Thieme

Dietary recommendations for persons with type 2 diabetes mellitus

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Preface

This practice guideline is aimed at all professional groups caring for people with type 2 diabetes mellitus (T2Dm). In addition to the multifaceted aspects of nutrition in diabetes, there is a particular call for individualization of therapy, counseling, empowerment, and diabetes self-management [1–3]. Therefore, the Nutrition Committee of the DDG has set the goal to compile practice guidelines on nutrition as target group-specific as possible with the highest available evidence. In doing so, it is considered necessary to treatment forms separately presentation since the therapeutic significance of nutrition differs significantly in each case and must be seen against the background of different drug therapy components.

T2Dm is characterized by a progressive course in terms of β-cell insufficiency, which progresses at different rates in different individuals [4–7]. Against this background, patients with T2Dm have both quite different characteristics and treatment regimens [8].

For patients with special life circumstances, e. g., sarcopenia and need for long-term care, diets must be designed taking strong consideration of personal preferences and with an emphasis on meeting protein requirements.

Overall, as a result, nutritional therapy needs to be highly individualized to realize its full potential.

The option of individualized nutritional counseling, including via telemedicine, should therefore be used more widely and intensively in people with T2Dm. The general goals are to promote balanced eating habits, provide training on appropriate portion sizes, and address individual dietary needs while maintaining enjoyment of food and providing practical tools for meal planning. Individualized nutrition counseling sessions include evidence-based topics

that should be provided by qualified and appropriately certified nutrition professionals (dietitian, nutritionist or ecotrophologist).

The nutritional therapy plan must also be coordinated and continuously aligned with the overall management strategy, including medications administered, physical activity, etc.

In addition, people with prediabetes and excess weight/obesity should be referred to an intensive lifestyle intervention program that includes individualized goal-setting components, as defined, for example, by the S3 Guideline Prevention and Therapy of Obesity (S3-Leitlinie Prävention und Therapie der Adipositas). Since this service is not yet a standard benefit of the statutory health insurance, at minimum individualized nutrition counseling should be provided with partial cost coverage according to § 43 German Social Security Code (SGB).

Another important recommendation is the referral of adults with diabetes to comprehensive diabetes self-management training and support (Diabetes-Selbstmanagementschulung und -unterstützung - DSMES) according to national standards.

This practice guideline represents the summary and evaluation of the literature by the Nutrition Committee of the DDG on selected nutritional aspects in the management of T2Dm. Regular updating and, if necessary, supplementation is planned. In doing so, the evidence - if available - was assessed in the context of literature research based on systematic reviews or meta-analyses. Original papers were also used for topics without the availability of such reviews.

Body weight recommendations

General recommendations

RECOMMENDATION

- In cases of excess weight, the goal of weight reduction should generally be pursued.
- Weight cycling should be avoided.

Comment

With age comes a weight gain leading to an increase in BMI of 5 points and is associated with a 3-fold (weight gain between 18 and 24 years) or 2-fold (weight gain ≥ 25 years) higher risk of T2Dm [9]. Obesity alone is an independent risk factor also for coronary heart disease (CHD). Moderate weight reduction, on the other hand (5–10 % of current weight), reduces risks such as insulin resistance, hyperglycemia, and dyslipidemia [10] and can reduce secondary complications. A very-low-calorie diet (VLCD; 624 kcal/d) for 8 weeks can also lead to a temporary diabetes remission of at least 6 months [11]. The effectiveness of a VLCD diet is greater with a shorter duration of diabetes and with higher fasting insulin and C-peptide levels [12]. Intensive weight management with a mixed diet and lifestyle intervention also leads to sustained remission [13]. In this context, a stable body weight seems to be associated with a better cardiovascular outcome than a high weight variability [14–16]. Weight gain or weight variability in T2Dm is associated with higher mortality [15, 17].

However, especially in elderly patients, greater weight loss (> 25 %) is associated with loss of muscle mass [18]. Studies also show that individuals with T2Dm with a normal weight have higher mortality than those with higher body weight [19, 20], which has been repeatedly described as the obesity paradox [21]. A possible explanation for this effect is a larger, more metabolically-active muscle mass in obese patients [22]; this must be factored into weight goals and, if necessary, included in a physical activity program for muscle maintenance [23].

Quantitative statements on targeted weight reduction, diabetes remission

RECOMMENDATION

- The extent of weight reduction is based on individual therapy goals. For diabetes remission, a target weight reduction of 15 kg of baseline overweight/obesity weight should be aimed for.

Comment

The association of obesity with all components of the metabolic syndrome makes weight reduction a priority therapeutic goal. The normal and realistic consensus was a 3–5 kg weight reduction in the context of dietary and exercise behavior modification. Achieving these goals allowed a reduction in T2Dm manifestation of about 60 % in people with prediabetes and has been demonstrated in large studies [24]. A greater weight loss of 10 kg was significantly more effective and prevented diabetes manifestation in over 90 % of study participants [25] over 3 years.

