

Macronutrient Composition and Management of Non-Insulin-Dependent Diabetes Mellitus (NIDDM): A New Paradigm for Individualized Nutritional Therapy in Diabetes Patients

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■ Abstract

Medical nutrition therapy constitutes an important lifestyle intervention in diabetes management. Several nutrition patterns have been effective in improving diabetes control, but there has been a debate about the optimal macronutrient composition in diabetes meal planning. For many years, the recommended diets for persons with and without diabetes were similar, i.e. heart-healthy and low in fat. For almost three decades, carbohydrates have been lauded, lipids demonized, and proteins considered of little importance. However, in the past few years, this concept has been questioned and reassessed. Modern nutritional recommendations for people with diabetes are headed towards individualization, but lack specific guidelines. Nutritional algorithms may help nutritionists in diabetes meal planning. This review aims to discuss: 1) the effects of the three major macronutrients

(carbohydrates, proteins, and lipids) on glucose levels, 2) current recommendations for macronutrient intake for people with diabetes, and 3) specific parameters that need to be taken into consideration when determining the macronutrient composition for a person with diabetes, for example body mass index, degree of insulin resistance, HbA1c value, and lipid profile (especially triglycerides and HDL cholesterol). These aspects are analyzed in the context of the results of recent studies, especially randomized controlled trials (RCTs). Finally, we introduce an individualized nutritional concept that proposes carbohydrate over lipid restriction, substitution of SFAs with MUFAs and PUFAs, and adequate intake of dietary fiber, which are key factors in optimizing diabetes management.

Keywords: diabetes · diet · macronutrients · carbohydrates · proteins · lipids

1. The role of medical nutrition therapy in diabetes management

The increase in type 2 diabetes incidence is mainly lifestyle-dependent [1]. Diet is considered a milestone in diabetes primary prevention, with various dietary patterns being effective in preventing diabetes development [2-4]. Medical nutrition therapy (MNT) after diabetes diagnosis is of major importance. The goals of MNT include the control of blood sugar, lipid, and blood pressure levels, as well as prevention or treatment of diabetes complications. Simultaneously, the considera-

tion of cultural and personal patient preferences and the maintenance of pleasure in eating represent further challenges in MNT [5].

A variety of eating patterns have been proposed as being effective in improving indices of cardiometabolic control. In 2013, a relatively new dietary pattern, the healthy Nordic diet, was studied in relation to cardiometabolic markers in patients with the metabolic syndrome, and found superior in improving lipid profile and inflammatory markers when compared with the typical Nordic diet [6]. In the same year, Ajala *et al.* conducted a meta-analysis of 20 randomized controlled trials (RCTs) with intervention periods >6 months. The

authors tested the effectiveness of several diets, including:

- Low-carbohydrate (low-carb)
- Vegetarian
- Vegan
- Low-glycemic index (low-GI)
- High-fiber
- Mediterranean
- High-protein

They compared the diets with various control diets, including:

- Low-fat
- High-GI
- Diet of the American Diabetes Association
- Diet of the European Association for the Study of Diabetes
- Low-protein

Low-carb, low-GI, Mediterranean, and high-protein diets were effective in improving markers of cardiovascular disease (CVD) in diabetes [7].

It is encouraging that such very different protocols can provide positive outcomes for cardiometabolic profile. However, it becomes increasingly difficult for health professionals to select the best approach. This diversity is an additional challenge in optimizing MNT for the individual patient. Also, the result of the meta-analysis needs to be interpreted with caution, and cannot readily be generalized, because of the heterogeneity of the studies included. Thus, it is inappropriate to combine these studies for the following reasons:

1. Dissimilarity of the control diets which impairs comparability, and thus makes universal statements regarding the superiority of one diet over the other impossible.
2. Heterogeneity of the study participants, in particular regarding baseline characteristics (weight, HbA1c, etc.), which demonstrates that there cannot be one diet that meets all patients' requirements.
3. Methodological discrepancies, in particular regarding the non-specific definition of the low-carb diet, with carbohydrate content ranging from 20 g (approximately 10-15% of total energy) to 45% (percentage close to the Mediterranean recommendation).

