLD, diet, lifestyle, review, mediterranean diet, recommendations.

### Introduction

The importance of non-alcoholic liver disease (NAFLD) as the largest non-communicable liver disease is undeniable and increasingly recognised by hepatologists, but also other medical specialists and even by policy makers (1). NAFLD encompasses a spectrum of disease going from simple steatosis via non-alcoholic steatohepatitis (NASH), where steatosis is accompanied by hepatocellular ballooning and inflammation, to fibrosis or cirrhosis (2). NASH and/or significant fibrosis (*i.e.*  $\geq$ F2) are associated with increased risk for end-stage liver disease, hepatocellular carcinoma and an high risk for cardiovascular or oncologic diseases (3,4). Consequently, finding and treating these patients is of importance (2).

As implied by the term non-communicable the environment and in case of NAFLD the diet and lifestyle of a patient, next to (genetic) susceptibility, are the main drivers of this disorder. This is also reflected in the vivid debate on the name and definition of the disease, where some propose to use metabolic-associated fatty liver disease (MAFLD) instead of NAFLD to reflect the observed and associated metabolic alterations (5,6).

In the absence of currently approved medicines for the treatment of NAFLD (7), therapy is now limited to the control of metabolic co-morbidities and lifestyle modification encompassing physical activity and diet.

This short review aims to describe the current knowledge on the impact of certain dietary habits and interventions on NAFLD in a succinct way.

### The impact of dietary habits on NAFLD

Many literature reviews, systematic reviews and meta-analysis are published on NAFLD and certain diets or food products (8-19). Most of the individual studies are observational while substantially less are randomised controlled trials (RCT). As a result, next to many challenges peculiar to nutritional studies, there is a wide array of outcomes described. Sometimes even contradicting each other. Moreover, one must be aware that described correlations are not always causal relations (20).

A meta-analysis of 60 observational studies found that total calorie intake was significantly higher in patients with NAFLD compared to controls. No differences could be found comparing individual macronutrient intake (proteins, carbohydrates, fat including comparison between saturated, poly- and monounsaturated fats) and micronutrient intake, nor in coffee or tea consumption (8). Patients with NASH had a non-significant trend towards lower total calory intake compared with patients with NAFLD, while intake of macro- and micronutrient intake was found similar (8). Given the variability of reported outcomes this meta-analysis was faced with important heterogeneity and robust conclusions cannot be drawn, *e.g.* the absence of differences in total and subtypes of fat intake might imply that low-fat diets are not more favourable than any other hypo-caloric diets (8). Others, while subscribing the concept that total energy intake *per se* rather than fat intake is key, conclude that the composition of dietary fat influences hepatic fat content. The intake of saturated fats is associated with hepatic fat content, while no firm conclusion was made on the dietary intake (not the supplementation with) mono- and polyunsaturated fats (21). Micronutrient deficits are described to be related to hepatic dysfunction and could

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Submission date: 29/01/2023

Acceptance date: 02/03/2023

be linked to NAFLD (9). Whereas the aforementioned meta-analysis did not detect a difference in micronutrient intake, a recent study on the antioxidants vitamin E and C found that sufficient vitamin E intake was associated with lower risk of NASH, intake of vitamin C was weaker associated with lower risk of both NAFLD and NASH (22).

When focussing on the macronutritional composition of the diet, comparing RCT's with isocaloric diets, it is found that unsaturated fats (mostly poly-unsaturated fats) and proteins over carbohydrates reduced liver fat content, while there was no difference when comparing high-carbohydrate/low-fat vs. low-carbohydrate/high-fat diets (10). The latter was recently confirmed with no significant differences in the NAFLD group, despite improved glycaemic and weight control in patients with low-carbohydrate/high-fat compared with high-carbohydrate/low-fat diet for 6 months (23).

