

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

185,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Low-Carbohydrate High-Fat (LCHF) Diet: Evidence of Its Benefits

Parijat De and Sagnik Mukhopadhyay

Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/intechopen.73138>

Abstract

Current dietary recommendations state that there is insufficient evidence to prescribe an exact percentage of calories from carbohydrate, protein and fat for people with diabetes from the choice of a variety of popular diets currently available. Over the years, many a research has focused on the relative importance of the right proportion of carbohydrates and fat combination in a balanced diabetic diet. Jury is still out regarding the relative merits and demerits of a diabetic diet – low carbohydrate, high fat or low fat, high carbohydrate diet. Evidence from various studies suggest that low carbohydrate diets improve cardiovascular (CVD) risk through lowering HbA1c levels, improving blood pressure and body weight. There is also a positive effect on lipid profile and reversal of non-alcoholic fatty liver disease (NAFLD). Whilst there are some significant metabolic benefits of LCHF diet, it is accepted that there needs to be more long-term studies before it can be used in daily clinical practice. This chapter focuses on basic physiology and metabolism of carbohydrate and fat content in normal and diabetic patients and a review of the literature on these two diet combinations with current thoughts and evidence on this core issue affecting insulin utilization and metabolic profile.

Keywords: carbohydrate, fat, diabetes, metabolic syndrome, insulin, insulin resistance, weight gain, lipids, NAFLD, cardiovascular disease

1. Introduction

Diet in diabetes has always been an area of much discussion. This is even more so now as there has been a lot of interest and research focusing on the relative contributions of carbohydrate and fat in diabetic diet affecting the overall metabolic profile. An area of confusion in diabetes diet is carbohydrates—Should one eat carbohydrates and to what extent or avoid

them? Another area that has traditionally always been important, although poorly understood, is the amount and type of fat that needs to be consumed; a lot of research is currently focussed on this matter.

It is currently unclear as to the exact percentage of calories that is required from carbohydrate, protein and fat in the diet for the diabetes patient—this should be based on metabolic needs and targets for the preferred individual. There are a variety of popular diets (low carb, intermittent fasting, low fat, ketogenic, mediterranean, vegetarian, DASH, very low calorie, Adkins, 5:2 and commercial food points) for patients to choose from in order to make informed decisions about their diet.

Over the years, many researches have focused on the relative importance of the right proportion of carbohydrates and fat combination in a balanced diabetic diet with some recent research challenging traditional viewpoint of the importance of one over the other. Jury is still out regarding the relative merits and demerits of a diabetic diet—low-carbohydrate high-fat or low-fat high-carbohydrate diet.

Low-carbohydrate high-fat (LCHF) diets are an upcoming although a debatable topic in current nutrition. Since the publication of Dr. Atkins' Diet Revolution in 1972 [1], LCHF diets have divided the opinion of medical fraternity significantly. Some believe that these diets effectively treat type 2 diabetes mellitus (T2DM), obesity and metabolic syndrome [2, 3], while others consider them too non-conventional and in conflict with current globally accepted dietary guidelines that advocate low-fat high-carbohydrate (LFHC) diets to reduce the risk of cardiovascular disease [4, 5]. Given such conflicting opinions, the medical profession may be unsure how to advise on the right diet for the individual patient with diabetes.

This chapter focuses on the basic physiology and metabolism of carbohydrate and fat in patients with diabetes and reviews the literature on these two diet combinations with current thoughts and evidence on this core issue affecting insulin utilisation in the individual with diabetes.

The aim of this chapter is to provide current thinking and evidence behind LCHF diets and in the process and to provide clinicians with additional evidence to inform their clinical decision-making and understanding the potential benefits of these eating plans for at least some patients.

2. Glycaemic index (GI) and diabetes

Carbohydrates have a direct influence on blood sugar levels—diabetes diet therefore tends to focus either on carbohydrate portion size or the speed at which carbohydrates are absorbed by the body. Patients with diabetes are generally advised to follow a low GI diet rather than a low-carb diet.

The glycaemic index [6] categorises food dependant on the rate at which the body breaks it down to form glucose. High GI foods (white bread, potatoes and biscuits) are those that are quickly broken down into glucose. Low GI foods (whole grain bread, milk, leafy vegetables) are typically those that are broken down more slowly by the body. A low glycaemic index diet is beneficial for people with diabetes in keeping their glycaemic control more stable since they are less likely to cause rapid surges in blood glucose levels compared to high GI foods. Low GI food keeps one more satisfied and makes one feel less hungry before the next meal. Other advantages of lower GI foods include a higher nutritional value, a varied diet and reduced immediate demand for insulin following eating.

3. Carbohydrate controlled diets

A carbohydrate controlled diet is a diet in which carbohydrate intake is either limited or set at a particular value, to help stabilise blood glucose levels in patients with diabetes. Examples of such diets are low-carbohydrate diets, Atkins diet, ketogenic diets, low-carb high-fat diet (LCHF), South beach diet and the Zone diet.

3.1. Fixed carbohydrate diet

This is a diet where intake of carbohydrate is pre-set, thereby offering less flexibility in terms of meals through the day. It is simple to follow and offer consistency and is especially useful for those on fixed-dose insulin regimens. People with type 1 diabetes do need to have competence in carbohydrate counting.

3.2. Restricted carbohydrate diets

Low-carbohydrate diets are a form of restricted carbohydrate diet. Restricted carbohydrate diets set a limit on how much carbohydrate can be consumed over the course of a day or for each meal. This can help reduce hunger and prevent wide swings in blood glucose levels responsible for causing hunger.

If carbohydrate and calorie intake is kept low enough, this form of dieting can not only help maintain good glucose control but also help promote regular ketosis and aid weight loss. It is important to maintain a healthy balance of nutrients including fruit and vegetables.

3.3. Low-carbohydrate diet

Many people with diabetes, both type 1 and type 2, are following a low-carb diet because of its benefits in improving diabetes control, weight loss, flexibility and simplicity. Carbohydrates, like proteins and fats, provide energy to help fuel the body. Carbohydrate is the nutrient which has the greatest effect on blood sugar levels and requires insulin to be produced by the

body. Lowering sugar levels reduces need for insulin and this can also help reduce insulin resistance and improve metabolic profile.

Insulin is also being the fat storage (anabolic) hormone in the body; thus, reducing insulin in the body with a low-carb diet can help with losing weight. People also generally reduce their calorie intake. This together with the satiating influence of fat helps with further weight loss. However, people on medications, such as insulin, sulphonylurea or glinides, should be careful about hypoglycaemia.