It is thus clear that such a study is unable to reach a sound conclusion regarding the optimal mix of macronutrients.

Abbreviations:

CVD	cardiovascular disease
CHD	coronary heart disease
DGAC	Dietary Guidelines Advisory Committee
DHA	docosahexaenoic acid
EPA	eicosapentaenoic acid
HDL	high-density lipoprotein
HFCS	high-fructose corn syrup
LDL	low-density lipoprotein
MD	Mediterranean diet
MUFA	monounsaturated fatty acid
PUFA	polyunsaturated fatty acid
RCT	randomized controlled trial
SFA	saturated fatty acid
TG	triglycerides

2. The effect of macronutrients on glucose levels

2.1 Carbohydrates

Carbohydrates are of major importance in diabetes as they are converted into blood glucose postprandially. Undoubtedly, the amount of carbohydrates ingested is the primary determinant of postprandial glycemic response. There are three main types of carbohydrates:

1. Starch (complex carbohydrates)
2. Sugar (simple carbohydrates)
3. Fiber

These types are found in different food groups, such as cereal, pasta, fruits, legumes, starchy vegetables, milk, yogurt and sweets, alone or in combination. Although carbohydrates should not be regarded as a homogenous component as they do not share identical properties regarding fiber content, glycemic index/load, micronutrient content, and others, all carbohydrate-rich foods affect blood glucose levels postprandially [5].

The quality of ingested carbohydrates is also important. Consumption of food with low-glycemic index, rich in fiber, and with low sugar content is preferable for people with diabetes as it interferes less with glycemic control. Furthermore, free fructose should not exceed 12% of total energy intake, and intake of sugar-sweetened beverages should be limited or avoided. Sugar-sweetened beverages contain large amounts of high-fructose corn syrup (HFCS) and sucrose, which are not recommended for individuals with diabetes to prevent the risk of weight gain and deterioration of the cardiometabolic risk profile [5]. In this regard, concerns have been raised against the increasing use of

HFCS in the US (approximately 40% of added sweeteners [8]). and the expected abolition of production quotas of HFCS in Europe (after 2017). On the one hand, HFCS is regarded as a high-fructose sweetener, with the potential to cause metabolic abnormalities, since fructose has been implicated in the development of insulin resistance and metabolic syndrome [9]. However, it is often overlooked that HFCS contains only 50% fructose, which makes it comparable to sucrose and honey rather than pure fructose. Also, there is no significant difference between HFCS and sucrose with respect to fasting plasma glucose, insulin, leptin, ghrelin, and energy and micronutrient intake [10]. The authors believe that sucrose may be as detrimental for the metabolism as HFCS, and that the latter should not be regarded as uniquely responsible for obesity and diabetes epidemic.

2.2 Proteins

Proteins have been associated with increased satiety and preservation of lean body mass during weight loss, but their role in the practical management of diabetes has not been completely clarified. Based on the experiments by Janney in the early 1900s, it was believed that >50% of proteins can be converted into glucose in the blood [11]. However, later studies supported the notion that a rise in plasma glucose following protein ingestion does not explain the theoretical glucose conversion by gluconeogenesis, emanating from the equivalent deaminated amino-acids [12]. This may be partially explained by the proteins' role as an insulin secretagogue. Specifically, among normal subjects, the ingestion of 50 g protein results in an insulin rise that amounts to 28% of that caused by ingesting 50 g glucose [13]. In diabetic subjects, in contrast, the insulin rise after ingesting the protein is equivalent to that caused by ingesting the same amount of glucose [14]. Finally, there seems to be a synergistic interplay between carbohydrates and proteins which reduces glucose levels. Mean insulin secretion was significantly greater when glucose and proteins were given together (50 g each) compared with the administration of glucose or proteins in the same quantity alone [14]. With these properties, proteins may represent a potential adjunct in practical diabetes management.