The metabolic pathways affected by certain macronutrients contributing to liver fat also differ, so do carbohydrates induce de novo lipogenesis in the liver, while fats increase adipose tissue lipolysis with consequent increased hepatic Influx of fat (11,24).

When zooming out to the diet and the different food groups, meta-analysis identified that consumption of nuts had a negative association with NAFLD, while both red meat and soft drinks (also called sugar sweetened beverages) had a positive association. The majority of the food groups, *e.g.* grains, eggs and dairy were neutral. If only cross-sectional studies were included, both vegetables and fruits were also negative associated with NAFLD (12). Ultra-processed foods are increasingly acknowledged to be associated with chronic diseases. They can be defined as foods that are industrial processed, often with sophisticated formulations, and by design contain low-cost ingredients, have a long shelf life and are ready to consume hyperpalatable foods. As such they form a group of high energy dens products with low nutritional quality (25). When healthy volunteers are challenged with ultra-processed foods compared to matched unprocessed diets, ad libitum food intakes increases from day 1 resulting in a significant different weight (ca. 2kg) already after 14 days (26). An increasing proportion of ultra-processed foods in the diet is also related to a higher risk for NAFLD (27). Fast food is a perfect example of ultra-processed food and is, especially in patients with diabetes or obesity, linked with steatosis (13).

In line with the above it is not unsurprising that diets that are rich in processed foods, red meat and dairy, and low intake of fruits and vegetables (so-called Western diets) can be linked with an increased risk for NAFLD (+56%). Similarly, diets that are considered either prudent or Mediterranean, containing high levels of fruits, vegetables, white meat, olive oil and fibres were linked with decreased risk for NAFLD (risk -22 to -23%) (14).

Finally, though non-alcoholic implies only limited alcohol intake a recent study demonstrates that there is a considerable number of patients with either moderate or even excessive alcohol use when screened for alcohol intake with alcohol metabolites (28). Alcohol contains a lot of empty calories. Furthermore, concomitant alcohol use (even within generally accepted safe amounts of <210g/week) has also been proven to be synergistically harmful in combination with obesity or type 2 diabetes mellitus leading to more NAFLD and more advanced fibrosis (29, 30).

A summary of the different observations is presented in figure 1.

### Dietary interventions in NAFLD

The goal of dietary/lifestyle interventions is to try to reverse or reduce the degree of steatohepatitis and to halt or even regress fibrosis, the two elements associated with co-morbidities and mortality, being in line with the primary end points in NAFLD trials. Other goals are the improvement of the cardiometabolic profile and reduction of the HCC risk (31,32). Goals are achieved by weight loss, improved glycaemic and lipid control and improvement of arterial blood pressure. Even a modest weight loss can already achieve important health benefits, improvement of steatosis can be observed from  $\geq 5\%$  weight loss, while a sustained weight loss of  $>10\%$  is able to reverse NASH or to improve fibrosis (31,33). This implies that in absence of a current approved drug for NAFLD (7) achieving weight loss is the primary goal of therapy.

Many interventional studies in NAFLD are not solely diet based but also encompass physical activity/exercises, hence making it difficult to distillate the effects of a diet as such. Even the best studied diet, the Mediterranean diet, is strictly a lifestyle with inclusion of regular physical activity. Regardless, there is enough evidence in observational and interventional studies to support the effect of diets at themselves. Likewise, there is also evidence that physical activity or exercise at itself can improve steatosis, hepatocellular ballooning or fibrosis independently (34). Moreover, and importantly, the effects of diet and physical activity work synergistically (35). For example, in a study that investigated the effect of diet with or without physical activity the Mediterranean diet decreased ectopic fat (in liver and extrahepatically) more than an isocaloric diet low in fat. Physical activity enhanced visceral adipose tissue loss and prevented rebound weight gain (36).