Low-carbohydrate diets have been said to provide diabetes patients with more energy levels through the day. There is less craving for sugary and snack foods. As a result of lower glucose results and improved HbA1c, there is clearer thinking process and less 'brain fog'. People have also found that low-carb diets can improve cholesterol and triglyceride levels.

There are various ways of following a low-carbohydrate diet—one will need to cut down on common foods like bread, pasta, rice, potatoes and sweet processed foods. There are a number of other ways to replace starchy foods—such as using swede or celeriac instead of potato and using cauliflower instead of rice. A healthy low-carb diet should also have a strong vegetable intake and moderate protein (unprocessed meat) and fat intake from natural sources (to provide a balance of monounsaturated, polyunsaturated and saturated fat).

In 2015, Diabetes UK launched the Low Carb Program [7], which has helped thousands of people with type 2 diabetes to improve their diabetes control and reduce their dependency on diabetes medication.

The counterargument against low-carb diets for people with diabetes is that there is not enough evidence to support the effectiveness and safety of low-carbohydrate diets in the medium to long term. However, more and more research and evidence seems to be favouring low-carb diets in general.

Diabetes UK has put together a position statement [8] to explain how low-carb diets might be used to help manage diabetes using the best level of evidence from systematic reviews, meta-analyses and randomised controlled trials.

Diabetes UK suggests that low-carb diets can be safe and effective for people with type 2 diabetes. They can help with weight loss and glucose management and reduce the risk of cardiovascular disease. So, they recommend a low-carb diet for some people with type 2 diabetes. But there is no consistent evidence that a low-carb diet is any more effective than other approaches in the long term, so it shouldn't be seen as the diet for everyone. Currently, there is no strong evidence to say that a low-carb diet is safe or effective for people with type 1 diabetes. Because of this, Diabetes UK does not recommend low-carb diets to people with type 1 diabetes.

Evidence for low-carb diets in children reports adverse effects such as poor growth, a greater risk of cardiovascular disease and psychological problems. So, low-carb diets are not recommended for children with diabetes.

4. The controversy about high fat intake

Consuming fats have very little direct effect on blood glucose levels, and as a result does not lead to an increase in insulin levels. The principle of LCHF diet is to replace carbohydrate intake with fat, thus reducing insulin levels and increase the body's ability to utilise its own fat stores for energy.

Metabolic syndrome is a conglomeration of three or more risk factors (elevated waist circumference, elevated triglycerides, low HDL-c, high blood pressure and elevated glucose). Metabolic syndrome is a condition of insulin resistance and can lead to obesity, type 2 diabetes, fatty liver and many other conditions [9]. A LCHF dietary approach can be used to reduce insulin levels and therefore can also be an effective method for treating or preventing the metabolic syndrome [10].

With LCHF diets, there is an increased intake from fats and proteins, and concerns have been raised about the potential dangers of their increased intake. As has been shown a number of times in the past [11–15], a reduction in dietary carbohydrate intake does not necessarily cause a concomitant increase in total fat and protein intake. The absolute amounts of energy intake often remain very similar, as total energy intake decreases on LCHF diets (although proportional amounts of energy supplied from fat and protein increase). Nevertheless, it is this absolute or relative increase in fat intake that causes a lot of anxiety within the medical profession.

Current dietary guidelines do not define a specific limit in terms of fat intake [16, 17]. Moreover, a few articles in the lay and scientific literature suggest that the intake of total fat (mainly, saturated fats) may not need to be limited [2, 18, 19]. American Diabetes Association position statement for type 2 diabetes recommends that a total fat intake of 20–35% may be desirable for reducing the risk of obesity and suggests minimising carbohydrate intake, but it has refrained from specifying ideal amounts of macronutrients [16].

The diet heart hypothesis based largely on Ancel Keys' original Seven Countries Study [20] suggested that saturated fat intake is the direct cause of coronary atherosclerosis. This theory is now being questioned as it is not supported by current evidence [21–31], which finds no association between saturated fat intake and all-cause mortality or progression of coronary atherosclerosis [32]. Instead, higher fat intakes have been associated with lower rates of ischaemic stroke in men [33] as evidenced by a continued decline in coronary mortality in the Japanese with high blood cholesterol levels [34] and high fat intake [35]. To the contrary, it has been shown that LCHF diets sometimes show significant improvements in coronary risk factors [36–39] and the fear of adverse effects from the increased (saturated) fat intake on this diet would appear to be groundless.

Benefits of replacing saturated fats with dietary polyunsaturated fats may not be as strong [40–44] and even harmful [44, 45]. Again, there is no evidence to suggest that the intake of moderate amounts of red meat has detrimental effects on conventional coronary risk factors [46, 47].

5. Low-carbohydrate high-fat (LCHF) diet

Low-carb high-fat diets are gaining popularity in Europe, especially Scandinavia, having originated in Sweden. The LCHF diet has been popularised by Swedish GP Dr Annika Dahlqvist, who has been recommending a low-carb high-fat diet to her patients for some years now. As this was a somewhat revolutionary concept, she had her opposition. The story goes that she was investigated by the Swedish Health authorities for any wrong doing but investigations cleared her based on their findings that her methods were scientifically sound [48].

As the name suggests, the diet suggests eating high fat and low carbohydrate foods. The LCHF diet is different to the Atkins diet as there are no 'stages' to work through, so the diet can be followed indefinitely. People are encouraged to eat full fat versions of dairy food and fatty meats with fat on rather than removing it.

The diet, because of its low requirement for insulin, has been recognised by the Swedish government as being suitable for people with type 2 diabetes and as helpful to individuals looking to lose weight or maintain a healthy weight. Lower carbohydrate consumption will invoke lower insulin release and thus lower storage of fat and rise in blood sugar levels [49, 50]. However, as the major contributors to hyperglycaemia in type 2 diabetes include a combination of insulin resistance and an inability of pancreatic β -cells to secrete enough insulin [51], it is important to clarify the impact of LCHFD on these important aspects of metabolic regulation.

Studies have shown that insulin-stimulated glucose uptake into muscle and adipose tissue is significantly improved by weight loss on a LCFD diet [52, 53]. LCHFD diet has not necessarily been shown to result in weight reduction in animal studies, regardless of effects on body weight. To the contrary, it has been shown to cause an increased accumulation of lipids in the liver, which negatively affects insulin's ability to reduce hepatic glucose production [54–56]. Thus, from animal studies at least, the proposed benefits versus potential negative effects of an LCHFD on blood glucose control are not very clear. Moreover, whether LCHFDs will prove beneficial for improving glucose control in type 2 diabetes in the longer term will also depend on their impact on glucose-induced insulin secretion.