The type of protein may also play a significant role. In mice, some amino acids, such as leucine, lysine, and alanine, acutely stimulate insulin secretion, whereas homocystein inhibits it [15]. In contrast, very high proline concentrations induce

insulin transcription and mitochondrial oxidative phosphorylation [16]. In non-insulin-dependent patients with diabetes, leucine induces insulin secretion to a greater extent than arginine [17], and glutamine has been suggested to be the most potent amino-acid in amplifying insulin secretion signaling [18]. Also, the observed insulinotropic effect of dairy protein is attributed to the amino acid composition of dairy products [19]. However, very limited data exist regarding the effectiveness of plant versus animal proteins on glycemic control in people with diabetes [20].

2.3 Lipids

Lipids, similarly to proteins, have minimal direct effects on plasma glucose levels *per se*. However, they have long been demonized. For many years, the primary goal of health professionals was to reduce total lipids <30% and limit the intake of saturated fatty acids (SFAs), trans fat, and dietary cholesterol in patients with diabetes to reduce the risk of CVD. Saturated and trans fats were considered to be the principal determinant of plasma LDL [21]. Low-fat research, conducted since 2002, does not clearly suggest the theoretical improvement in lipid profile in patients with diabetes. Adopting a low-fat diet may improve total cholesterol and LDL, but may also lower HDL [20]. In 2010, a meta-analysis of prospective studies found that there is no significant evidence associating dietary SFAs with increased risk of CHD or CVD [22]. Therefore, lipid profile improvement may not be attributed to SFA restriction *per se*, but rather to their replacement by other types of lipids. Not all lipids are homogenous, and the impact of different types of lipids on glycemic control remains to be clarified, but lipids do play a role in glucose metabolism.

Impairment of insulin binding or glucose transport has been associated with changes in the fatty acid composition of cell membranes, which is highly dependent on dietary fat consumption [23]. In healthy adults, SFAs have caused insulin sensitivity to deteriorate, whereas monounsaturated fatty acids (MUFAs) or n-3 fatty acids have no effect [24]. In studies that included patients with type 2 diabetes, substitution of SFAs by polyunsaturated fatty acids (PUFAs) [25] and carbohydrates by MUFAs [26] has decreased insulin resistance. The Mediterranean diet, typical for its high MUFA content, has been shown to improve insulin sensitivity better than very low-carb and low-fat diets [26, 27]. Generally, the relationship between dietary fat and glucose metabolism has not been

fully elucidated. However, the key seems to be quality over quantity.

3. Current macronutrient recommendations

3.1 Carbohydrates

For insulin-dependent individuals with type 1 or 2 diabetes, carbohydrate counting (exchanges or grams) is considered the gold standard for glycaemic control. Therefore, participation in an intensive flexible insulin therapy education program, focusing on the carbohydrate counting approach to meal planning should be encouraged by healthcare professionals [5]. In these cases, carbohydrate intake is primarily determined by personal dietary habits and other health problems that the individual may have. The recommended dietary allowance (RDA) for digestible carbohydrate is 130 g/day (≈ 8 exchanges), which is based on calculations of adequate glucose provision as the required fuel for the central nervous system regardless of glucose production from ingested proteins or lipids [28].

In 2010, the European Food and Safety Authority (EFSA) proposed that the total intake of carbohydrates should range between 45% to 60% of the total energy intake (25 g of which should be fiber) [29]. However, this recommendation has been questioned, at least for the management of type 2 diabetes. While the recommendations for carbohydrate intake vary significantly between organizations, ranging from 40% (Joslin Diabetes Center) [30] to 60% (Diabetes and Nutrition Study Group of EASD and Diabetes Association in UK) [31, 32], medical centers have departed from the recommendation of moderate to high carbohydrate intake, proposing an individualization of nutritional needs instead. Since 2008, the ADA guidelines have not indicated a specific percentage range for carbohydrate intake therefore. The ADA 2014 position statement explained that there is no “first-line” approach with respect to the optimal carbohydrate quantity in the diet plan, because evidence remains inconclusive [5].

3.2 Proteins

The RDA for digestible proteins for adults is 10-35% of energy intake, or a minimum of 0.8 g/kg body weight [28], or 0.83 g/kg based on the EFSA 2010 position statement [33]. The previous ADA position statement suggested that patients with diabetes and normal renal function should con-

sume 15-20% of their energy intake through proteins, as intakes $>20\%$ may have undesirable long-term effects. The statement also suggested that protein intake for patients with early-stage chronic kidney disease (CKD) should be in the range of 0.8-1.0 g/kg/day, and should not exceed 0.8 g/kg/day for patients with late-stage CKD [21]. However, the 2014 protein recommendation is less strict because the evidence is inconclusive, which is also the situation with carbohydrate. Even for patients with diabetic kidney disease, a reduction in proteins is not strongly recommended. Again, the key is individualization [5].