Several detailed reviews provide an extended and in depth background on the evidence for the use of certain diets in NAFLD (15,16,37). Evidence can be briefly summarised as follows:

- The Mediterranean diet is the most studied diet so far. It provides a diet rich in fruits and vegetables, whole grains and the use of olive oil. Furthermore, it means frequent consumption of white meat/sea foods and a

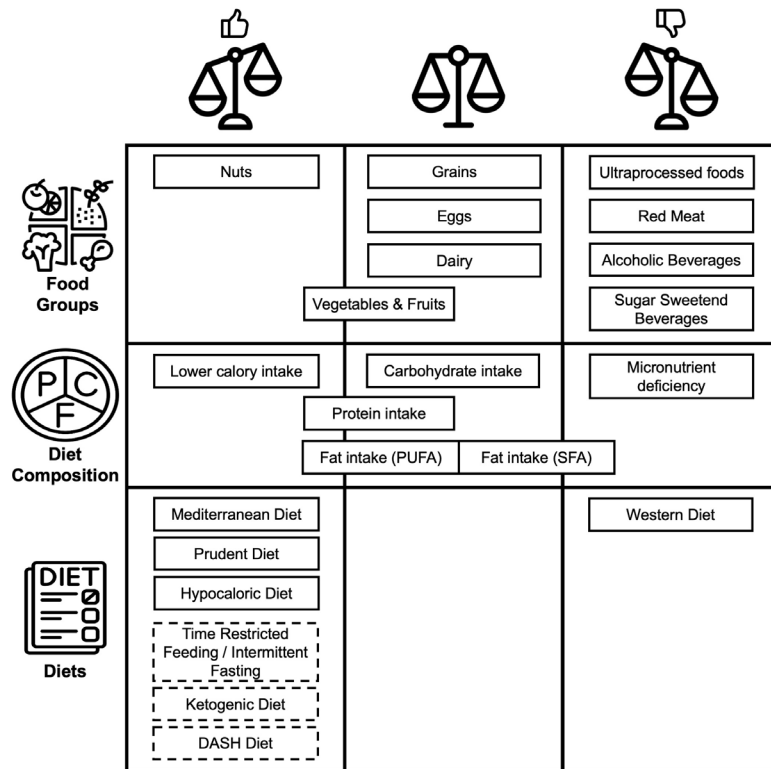


Figure 1. — Schematic overview of the observations and interventions that associate with higher or lower risk of NAFLD Associations are organised by a lower or higher risk, or a neutral association with NAFLD and presented in 3 levels reflecting either certain food groups, individual nutrients that compose diet and diets itself. See the main text for detailed description. Diets in dashed boxed have less or weaker evidence on their effects. PUFA, poly-unsaturated fatty acids; SFA, saturated fatty acids; DASH, dietary approach to stop hypertension.

limited intake of red meat and sweets. Consequently this diet is also characterised by high content of fibres and low content of refined carbohydrates (31). The Mediterranean diet is related to a lower prevalence and severity of NAFLD (38). The Mediterranean diet can improve steatosis, even without the reduction of weight loss *per se* (39). Other indices of the liver such as transaminase levels or liver stiffness reduced as well with the Mediterranean diet (17). Finally, the beneficial effects of this diet on metabolic health, diabetes and cardiovascular disease are well established (18).

- As discussed above total energy intake and weight loss *per se* are key determinants for the risk of NAFLD. Hypocaloric, or calory-restricted, diets are defined by an energy deficit of average 500 kcal/day, but restrictions can be higher. These diets induce weight loss effectively corresponding to biochemical and histological improvements in a dose-dependent way (17,33). Note that both the Mediterranean and the hypocaloric diets had an acceptable attrition rate of 14%, implying that long term adherence is feasible (17).
- The ketogenic diet is an example of a low-carbohydrate diet where carbohydrates are limited to maximum 40% of total daily energy intake that at itself can be additionally restricted (*i.e.* hypocaloric)

as well (15). In patients with obesity there is evidence of improved metabolic parameters (40). Data in patients with NAFLD are scarce but seem to point to weight loss and the loss of intrahepatic fat but not improved serum liver biochemistry (19,41,42).