It is still not very clear that very low carbohydrate intake improves metabolic profile in every diabetes patients, and we need further scientific evidence for this [2, 36]. Although LCHFDs have been shown to reduce post-meal glucose excursions but without any improvement in β -cell function or mass [49, 50, 57], high-dietary fat has been shown, in multiple animal studies, to cause impairments in the ability of insulin to reduce blood glucose resulting in glucose intolerance [58, 59]. Thus, these results from animal studies do not support the recommendation of an LCHFD for use in prediabetes; rather, interventions aimed specifically at reducing obesity and improving insulin sensitivity need to be pursued.

6. What foods are encouraged in LCHF diet plan?

Reduced carbohydrate diets are those that have carbohydrate intakes below the Dietary Guidelines for Americans (DGA) recommendations (of 45–65% of total energy intake). 'Low'

carbohydrate is defined as less than 130 g per day, whereas 'very low' carbohydrate is less than 50 g per day [60]. Although individual responses vary, ketosis usually occurs in people who restrict their carbohydrate intake to below 20–50 g/day with some degree of protein restriction (nutritional ketosis).

Contrary to what many people think, most LCHF diets are not high in protein. In fact, for every 100 g of protein consumed, 56 g of glucose can be produced [61]; thus, having too much can affect blood glucose and undermine the principle of LCHF. Protein can also directly stimulate insulin resistance. Moderate protein consumption, 2–3 portions per day, is therefore usually recommended. Protein can also increase satiety, i.e. it can help you to feel fuller.

When carbohydrate is restricted, it is important to increase the levels of fat consumed—a low carbohydrate AND low fat diet inevitably lead to hunger. Fat should be consumed to satiety. Healthy natural sources of fat include olive oil, butter, grass-fed meats, eggs and dairy products. There is no need to be afraid of fats, including saturated fats and cholesterol, though trans-fats and hydrogenated or partly hydrogenated vegetable oils (often found in junk foods) should be avoided!

A LCHF diet should also include a lot of green leafy vegetables, although consumption of starchy vegetables (such as potatoes and other root vegetables) and fruit should be limited due to their higher carbohydrate content.

According to the Banting diet eating plan [62], foods that can be consumed liberally on the LCHF diet include dairy like natural yoghurt, cheese, cream, butter, along with meat, fish, eggs, vegetables and olive oil. Foods that can be consumed in moderate amounts are bean and lentils, nuts, almonds and sunflower seeds, fruits (not dried fruit), chocolate with a high cocoa quantity (65–90%), sausages and moderate amounts of alcohol. Foods to be avoided are potato; rice; bread; flour and corn-based products; cereal-based products, such as pasta, pastry, biscuits and breakfast cereals; sweets and cakes; sugary drinks; margarines and omega-6 based oils such as corn, sunflower, safflower, soybean and peanut oil. More information about the LCHF diet can be found in the book, 'Diabetes, No thanks' [63]—description of one man's journey from his diagnosis of diabetes to controlling his diabetes with the diet alone.

7. Mechanisms for weight loss on the LCHF eating plan

Increased satiety, allowing a lower energy intake without hunger and a specific metabolic advantage have been proposed to explain how LCHF diets produce weight loss, despite an increased consumption of energy-dense 'fatty' foods.

A recent systematic review compared weight loss between participants on 'LCHF diets' and 'low fat balanced diets' [64] but excluded all trials that were not isoenergetic. Although the original study did not find any differences in weight loss between the different diets, a reanalysis [64] of the same data found a small but significantly great weight loss on the lower carbohydrate diet.

Greater satiety on LCHF diets in persons responding to the diet may result from a number of mechanisms, including increased protein intake, which promotes satiety [65]; ketogenesis, which suppresses appetite [66] and fewer instances of rebound hypoglycaemia.

Although still controversial, it has been suggested that LCHF diets may provide a metabolic 'advantage' favouring greater weight loss, despite the ingestion of an equal number of calories. This metabolic advantage could be related to thermogenic effects of protein intake, greater protein turnover for gluconeogenesis and loss of energy through excretion of ketones in sweat or urine [67, 68]. This state of increased lipolysis with reduced lipogenesis contributes to a metabolic milieu theoretically favouring fat loss. This effect is dependent on reduced blood insulin concentrations, uniquely produced by the LCHF diet.

8. LCHF diets in the management of T2DM

Any diet that reduces carbohydrate load and insulin concentrations will have a beneficial effect on diabetes. Therefore, LCHF diets are currently being discussed as a potential first-line treatment for T2DM [69, 70].

Three hundred and sixty-three patients, who were overweight and obese, were given either a ketogenic LCHF diet or a 'low calorie, high nutritional value' diet in a 6-month trial [71]. Those with T2DM (102 patients) had significantly lower HbA1c and fasting glucose levels and also lost more weight (−12.0% vs. −7.0%) with the LCHF diet.

Thirty-four prediabetic or T2DM patients were randomised to a calorie-restricted diet according to American Diabetes Association (ADA) guidelines or a very LCHF diet in another 3-month trial [72]. HbA1c did not alter in the ADA group, whereas in the very LCHF group, there was a significant reduction (6.6–6.0%) in HbA1c, decrease in the use of anti-diabetic medications and weight loss (−5.5 vs. −2.6 kg).

Westman et al. [73], in their 24-week trial comparing a very LCHF diet with a low GI diet, similarly showed greater decreases in HbA1c (−1.5% vs. −0.5%, $p = 0.03$) with the very LCHF diet, despite more patients reducing or stopping their diabetes medications.

In another study, 115 obese adults with T2DM were randomised to either LCHF or LFHC diet for 1 year [74]. Both diets showed significant weight loss and HbA1c reduction. LCHF diet, however, resulted in better blood glucose stability, greater reductions in diabetes medication requirements and significant improvements in all aspects of lipid concentrations.

Although it could be assumed that all the above positive metabolic changes with an LCHF diet is attributable to its associated weight loss, it is also well established that carbohydrate restriction in diabetes patients per se improves glycaemic control even in the absence of weight loss [75, 76].

9. LCHF diets and cardiovascular risk factors

An understandable concern with any increased dietary fat intake on the LCHF diet is the increased risk of future cardiovascular disease. This is largely based on the Ancel Keys' original seven countries study [20], which led to the development of traditional LFHC dietary guidance. However, there is good evidence emerging now that LCHF diets significantly alter cardiovascular risk more so than LFHC diets, especially in those with T2DM and metabolic syndrome.