However, what does individualization of diet or nutrition therapy actually mean in concrete terms? Which clinical parameters and other factors may need to be taken into consideration to find a macronutrient consumption plan that aims to minimize the individual patient's risk of developing diabetes – height, weight, BMI, duration of diabetes, type of diabetes, insulin-dependent or not? In fact, there is no general instruction on how to create an individual diet for diabetes patients. This situation is unsatisfactory, and may cause harm to patients in daily medical practice. Therefore, the aim of this article is to propose an individualized nutritional concept that is oriented at the most relevant factors determining the association between macronutrient intake and the development of diabetes and diabetes complications. The concept is presented in section 4.

3.3 Lipids

For healthy individuals, the EFSA proposed in 2010 that lipids should be in the range of 20-35%, and that the replacement of SFA by MUFAs and PUFAs was considered to be crucial. This recommendation was similar to the 2008 nutrition therapy recommendations by the ADA [34]. In fact, individuals with diabetes were treated like people with pre-existing CVD, as they face similar CVD risk. Low-fat diets dominated in this treatment, and the following were considered essential:

- Reducing SFAs to $<7\%$
- Trans fat intake as low as possible
- Dietary cholesterol <200 mg

The main argument was that SFAs and cholesterol have been strongly linked to increased CVD risk [21]. In a 2013 nutritional recommendation for persons with diabetes, no specific percentage of lipids was recommended, but it was suggested that the quality of lipids should tend more towards

Table 1. Summary of recommendations regarding macronutrient composition of a diet

Macronutrient	Recommendation	Issues to consider
Carbohydrates	<ul style="list-style-type: none"> Restriction as low as deemed necessary Emphasis on low GI foods Emphasis on starchy foods Limitation of sugar and fructose Intake of ≥ 25 g fiber/day 	<ul style="list-style-type: none"> BMI Insulin resistance HbA1c Lipid profile Other - not discussed in this review (personal preferences, cultural background, family history of diabetes, physical activity, age, blood pressure, medication used)
Protein	<ul style="list-style-type: none"> ≥ 0.83 g/kg Combination with carbohydrates to improve postprandial glycemic response 	
Fat	<ul style="list-style-type: none"> Reciprocal increase to carbohydrate restriction Substitution of SFA and trans fat over MUFA and PUFA 	

Legend: BMI – body mass index, GI – glycemic index, HbA1c – glycosylated hemoglobin, MUFA – monounsaturated fatty acid, PUFA – polyunsaturated fatty acid, SFA – saturated fatty acid.

omega-3 fatty acids, including eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and linolenic acid, and the intake of SFA, cholesterol, and trans fat should be the same as in the general population [5]. Two years later, recommendations for lipid intake were further toned down; the 2015 Dietary Guidelines Advisory Committee (DGAC) did not recommend limiting dietary cholesterol to <300 mg/day because of insufficient evidence. Regarding SFAs, the DGAC encouraged the maintenance of 10% total calories from SFAs, but did not actually ban them. These proposals were based on the beneficial effects (in terms of a healthy heart) of replacing SFA by unsaturated fatty acids, in particular PUFAs [35].

4. A step-by-step approach

It is clear that the individualized approach proposed by the ADA requires clinical experience and the consideration of relevant clinical parameters. Therefore, the third part of this review aims to specify the parameters that are important for an individualized nutrition approach. It is suggested that these criteria are considered step by step when determining the macronutrient composition of the diet for an individual person with diabetes. This concept has been developed on the basis of recent studies, especially RCTs, and includes four steps to determine the patient's clinical profile (regarding obesity- and diabetes-related parameters) and to initiate adequate treatment measures (**Table 1, Figure 1**).