- The DASH (dietary approach to stop hypertension) diet is a low energy-dense diet with a low glycaemic index originating within the cardiovascular field. It has some similarities with the Mediterranean diet with high intake of fruit, vegetables and whole grains, and with low intake of fat products, added sugars or red/processed meat (15). It is not much studied in NAFLD but the available evidence points to an reduced risk for NAFLD and an improved metabolic profile (43, 44).
- Time restricted feeding/intermittent fasting are characterised by regular periods of fasting either as a part of the day, either whole days (15). Via the activation to the metabolic switch where fatty acid-derived ketones become the preferential energy source, these regimens lead to weight loss and metabolic improvements. Fasting approaches (by alternate fasting or 5:2 diet) in patients with NAFLD lead to rapid improvement of dyslipidaemia, weight loss and lead to reduced steatosis (42,45). Beneficial effects might be enhanced when combined with exercise (46). Importantly, intermittent calory

restriction is better tolerated than a ketogenic diet (42), hence implying that these diets might become superior on the long-term.

The position of the different discussed diets with respect to NAFLD is presented in figure 1.

### Conclusions and practical advice

Since the best evidence exists on the Mediterranean diet in NAFLD and its proven benefits on diabetes and cardiovascular diseases, the guidelines recommend the use of this diet (31,32). Though, it is acknowledged that many diets are faced with challenges related to long term adherence, costs (on average healthy foods are more expensive) or balanced nutrition (*i.e.* too restrictive) (47). Magical diets do not exist, but diets that are tailored to the patients' needs and beliefs will charm the most and are likely to have success. In other words, the best diet is the patients preferred diet. One must aim for diets that are adhered and maintained and even might lead to lasting behavioural changes. It makes sense that in this tailored diet weight loss is pursued, food that is associated with NAFLD or worse outcomes is avoided and food that is linked to the opposite is favoured.

Of note, this review did not include or discuss NAFLD-cirrhosis as this has a specific approach. Specific guidelines, including some dedicated sections on patients with obesity or NAFLD exist (32,48).

An approach with SMART (specific, measurable, achievable, relevant, timely) goals can help to induce and uphold the right changes. Based on the current evidence table 1 gives a set of ready to go and easily implemented recommendations to improve dietary/lifestyle habits of patients with NAFLD.

### Acknowledgements

The author wishes to thank Jolien Derdeyn for reading the manuscript and her valuable feedback to improve the manuscript.

### Conflict of Interest

The author declares not have a conflict of interest related to this paper.

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Table 1. — Recommendations for daily practice

Be supportive and realistic <i>E.g.</i> A smaller weight goal that is easier achieved and maintained might be more successful and propel further weight loss
Give practical and understandable advice
Organise follow-up to evaluate the effect and motivation, adapt strategy if needed
Do not judge if a patient does not reach his goal (yet) or makes a mistake, turn it into a teaching point
Allow certain 'forbidden fruits' with large social or mental impact (though on the premise of infrequency or exception) <i>E.g.</i> religious meals or birthday parties
Stimulate the intake of vegetables, fruits, nuts, plant-based proteins
Stimulate 'flexitarianism' <i>E.g.</i> skip any meat 1-2 days a week, eat more often white instead of red meat
Stimulate and look for healthier alternatives <i>E.g.</i> an apple instead of a chocolate bar
Discourage (pre)packed and/or processed foods, stimulate self-cooked meals with fresh ingredients
Discourage soft drinks
Discourage intake of 'empty' alcoholic calories
Promote a daily (routine) activity <i>E.g.</i> a walk, biking, hometrainer. Think of the commute ( <i>e.g.</i> bike to work instead of car)

A set of recommendations that can be implemented easily to support the shift to a healthier diet/lifestyle in a patient with NAFLD.

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