Many RCTs show that LCHF diets lower blood triglyceride [77] and blood apoprotein B concentrations significantly more than do LFHC diets [3, 78–81]. Furthermore, no other diet increases HDL-C concentrations as effectively as do LCHF diets, which outperform LFHC [79, 82, 83] low glycaemic index [84] and many other diets.

Tay et al. [79] compared a very LCHF with an LFHC diet over a 1-year period—despite similar weight loss, there was significantly more lowering of blood TG concentrations (−0.58 vs. −0.22 mmol/L) and greater increase in HDL-C concentrations (+0.30 vs. +0.07 mmol/L) with the LCHF diet. This has huge connotations for reducing coronary artery disease and would be especially beneficial for those with insulin resistance.

A contentious issue regarding the LCHF diet is the variable LDL-C response to the increase in dietary fat intake. Some trials show a decrease or non-significant change in LDL-C concentrations [38, 85], whereas others report a more marked increase in LDL-C levels [86]. Tay et al. [79], in their study, have demonstrated that both LDL-C (+0.6 vs. +0.1 mmol/L) and total cholesterol (+0.7 vs. +0.1 mmol/L) concentrations increased significantly more in those following the LCHF diet.

Many other systematic reviews [87] and trials [88] have confirmed similar positive effects on overall lipid profile. However, one needs to remember that LDL-C concentrations predicted by the Friedewald equation becoming increasingly inaccurate at low blood TG concentrations [89] as seen with the LCHF diet. It has been shown that LCHF diets consistently reduce the proportion of small, dense LDL particles while increasing the number of large, buoyant LDL particles [3, 81, 85, 90–92].

Additionally, LCHF diets have been associated with improvements in flow-mediated arteriolar dilation [80], decreased inflammatory biomarkers [14], lower systolic and diastolic blood pressures [3], improved glycaemic control with reduced HbA1c, plasma glucose and insulin concentrations [87] and preferential reduction in visceral and liver fat—changes in these surrogate markers would be expected to reduce cardiovascular risk significantly [3, 93].

10. LCHF and non-alcoholic fatty liver disease (NAFLD)

Non-alcoholic fatty liver disease (NAFLD) is characterised by elevated TG and low HDL-C concentrations with overproduction of VLDL and impaired clearance of TG-rich lipoproteins

[94, 95]. It is also recognised that cardiovascular disease is the leading cause of death in NAFLD [96]. It has been shown that NAFLD with insulin resistance is the cause of atherosclerotic disease characterised by many of these features [97]. Since NAFLD is caused by excessive carbohydrate, especially fructose intake [98–100], it is postulated that a carbohydrate-restricted LCHF diet can reverse NAFLD.

Thus, LCHF diet is likely to benefit patients with high TG to HDL-C ratios and NAFLD, all of which are common in the insulin-resistant individual. A recent lifestyle intervention trial reduced the prevalence of metabolic syndrome from 58 to 19% among obese and overweight patients treated with LCHF for 3–8 months, showing how quickly carbohydrate restriction can improve health in those with metabolic syndrome [37].

11. What are the drawbacks of LCHF diet?

As with any dietary approach, there are some caveats to following a LCHF approach. The concept of LCHF is relatively new and not everyone is fully familiar with it. The following are some of the common concerns.

11.1. Hunger

Some people experience increased hunger on a LCHF diet. However, if they eat fat to true fullness, hunger should not be an issue. Lowering insulin levels and reducing insulin resistance can reduce hunger, and also protein and high-fibre green leafy vegetables can reduce this sense of hunger [101].

11.2. Lack of variety

It is assumed that eating the same thing all the time following a LCHF diet will reduce variety and enjoyment. This can be circumvented as there are a wide variety of meals and foods in the LCHF diet to choose from.

11.3. Nutritional deficiencies

It has also been suggested that following a LCHF approach can lead to deficiencies of certain vitamins and minerals. However, there is no evidence of this from trials [60]. An LCHF diet based on meat, seeds/nuts and dairy should provide a diet rich in all the essential nutrients. An online survey found that most people using LCHF diet substituted carbohydrates like bread, rice and pasta with green leafy vegetables, thus reducing likelihood of nutritional deficiencies [102].

11.4. 'Low carb flu': headache, fatigue and muscle cramping

These are potential side effects of LCHF diets at the start of dieting. This is simply because the body is used to using glucose as a primary fuel source and needs some time to adapt to

using fats. However, these symptoms may be especially prevalent only in the period of adaptation to the diet, after which most subside. Some suggest additional sodium (especially for cramping) and fluid intake to minimise side effects, since excretion of water and sodium are increased on these diets as a result of reduction in insulin levels with LCHF diet [103].

11.5. Weight loss on LCHF diets is due to increased water loss

Some have suggested that weight loss on LCHF diets is the result mainly of water loss. This increased diuresis may be true in the first weeks of carbohydrate restriction [104]. However, body composition by DEXA analysis indicates that long-term weight loss on the LCHF diet is predominantly the result of the loss of fat mass with some loss of fat-free mass [3].

11.6. Sustainability

Trials show that adherence to LCHF and LFHC diets are similar [13, 72, 105]. On the other hand, a recent systematic review found a higher attrition rate from LFHC than from LCHF diets [106]. Therefore, sticking to a LCHF diet is perhaps as convenient as any other dietary plan and thus may be more sustainable as it tends to reduce hunger without need for specific calorie restriction. In fact, studies of long-term adherence of up to a year [38, 39] on the LCHF have not identified any evidence of harm.

12. Summary

From the current evidence and above reviews of lower carbohydrate diets, it can be postulated that LCHF diets reduce insulin resistance, improves glycaemic regulation and has positive effects on reducing cardiovascular risk factors, including reducing serum triglyceride, increasing HDL cholesterol, increasing LDL particle size and reducing blood pressure. A substantial proportion of individuals have also been shown to discontinue one or more diabetes medication.

Low-carbohydrate high-fat (LCHF) diet has been shown to be as effective as other diets for weight reduction, through increased satiety and reduction in calorie intake. LCHF diet also helps improve glycaemic control in type 2 diabetes mellitus and in otherwise healthy patients with insulin resistance.

Some of the benefits of the LCHF diet results from the often large weight loss typically produced by this diet. Therefore, at least some of the beneficial changes from LCHF diet would also be experienced by patients prepared to adhere to any calorie-restricted diet. LCHF diets control energy balance through increased satiety and reduced ad libitum energy intake while encouraging the ingestion of a nutrient-dense diet by replacing refined foods with natural foods.

LCHF diets have beneficial effects on cardiovascular risk factors through their effect on blood lipid concentrations. They decrease triglycerides, apoprotein B and saturated fat levels in

blood, together with reduction in small dense LDL particles and increase in HDL-C concentrations. Their effect on LDL-C concentration seems to be variable.