4.1 Step 1: is the patient overweight (BMI ≥ 25)?

In practice, the answer to this question is mostly yes. More than 75% of adults with diabetes are overweight or obese [36]. The link between body weight (i.e., adiposity) and insulin resistance is well established. Thus, weight loss has long been a recommended strategy for those individuals [37]. Based on the 2013 Report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines and the Obesity Society, a variety of dietary approaches

can produce weight loss in overweight and obese adults. Prescription of 1200-1500 kcal/d for women and 1500-1800 kcal/d for men, a 500-750 kcal energy deficit, or a diet low in certain foods (e.g. high-carbohydrates, low-fiber, high-fat foods) are effective ways of dealing with overweight and obesity. Of course, calorie restriction remains the common denominator. Sustained weight loss of 3-5% can result in clinically significant health benefits, such as lowered triglycerides, blood glucose, HbA1c, and risk of developing type 2 diabetes [38].

Low-fat diets have traditionally been used to promote weight loss. However, for an individual with diabetes, the effects may be different. When the macronutrient composition of a diet changes by reducing lipids, nutritionists usually replace the energy from this source primarily by carbohydrates as high-energy intake from proteins is both hard to maintain in the long term and potentially dangerous for patients with diabetic kidney disease. However, a high-carb diet, particularly one with a lot of rapidly digested sugars and refined starches, leads to an increased demand for insulin to maintain normal metabolic homeostasis. Nutrition high in carbohydrates is therefore not appropriate for people with diabetes to achieve weight loss and metabolic control because of the body's decreased insulin sensitivity and secretion from beta-cells. For this reason, in the past 15 years, many RCTs have proposed low-carb diets as equally effective as or even more effective than low-fat.

Low-carb diets were defined as those with carbohydrate content <50 g, which may promote nu-

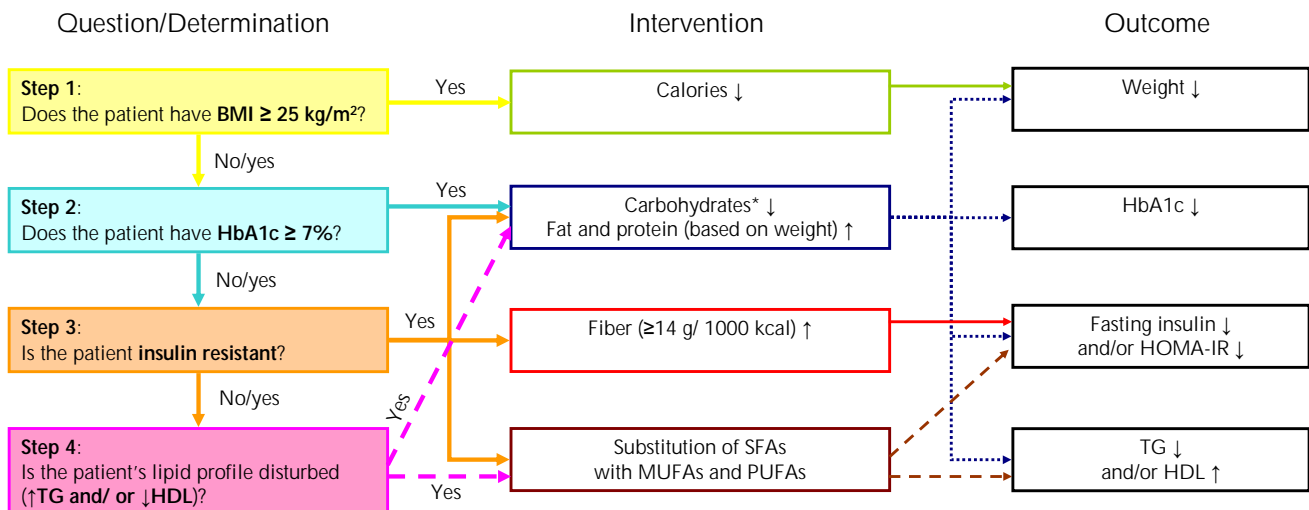


Figure 1. Conceptual framework for determining the macronutrient composition of a diet in diabetes meal planning. This framework includes the four parameters discussed in the article. It is based on results from relevant studies. * Degree of carbohydrate restriction may be dependent on the degree of obesity, insulin resistance, HbA1c, TG, and HDL levels.