LCHF diet, thus far, has proven to be a safe and efficacious strategy for weight loss and improved health outcomes especially for those with metabolic syndrome and NAFLD. Thus, LCHF diets may be the ideal choice for patients who have struggled to lose weight on traditional diets, especially T2DM with or without cardiovascular risk factors. A life-long completely carbohydrate-free diet is unlikely to be achievable but a LCHF, through reducing post-meal glucose excursions, could potentially have some benefit for improving glucose control in diabetes. However, from animal models, it has been shown that there are no longer term benefits for β -cell function or glucose metabolism.

Notably, most diets are effective at inducing at least short-term weight loss, usually followed by some weight regain as adherence diminishes. However, it can be argued that LCHF diets perform at least as well as do any other dietary approaches. In practice, beneficial responses to any diet is entirely dependent on the degree of patients' adherence, so a LCHF diet is only likely to benefit patients motivated to comply.

A growing understanding that obesity/hypertension/T2DM/non-alcoholic fatty liver disease/atherogenic dyslipidaemia and metabolic syndrome may all be substantially influenced by a high-carbohydrate diet, acting on a single metabolic state, insulin resistance—could revolutionise the dietary management of these conditions over the next few years. It can therefore be argued that the LCHF eating plan should form an integral part of medical management for all these conditions.

LCHF diet may not be an answer for everyone as every individual metabolic profile is different. However, it may present a sensible dietary option for weight loss and health improvement in certain group of patients. Despite its numerous benefits, individual LDL-C responses need to be monitored and continued emphasis should be placed on nutrient-rich choices, avoiding ultra-processed foods. We need more well-designed comparative studies to confirm whether the metabolic changes from LCHF diet will be sustained long term.

Author details

Parijat De^{1,2*} and Sagnik Mukhopadhyay¹

*Address all correspondence to: p.de@nhs.net

1 Department of Diabetes, Endocrinology and Lipid Metabolism, Sandwell and West Birmingham NHS Trust, Birmingham, UK

2 University of Birmingham, UK

References

- [1] Atkins RC. Dr Atkins Diet Revolution. 1st ed. New York: David McKay Company; 1972. pp. 1-310
- [2] Feinman RD, Pogozelski WK, Astrup A, et al. Dietary carbohydrate restriction as the first approach in diabetes management: Critical review and evidence base. *Nutrition*. 2015;**31**:1-13
- [3] Volek JS, Phinney SD, Forsythe CE, et al. Carbohydrate restriction has a more favorable impact on the metabolic syndrome than a low fat diet. *Lipids*. 2009;**44**:297-309
- [4] Blackburn GL, Phillips JC, Morreale S. Physician's guide to popular low-carbohydrate weight-loss diets. *Cleveland Clinic Journal of Medicine*. 2001;**68**:761, 765-6, 768-9, 773-4
- [5] Smith SR. A look at the low-carbohydrate diet. *The New England Journal of Medicine*. 2009;**361**:2286-2288
- [6] Kirpich AR, Maryniuk MD. The 3 R's of Glycemic index: Recommendations, research, and the real world. *Clinical Diabetes*. 2011;**29**(4):155-159
- [7] Low Carb Program—Free 10 Week Education Program—Diabetes.co.uk. <https://www.diabetes.co.uk/lowcarb/>
- [8] Diabetes UK 2017 Position statement: Low carb diets for people with diabetes. <https://www.diabetes.org.uk/.../Position.../Low-carb-diets-for-people-with-diabetes>
- [9] Roberts CK, Hevener AL, Barnard RJ. Metabolic syndrome and insulin resistance: Underlying causes and modification by exercise training. *Comprehensive Physiology*. 2013;**3**(1):1-58
- [10] Volek JS, Feinman RD. Carbohydrate restriction improves the features of metabolic syndrome. Metabolic Syndrome may be defined by the response to carbohydrate restriction. *Nutrition & Metabolism*. 2005;**2**:31
- [11] Stock AL, Yudkin J. Nutrient intake of subjects on low carbohydrate diet used in treatment of obesity. *The American Journal of Clinical Nutrition*. 1970;**23**:948-952
- [12] Saslow LR, Kim S, Daubenmier JJ, et al. A randomized pilot trial of a moderate carbohydrate diet compared to a very low carbohydrate diet in overweight or obese individuals with type 2 diabetes mellitus or prediabetes. *PLoS One*. 2014;**9**:e91027
- [13] Gardner CD, Kiazand A, Alhassan S, et al. Comparison of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women: The A to Z Weight Loss Study: A randomized trial. *JAMA*. 2007;**297**:969-977
- [14] Forsythe CE, Phinney SD, Fernandez ML, et al. Comparison of low fat and low carbohydrate diets on circulating fatty acid composition and markers of inflammation. *Lipids*. 2008;**43**:65-77

- [15] Larosa JC, Fry AG, Muesing R, et al. Effects of high-protein, low-carbohydrate dieting on plasma lipoproteins and body weight. *Journal of the American Dietetic Association*. 1980;**77**:264-270
- [16] Panel on dietary reference intakes for macronutrients. *Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients)*. Washington, DC, USA: The National Academies Press; 2005
- [17] Evert AB, Boucher JL, Cypress M, Dunbar SA, Franz MJ, Mayer-Davis EJ, et al. Nutrition therapy recommendations for the management of adults with diabetes. *Diabetes Care*. 2014;**37**(Suppl 1):S120-S143
- [18] Kromhout D. Where the latest US dietary guidelines are heading. *BMJ*. 2015;**351**:h4034
- [19] Smith R. Are some diets “mass murder”? *BMJ*. 2014;**349**:g7654
- [20] Keys A, Menotti A, Karvonen MJ, et al. The diet and 15-year death rate in the seven countries study. *American Journal of Epidemiology*. 1986;**124**:903-915
- [21] Siri-Tarino PW, Sun Q, FB H, et al. Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease. *The American Journal of Clinical Nutrition*. 2010;**91**:535-546
- [22] Hooper L, Summerbell CD, Thompson R, et al. Reduced or modified dietary fat for preventing cardiovascular disease. *Cochrane Database of Systematic Reviews*. 2012;**5**: CD002137
- [23] Hooper L, Summerbell CD, Thompson R, et al. Reduced or modified dietary fat for preventing cardiovascular disease. *Cochrane Database of Systematic Reviews*. 2011;**7**: CD002137
- [24] Skeaff CM, Miller J. Dietary fat and coronary heart disease: Summary of evidence from prospective cohort and randomised controlled trials. *Annals of Nutrition & Metabolism*. 2009;**55**:173-201
- [25] Jakobsen MU, O'Reilly EJ, Heitmann BL, et al. Major types of dietary fat and risk of coronary heart disease: A pooled analysis of 11 cohort studies. *The American Journal of Clinical Nutrition*. 2009;**89**:1425-1432
- [26] De Souza RJ, Mente A, Maroleanu A, et al. Intake of saturated and trans unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: Systematic review and meta-analysis of observational studies. *BMJ*. 2015;**351**:h3978
- [27] Praagman J, Beulens JW, Alssema M, et al. The association between dietary saturated fatty acids and ischemic heart disease depends on the type and source of fatty acid in the European Prospective Investigation into Cancer and Nutrition-Netherlands cohort. *The American Journal of Clinical Nutrition*. 2016;**103**:356-365
- [28] Mente A, De Koning L, Shannon HS, et al. A systematic review of the evidence supporting a causal link between dietary factors and coronary heart disease. *Archives of Internal Medicine*. 2009;**169**:659-669

- [29] Chowdhury R, Warnakula S, Kunutsor S, et al. Association of dietary, circulating, and supplement fatty acids with coronary risk: A systematic review and meta-analysis. *Annals of Internal Medicine*. 2014;**160**:398-406
- [30] Ptaschitz NG, Strand E, Norekval TM, et al. Dietary intake of saturated fat is not associated with risk of coronary events or mortality in patients with established coronary artery disease. *The Journal of Nutrition*. 2015;**145**:299-305
- [31] Schoenaker DA, Toeller M, Chaturvedi N, et al. Dietary saturated fat and fibre and risk of cardiovascular disease and all-cause mortality among type 1 diabetic patients: The EURODIAB Prospective Complications Study. *Diabetologia*. 2012;**55**:2132-2141
- [32] Mozaffarian D, Rimm EB, Herrington DM. Dietary fats, carbohydrate, and progression of coronary atherosclerosis in postmenopausal women. *The American Journal of Clinical Nutrition*. 2004;**80**:1175-1184
- [33] Gillman MW, Cupples LA, Millen BE, et al. Inverse association of dietary fat with development of ischemic stroke in men. *JAMA*. 1997;**278**:2145-2150
- [34] Sekikawa A, Miyamoto Y, Miura K, et al. Continuous decline in mortality from coronary heart disease in Japan despite a continuous and marked rise in total cholesterol: Japanese experience after the Seven Countries Study. *International Journal of Epidemiology*. 2015;**44**:1614-1624
- [35] Natella S, Divan V, Giraldo M. Fat: The new health paradigm. Zurich, Switzerland: Research Institute; 2015:1-73. cs.researchinstitute@credit-suisse.com
- [36] Noakes TD. Low-carbohydrate and high-fat intake can manage obesity and associated conditions: Occasional survey. *South African Medical Journal*. 2013;**103**:826-830
- [37] Mark S, TS D, Noakes TD, et al. A successful lifestyle intervention model replicated in diverse clinical settings. *South African Medical Journal*. 2016;**106**:763-766
- [38] Dashti HM, Mathew TC, Hussein T, et al. Long-term effects of a ketogenic diet in obese patients. *Experimental and Clinical Cardiology*. 2004;**9**:200-205
- [39] Grieb P, Klappinska B, Smol E, et al. Long-term consumption of a carbohydrate-restricted diet does not induce deleterious metabolic effects. *Nutrition Research*. 2008;**28**:825-833
- [40] Harcombe Z, Baker JS. Plant sterols lower cholesterol, but increase risk for coronary heart disease. *OnLine Journal of Biological Sciences*. 2016;**14**:167-169
- [41] DiNicolantonio JJ. The cardiometabolic consequences of replacing saturated fats with carbohydrates or omega-6 polyunsaturated fats: Do the dietary guidelines have it wrong? *Open Heart*. 2014;**1**:1-4
- [42] Ravnskov U, DiNicolantonio JJ, Harcombe Z, et al. The questionable benefits of exchanging saturated fat with polyunsaturated fat. *Mayo Clinic Proceedings*. 2014;**89**:451-453
- [43] Ramsden CE, Zamora D, Leelarthaepin B, et al. Use of dietary linoleic acid for secondary prevention of coronary heart disease and death: Evaluation of recovered data from the Sydney Diet Heart Study and updated meta-analysis. *BMJ*. 2013;**346**:e8707

- [44] Ramsden CE, Zamora D, Majchrzak-Hong S, et al. Re-evaluation of the traditional diet-heart hypothesis: Analysis of recovered data from Minnesota Coronary Experiment (1968-73). *BMJ*. 2016;**353**:i1246
- [45] Shapira N. Israeli 'cancer shift' over heart disease mortality may be led by greater risk in women with high intake of n-6 fatty acids. *European Journal of Cancer Prevention*. 2007;**16**:486-494
- [46] Binnie MA, Barlow K, Johnson V, et al. Red meats: Time for a paradigm shift in dietary advice. *Meat Science*. 2014;**98**:445-451
- [47] O'Connor LE, Kim JE, Campbell WW. Consuming < or >0.5 servings of red meat per day does not have a negative impact on cardiovascular disease risk factors; a systematic review and meta-analysis of randomized controlled trials. *The FASEB Journal*. 2016; **30**:S904.1
- [48] Low Carb High Fat Cooking for Healthy Aging: 70 Easy and Delicious Recipes to Promote Vitality and Longevity—20 Aug 2015 by Annika Dahlqvist and Birgitta Höglund (amazon.co.uk)
- [49] Gannon MC, Nuttall FQ. Effect of a high-protein, low-carbohydrate diet on blood glucose control in people with type 2 diabetes. *Diabetes*. 2004;**53**:2375-2382
- [50] Nuttall FQ, Almokayyad RM, Gannon MC. Comparison of a carbohydrate-free diet vs. fasting on plasma glucose, insulin and glucagon in type 2 diabetes. *Metabolism*. 2015;**64**: 253-262
- [51] Kahn SE. The relative contributions of insulin resistance and beta-cell dysfunction to the pathophysiology of type 2 diabetes. *Diabetologia*. 2003;**46**:3-19
- [52] Samaha FF, Iqbal N, Seshadri P, Chicano KL, Daily DA, McGrory J, et al. A low-carbohydrate as compared with a low-fat diet in severe obesity. *New England Journal of Medicine*. 2003;**348**:2074-2081
- [53] Shai I, Schwarzfuchs D, Henkin Y, Shahar DR, Witkow S, Greenberg I, et al. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. *The New England Journal of Medicine*. 2008;**359**:229-241
- [54] Bielohuby M, Sisley S, Sandoval D, Herbach N, Zengin A, Fischereder M, et al. Impaired glucose tolerance in rats fed low-carbohydrate, high-fat diets. *American Journal of Physiology. Endocrinology and Metabolism*. 2013;**305**:E1059-E1070
- [55] Garbow JR, Doherty JM, Schugar RC, Travers S, Weber ML, Wentz AE, et al. Hepatic steatosis, inflammation, and ER stress in mice maintained long term on a very low-carbohydrate ketogenic diet. *American Journal of Physiology. Gastrointestinal and Liver Physiology*. 2011;**300**:G956-G967
- [56] Jornayvaz FR, Jurczak MJ, Lee HY, Birkenfeld AL, Frederick DW, Zhang D, et al. A high-fat, ketogenic diet causes hepatic insulin resistance in mice, despite increasing energy expenditure and preventing weight gain. *American Journal of Physiology. Endocrinology and Metabolism*. 2010;**299**:E808-E815