tritional ketosis. The first study to assess the efficacy of a very low-carb diet (<20 g carbs gradually increasing) over the conventional low-fat diet (60% carbs, 15% proteins, 25% lipids) in 63 obese individuals was conducted by Foster *et al.* in 2003. The participants in the intervention group lost more weight than those in the control group at 3 and 6 months, but at 1 year, the results were not significant [39]. The faster weight loss after 3 months achieved with the very low-carb protocol, but similar results at 1 year, were confirmed later in an RCT that included 105 overweight individuals with type 2 diabetes [40]. However, the non-sustainability weight loss was no longer a limitation, after a recent meta-analysis of 13 RCTs (around half of the studies included patients with type 2 diabetes in addition to high BMI) found that very low-carb diets (<50 g carbs/d) were more effective in producing weight loss even at 1 year than low-fat diets [41]. The fact that the meta-analysis also included studies with individuals without diabetes is not considered to be a limitation in this case.

Apart from the very low-carb diets, patterns with higher percentages of carbohydrates such as the Mediterranean diet (MD) have been compared with usual care, but results are limited. A high-MUFA diet (typical of MD composition, with 45% carbs, 15% proteins, 40% lipids) failed to promote greater weight loss than a typical low-fat diet (60% carbs, 15% proteins, 25% lipids) at 1-year follow-

up in overweight/obese adults with type 2 diabetes [42]. However, when a low-carb MD (35% carbs, 45% lipids) was compared with the standard low-fat diet in a similar group of participants, it was found to be more effective, while the traditional MD (50-55% carbs, 30% lipids) and low-fat diet produced similar results [43]. On the other hand, it was observed that patients with diabetes had lost approximately the same weight at 2 years' follow-up with a low-carb (20% carbs, 30% proteins, 50% lipids) and a high-carb diet (55-60% carbs, 10-15% proteins, 30% lipids) [44]. However, in this study, only 4 follow-up sessions were performed within the period of 2 years, which raises questions about compliance with the diet. After performing an additional analysis among participants who complied with the energy restriction, the low-carb diet exerted a greater benefit, even after 2 years [44]. Shai *et al.* studied 322 obese individuals for 2 years, in a three-arm RCT, prescribing a very low-carb diet (<20 g, gradually increasing), an MD, and a low-fat diet [27]. Again, the low-fat diet was least effective in promoting weight loss, while the very low-carb diet was most effective, particularly among the 272 participants that completed the study at 2 years. However, no results were provided for patients with diabetes [27].

Finally, in three different studies, the effect of protein variance has been studied in relation to weight loss in overweight or obese individuals with diabetes. A low-protein diet (15%) was compared

with a high-protein diet (30%), using the same amount of lipids (30%), but no significant difference in weight loss was observed [42, 45, 46]. This finding confirmed that the key in weight loss probably lies in the balance of carbohydrates and lipids.

Even though carbohydrates are usually the major part of a diet for achieving weight loss, the aforementioned results indicate that low-fat, high-carb diets, commonly administered in usual care, are not the optimal choice for a group of “carbohydrate intolerant” people or diabetes patients. There is also a significant effect of carbohydrate restriction on leptin levels; it promotes satiety and appetite suppression [27]. It may be that high amounts of carbohydrates are able to render a diet ineffective. Probably, there is a specific cut-off value, under which the carbohydrate restriction offers additional benefits for weight-loss in a person with diabetes.

4.2 Step 2: does the patient have high HbA1c?

Although HbA1c has some limitations in monitoring glycemic control (i.e., it does not provide a measure of glucose variability or hypoglycemia), it is still considered the best variable to evaluate a 3-month glycemic course in everyday clinical practice. Achieving an HbA1c $\leq 7\%$ is considered to maintain low risk of microvascular complications and long-term macrovascular complications of diabetes (when implemented soon after the diagnosis) [37]. It is clear that if a person has a high HbA1c, overall management, including dietary intervention, should be more intensive.