- [57] Lamont BJ, Waters MF, Andrikopoulos S. A low-carbohydrate high-fat diet increases weight gain and does not improve glucose tolerance, insulin secretion or β -cell mass in NZO mice. *Nutrition & Diabetes*. 2016;**6**:e194. DOI: 10.1038/nutd.2016.2 Published online 15 February 2016
- [58] Ellenbroek JH, van Dijk L, Tons HA, Rabelink TJ, Carlotti F, Ballieux BE, et al. Long-term ketogenic diet causes glucose intolerance and reduced beta- and alpha-cell mass but no weight loss in mice. *American Journal of Physiology-Endocrinology and Metabolism*. 2014;**306**:E552-E558
- [59] Andrikopoulos S, Blair AR, Deluca N, Fam BC, Proietto J. Evaluating the glucose tolerance test in mice. *American Journal of Physiology. Endocrinology and Metabolism*. 2008;**295**:E1323-E1332
- [60] Feinman RD, Pogozelski WK, Astrup A, Bernstein RK, Fine EJ, Westman EC, et al. Dietary carbohydrate restriction as the first approach in diabetes management. Critical review and evidence base. *Nutrition (Burbank, Los Angeles County, Calif)*. 2015 Jan;**31**(1):1-13. DOI: 10.1016/j.nut.2014.06.011. [Epub 2014 Jul 16]
- [61] Institute of Medicine of the National Academies. Dietary Reference Intakes for Energy, Carbohydrate, Fiber, Fat, Fatty Acids, Cholesterol, Protein, and Amino Acids (Macronutrients). Washington, DC: National Academy Press; 2005
- [62] Noakes T, Proudfoot J, Creed S, Greer D. *The Real Meal Revolution: The Radical, Sustainable Approach to Healthy Eating*. Cape Town, South Africa: Quivertree Publications; November 2013
- [63] *Diabetes, No Thanks!* by Lars-Erik Litsfeldt, Rob Dinsdale (Editor), Janis Abens (Translator). Paperback, 208 pages. Published October 1st 2011 by Little Moon Publishing Limited
- [64] Naude CE, Schoonees A, Senekal M, et al. Low carbohydrate versus isoenergetic balanced diets for reducing weight and cardiovascular risk: A systematic review and meta-analysis. *PLoS One*. 2014;**9**:e100652
- [65] Weigle DS, Breen PA, Matthys CC, et al. A high-protein diet induces sustained reductions in appetite, ad libitum caloric intake, and body weight despite compensatory changes in diurnal plasma leptin and ghrelin concentrations. *The American Journal of Clinical Nutrition*. 2005;**82**:41-48
- [66] Johnstone AM, Horgan GW, Murison SD, et al. Effects of a high-protein ketogenic diet on hunger, appetite, and weight loss in obese men feeding ad libitum. *The American Journal of Clinical Nutrition*. 2008;**87**:44-55
- [67] Feinman RD, Fine EJ. Thermodynamics and metabolic advantage of weight loss diets. *Metabolic Syndrome and Related Disorders*. 2003;**1**:209-219
- [68] Feinman RD, Fine EJ. 'A calorie is a calorie' violates the second law of thermodynamics. *Nutrition Journal*. 2004;**3**(9). <https://doi.org/10.1186/1475-2891-3-9>
- [69] Hamdy O. Nutrition revolution—The end of the high carbohydrates era for diabetes: Prevention and management. *US Endocrinology*. 2014;**10**:103-104

- [70] Schofield G, Henderson G, Thornley S, et al. Very low-carbohydrate diets in the management of diabetes revisited. *New Zealand Medical Journal*. 2016;**129**:67-73
- [71] Hussain TA, Mathew TC, Dashti AA, et al. Effect of low-calorie versus low-carbohydrate ketogenic diet in type 2 diabetes. *Nutrition*. 2012;**28**:1016-1021
- [72] Daly ME, Paisey R, Paisey R, et al. Short-term effects of severe dietary carbohydrate-restriction advice in Type 2 diabetes—A randomized controlled trial. *Diabetic Medicine*. 2006;**23**:15-20
- [73] Westman EC, Yancy WS Jr, Mavropoulos JC, et al. The effect of a low-carbohydrate, ketogenic diet versus a low-glycemic index diet on glycemic control in type 2 diabetes mellitus. *Nutrition & Metabolism (London)*. 2008;**5**:36
- [74] Tay J, Luscombe-Marsh ND, Thompson CH, et al. Comparison of low- and high-carbohydrate diets for type 2 diabetes management: A randomized trial. *The American Journal of Clinical Nutrition*. 2015;**102**:780-790
- [75] Gannon MC, Nuttall FQ. Control of blood glucose in type 2 diabetes without weight loss by modification of diet composition. *Nutrition & Metabolism (London)*. 2006;**3**:16
- [76] Guldbrand H, Dizdar B, Bunjaku B, et al. In type 2 diabetes, randomisation to advice to follow a low-carbohydrate diet transiently improves glycaemic control compared with advice to follow a low-fat diet producing a similar weight loss. *Diabetologia*. 2012;**55**:2118-2127
- [77] Brinkworth GD, Noakes M, Buckley JD, et al. Long-term effects of a very-low-carbohydrate weight loss diet compared with an isocaloric low-fat diet after 12 mo. *The American Journal of Clinical Nutrition*. 2009;**90**:23-32
- [78] Foster GD, Wyatt HR, Hill JO, et al. A randomized trial of a low-carbohydrate diet for obesity. *The New England Journal of Medicine*. 2003;**348**:2082-2090
- [79] Tay J, Brinkworth GD, Noakes M, et al. Metabolic effects of weight loss on a very-low-carbohydrate diet compared with an isocaloric high-carbohydrate diet in abdominally obese subjects. *Journal of the American College of Cardiology*. 2008;**51**:59-67
- [80] Keogh JB, Brinkworth GD, Noakes M, et al. Effects of weight loss from a very-low-carbohydrate diet on endothelial function and markers of cardiovascular disease risk in subjects with abdominal obesity. *The American Journal of Clinical Nutrition*. 2008;**87**:567-576
- [81] Volek JS, Fernandez ML, Feinman RD, et al. Dietary carbohydrate restriction induces a unique metabolic state positively affecting atherogenic dyslipidemia, fatty acid partitioning, and metabolic syndrome. *Progress in Lipid Research*. 2008;**47**:307-318
- [82] Bazzano LA, Hu T, Reynolds K, et al. Effects of low-carbohydrate and low-fat diets: A randomized trial. *Annals of Internal Medicine*. 2014;**161**:309-318
- [83] Yancy WS Jr, Olsen MK, Guyton JR, et al. A low-carbohydrate, ketogenic diet versus a low-fat diet to treat obesity and hyperlipidemia: A randomized, controlled trial. *Annals of Internal Medicine*. 2004;**140**:769-777

- [84] Feinman RD, Volek JS, Westman EC. Dietary carbohydrate restriction in the treatment of diabetes and metabolic syndrome. *Clinical Nutrition Insight*. 2008;**34**(5):1-5
- [85] Forsythe CE, Phinney SD, Feinman RD, et al. Limited effect of dietary saturated fat on plasma saturated fat in the context of a low carbohydrate diet. *Lipids*. 2010;**45**:947-962
- [86] Hernandez TL, Sutherland JP, Wolfe P, et al. Lack of suppression of circulating free fatty acids and hypercholesterolemia during weight loss on a high-fat, low-carbohydrate diet. *The American Journal of Clinical Nutrition*. 2010;**91**:578-585
- [87] Santos FL, Esteves SS, Da Costa PA, et al. Systematic review and meta-analysis of clinical trials of the effects of low carbohydrate diets on cardiovascular risk factors. *Obesity Reviews*. 2012;**13**:1048-1066
- [88] Hu T, Mills KT, Yao L, et al. Effects of low-carbohydrate diets versus low-fat diets on metabolic risk factors: A meta-analysis of randomized controlled clinical trials. *American Journal of Epidemiology*. 2012;**176**(Suppl 7):S44-S54
- [89] Sniderman AD, Blank D, Zakarian R, et al. Triglycerides and small dense LDL: The twin Achilles heels of the Friedewald formula. *Clinical Biochemistry*. 2003;**36**:499-504
- [90] Aude YW, Agatston AS, Lopez-Jimenez F, et al. The national cholesterol education program diet vs a diet lower in carbohydrates and higher in protein and monounsaturated fat: A randomized trial. *Archives of Internal Medicine*. 2004;**164**:2141-2146
- [91] Wood RJ, Volek JS, Liu Y, et al. Carbohydrate restriction alters lipoprotein metabolism by modifying VLDL, LDL, and HDL sub-fraction distribution and size in overweight men. *The Journal of Nutrition*. 2006;**136**:384-389
- [92] Volek JS, Sharman MJ, Forsythe CE. Modification of lipoproteins by very low-carbohydrate diets. *The Journal of Nutrition*. 2005;**135**:1339-1342
- [93] Volek JS, Sharman MJ, Gomez AL, et al. Comparison of a very low-carbohydrate and low-fat diet on fasting lipids, LDL subclasses, insulin resistance, and postprandial lipemic responses in overweight women. *Journal of the American College of Nutrition*. 2004;**23**:177-184
- [94] Taskinen MR, Adiels M, Westerbacka J, et al. Dual metabolic defects are required to produce hypertriglyceridemia in obese subjects. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2011;**31**:2144-2150
- [95] Yki-Jarvinen H. Non-alcoholic fatty liver disease as a cause and a consequence of metabolic syndrome. *The Lancet Diabetes and Endocrinology*. 2014;**2**:901-910
- [96] Targher G, Marra F, Marchesini G. Increased risk of cardiovascular disease in non-alcoholic fatty liver disease: Causal effect or epiphenomenon? *Diabetologia*. 2008;**51**:1947-1953
- [97] Bril F, Lomonaco R, Orsak B, et al. Relationship between disease severity, hyperinsulinemia, and impaired insulin clearance in patients with nonalcoholic steatohepatitis. *Hepatology*. 2014;**59**:2178-2187

- [98] Bian H, Hakkarainen A, Lundbom N, et al. Effects of dietary interventions on liver volume in humans. *Obesity (Silver Spring)*. 2014;**22**:989-995
- [99] Neuschwander-Tetri BA. Carbohydrate intake and nonalcoholic fatty liver disease. *Current Opinion in Clinical Nutrition and Metabolic Care*. 2013;**16**:446-452
- [100] Browning JD, Baker JA, Rogers T, et al. Short-term weight loss and hepatic triglyceride reduction: Evidence of a metabolic advantage with dietary carbohydrate restriction. *The American Journal of Clinical Nutrition*. 2011;**93**:1048-1052
- [101] Chambers L, McCrickerd K, Yeomans MR. Optimising foods for satiety. *Trends in Food Science & Technology*. 2015;**41**(2):149-160
- [102] Feinman RD, Vernon MC, Westman EC. Low carbohydrate diets in family practice: What can we learn from an internet-based support group. *Nutrition Journal*. 2006;**5**(26). <https://www.ncbi.nlm.nih.gov/pubmed/17014706>
- [103] Westman EC, Feinman RD, Mavropoulos JC, et al. Low-carbohydrate nutrition and metabolism. *The American Journal of Clinical Nutrition*. 2007;**86**:276-284
- [104] Yang MU, Van Itallie TB. Composition of weight lost during short-term weight reduction. Metabolic responses of obese subjects to starvation and low-calorie ketogenic and nonketogenic diets. *The Journal of Clinical Investigation*. 1976;**58**:722-730
- [105] Krebs NF, Gao D, Gralla J, et al. Efficacy and safety of a high protein, low carbohydrate diet for weight loss in severely obese adolescents. *The Journal of Pediatrics*. 2010;**157**:252-258
- [106] Hession M, Rolland C, Kulkarni U, et al. Systematic review of randomized controlled trials of low-carbohydrate vs. low-fat/low-calorie diets in the management of obesity and its comorbidities. *Obesity Reviews*. 2009;**10**:36-50