However, what is the most effective dietary therapy for lowering HbA1c levels? Consistently with the aforementioned results, most RCTs in patients with diabetes have reported that a greater reduction in HbA1c levels is achieved after carbohydrate restriction rather than after protein or lipid restriction. Specifically, significant reductions in HbA1c have been detected at 3 and 6 months using very low-carb or low-carb diets versus low-fat diets [47-49], even when there was no upper limit for SFA intake [44]. Similarly, Elhanyay *et al.* found that a low-carb MD produced a greater improvement in HbA1c than a traditional MD or a low-fat diet at 1 year [43], whereas studies comparing diets with $\geq 40\%$ carb percentage, differing mainly in protein and lipid content, have reported similar reduction rates of HbA1c at 1 year [42, 45, 50]. Finally, in the study by Shai *et al.*, with a longer follow-up of 2 years, in the subgroup of individuals with diabetes, HbA1c decreased in the

very low-carb group only, but not in the MD and low-fat group [27].

4.3 Step 3: what is the degree of insulin resistance?

Insulin resistance, characterized by reduced responsiveness to normal plasma insulin concentrations, is a typical feature in type 2 diabetes. It is measured using fasting insulin levels or homeostatic model assessment for insulin resistance (HOMA-IR). The predecessor of insulin resistance is usually high BMI, especially visceral obesity. However, individuals who are not obese according to standard BMI criteria may have an increased percentage of body fat distributed predominantly in the abdominal region; they may be insulin resistant as well. Apart from pharmacological treatment, this condition may improve by weight reduction [37]. With regard to diabetes onset, high-carb diets have not been found to affect insulin sensitivity adversely; they may even be beneficial. On the contrary, high lipid intake, especially SFA, may be related to impaired insulin sensitivity [51].

The questions that arise are (i) whether the same applies to people with established type 2 diabetes, and (ii) what the best diet is to delay the progress of insulin resistance in patients with type 2 diabetes. There are no conclusive answers to these questions. RCTs that have examined dietary patterns with different macronutrient compositions in individuals with diabetes are limited. Shai *et al.* included a subgroup of 36 participants with diabetes. It was reported that the Mediterranean diet, compared with the very low-carb diet and the low-fat diet, was the only one to induce a significant reduction in HOMA-IR after 2 years of follow-up [27]. In contrast, in 124 overweight/obese individuals with type 2 diabetes, randomized to follow either a Mediterranean diet or a low-fat diet, no significant differences in insulin levels were detected between the groups after 1 year [42]. However, a 2009 meta-analysis, which examined 19 RCTs and 306 participants, concluded that a high-fat/low-carb diet is more effective in lowering fasting insulin levels than a high-carb/low-fat diet [52].

Nevertheless, it seems that the key to improving insulin sensitivity through diet may be quality rather than quantity alone. As mentioned in the first section, lipid quality has been implicated in insulin resistance. Specifically, the addition substitution of SFAs and carbohydrates with MUFAs or PUFAs has been found to improve insulin sensitivity [25-27]. It would be interesting to study

whether the Mediterranean diet, which is traditionally high in MUFAs, is superior to a well-formulated low-carb diet, rich in MUFAs and PUFAs instead of SFAs.

Furthermore, carbohydrate quality may contribute to some extent to the reduction of insulin resistance in people with diabetes. A large, cross-sectional study in 979 individuals, with normal or impaired glucose tolerance, revealed a significant positive association of fiber intake with insulin sensitivity, and a negative association between fiber intake and fasting insulin levels, whereas glycemic load and index were not related to any index of insulin sensitivity or secretion [53]. In a cross-over RCT in 15 adults with insulin resistance, supplementation of 40 g/day of a specific type of resistant starch (HAM-RS2) compared with a matched placebo for 8 weeks was found to improve peripheral insulin sensitivity in the forearm muscle and adipose tissue [54].

The aforementioned results support current nutrition recommendations for diets rich in fiber (14 g fiber/1000 kcal/day) and unsaturated fatty acids for individuals with diabetes. Consequently, it is suggested that nutrition counseling should emphasize substitution of SFAs with unsaturated fatty acids and fiber, particularly in people with increased insulin resistance. Since carbohydrate restriction may be necessary (considering parameter 1 and 2), it is essential for nutritional professionals to identify carbohydrate-rich sources with high fiber concentrations, so as to ensure increased fiber intake (25 g/day), despite a potential decrease in carbohydrates.

4.4 Step 4: does the patient have a disturbed lipid profile?

A common condition coexisting with type 2 diabetes is dyslipidemia, which significantly increases CVD risk. A combination of low HDL and high triglycerides (TG) is identified as the most prevalent pattern of dyslipidemia among patients with diabetes. Pharmacological treatment successfully improves this disturbed lipid profile [37]. However, which dietary modifications may beneficially alter plasma lipids? So far, carbohydrate restriction has been shown to exert a positive effect on body weight and HbA1c, but if lipids are simultaneously increased when carbohydrate is reduced, this may be detrimental for people at high CVD risk, even compared to a conventional low-fat diet.

In 2006, a meta-analysis comprising 5 RCTs and 477 overweight or obese participants found that low-carb diets (20-50 g/carb) versus low-fat

diets had a favorable effect on TG and HDL, whereas low-fat diets were more effective in improving LDL and TC [55]. A larger meta-analysis in 2009 comprising 19 RCTs and 306 participants with type 2 diabetes concluded that low-fat diets (>50% carbs) increase TG and lower HDL compared with low-carb diets (defined as >30% carbs), whereas LDL and TC are not significantly altered [52]. The difference in the definition of "low-carb" between the two meta-analyses is obvious, and explains the different studies included in each meta-analysis and the different conclusions. However, a common message is that high carbohydrate intake (>50%) does not favorably affect TG and HDL in patients with diabetes. A benefit of low-carb versus low-fat diets has also been reported in other studies regarding HDL levels [40, 43, 48, 56], TC/HDL ratio [27, 56], and triglycerides [27, 43, 48, 56].

Similar changes in lipids were seen when the protein content was stable (15%) and carbohydrate intake >45%. Specifically, a Mediterranean diet (45% carbs, 40% lipids) achieved the same improvement in HDL as a low-fat diet (60% carbs, 25% lipids) [39], implying that moderate restriction of carbohydrates may not be enough. Finally, proteins *per se* do not seem to be responsible for the significant changes in lipid profile; i.e., similar changes in HDL, TG, total cholesterol (TC), and TC/HDL ratio were seen when two low-fat diets (30% lipids), high or low in protein (30% vs. 15%), were compared in overweight or obese individuals with type 2 diabetes, in 3 different studies at 1 year of follow-up [45, 46, 50].

5. Conclusions

Macronutrient composition is a highly debated issue in diabetes meal planning. The existing results suggest that both quality and quantity of carbohydrates play a significant role in diabetes management. In the majority of the studies, carbohydrate restriction had a favorable effect on weight reduction and glycemic control. A number of studies have indicated that restricting carbohydrates and replacing them primarily by unsaturated fats and secondarily by high-biological value proteins (considering kidney function) has beneficial effects on glycemic control indices in patients with diabetes. Therefore, an increase in healthy lipids (i.e., rich in MUFA and PUFA and low in SFA) and specific proteins high in biological value seems to be beneficial for at least those diabetic patients without chronic kidney disease. This conclusion does not rule out the results of numerous studies,

which have supported carb-rich patterns, for example the Mediterranean diet or the healthy Nordic diet in diabetes secondary prevention.

Following the 2014 recommendations and the trend towards individualization, it is obvious that a nutritional algorithm designed for health professionals is needed to guide them through the process of meal planning, and to help them determine the optimal macronutrient composition. The authors believe that the precise amount of carbohydrates in the diet should be the starting point in diabetes meal planning. That is why a collaborative effort to create a standardized formula of car-

bohydrate calculation for a person with established type 2 diabetes is necessary. The parameters discussed in the present review may be considered in the first instance, i.e., body weight, level of insulin resistance, HbA1c, lipid profile. The consideration of other parameters, including age, physical activity level, blood pressure, family history of diabetes, medication, inflammatory markers, and time of diagnosis, may be a second step in optimizing and tailoring medical nutrition therapy in individual patients (**Table 1**).

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