Remission of T2Dm after an average of 5 years of diabetes duration and 1 year of intensive lifestyle modification program with 8.9 % weight reduction (baseline BMI 35 kg/m²) was 11.5 % in the Look Ahead trial. After 4 years, weight reduction was still 4.7 % of baseline weight, and 7.3 % showed remission defined as fasting blood glucose below 126 mg/dl without diabetes medications [26].

In the DIRECT study, a weight reduction of 15 kg with formula diets resulted in an 86 % remission of T2Dm after a maximum of 6 years of previous diabetes. Lower weight loss resulted in greatly lower success rates, but only a few patients were able to achieve significant weight loss. The data shows a quantitative effect of weight loss on diabetes remission [13]. Patients should therefore be offered appropriate therapy as early as possible after diagnosis of T2Dm [21].

What is the role of the weight loss strategy of a formula diet versus slow moderate weight loss? In the long term, the likelihood of regaining weight after cessation of the diet program is more than 80 %. Formula diets result in faster and more significant weight loss and still show greater weight loss in the long term [27].

Weight loss leads to rapid improvement in hepatic insulin resistance, so that blood glucose levels decrease rapidly while the insulin secretory capacity remains unchanged. With insulin therapy and insulin resistance, insulin levels must be reduced rapidly (1–5 days), often by two-thirds of the initial dose. The patient must either be prepared for this or the therapy should be performed as an inpatient for the first few days, and as an outpatient only with daily patient contact.

Using telemedicine for type 2 diabetes mellitus

RECOMMENDATION

- Telemedicine applications can support the implementation of behavioral modifications recommended in the treatment of T2Dm.
- Telemedicine can increase adherence to weight loss programs and accessibility.

Comment

The COVID-19 pandemic has increased the need for digital consultation methods in the therapy of diabetes mellitus. Telemedicine refers to the use of audio-visual communication technologies for the purpose of diagnosis, consultation, and emergency medical services [28]. Telemedicine care for diabetes patients had already been used before the COVID-19 pandemic and has established itself as a proven form of therapy.

As part of a telemedicine program, therapy-relevant data (e. g., blood glucose level, insulin dose, body weight) is transmitted to the healthcare professional, whereupon the patient receives feedback. A distinction is made between telemedical therapy via text messages/e-mail and via telephone/video conferencing.

A meta-analysis by Su et al. from 2015 with 92 included studies showed a significant reduction of the HbA_{1c} value in type 1 and type 2 diabetes patients through telemedical nutrition therapy [29]. However, no significant difference was found between telemedicine programs via messaging (cell phone or email) and a face-to-face consultation (telephone call or video conference).

In Germany, a randomized controlled trial by Kempf et al. reported a 0.6 % lower HbA_{1c} value and a 5 kg greater weight reduction at the 1-year follow-up in the telemedicine-assisted group vs. standard therapy [30].

Telemedical applications can be prescribed by physicians and psychotherapists and reimbursed by the statutory health insurance companies if they are included in the Federal Institute of Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte - BfArM) directory as digital health applications (Digitale Gesundheitsanwendungen - DiGA). This is regulated in the Digital Health Care Act (Digitales Versorgungsgesetz - DVG), which came into effect in December 2019. Digital health applications are usually used by the patients on their own. However, it is also possible for patients and providers to make use of digital health applications together, for example in the form of teleconsultation or chats. At the time of publication of these practice guidelines, no digital health applications with the indication “diabetes” are listed in the BfArM directory, but several diabetes digital health applications (Diabetes-DiGA) are currently being evaluated.

The DiGA “Zanadio” with the indication “obesity” is provisionally included in the BfArM directory. Zanadio works on the basis of the guideline recommendations for the therapy of obesity and supports a conservative obesity therapy consisting of exercise, diet and behavioral change. Zanadio includes telemedicine elements in that users are supported by a dietitian via a chat function.

An example of a telemedicine application - though not approved as a digital health application - is the TeLiPro telemedicine lifestyle intervention program. In this program, patients are provided with an app that is used to monitor lifestyle activities. Bluetooth-compatible blood glucose meters, scales, blood pressure monitors and pedometers are used for this purpose. A cloud enables the diabetes coach (diabetes advisor) to view the data and interact directly with the patient via a chat function or by telephone.

In the TeLiPro study, both groups received the app, scales, pedometers, blood glucose and blood pressure monitors. However, the groups differed in that a diabetes coach was only available to patients in the intervention group [29].

As a result, it can be seen that the intervention group, in contrast to the control group, had a significant reduction in HbA_{1c} (mean ± SD − 1.1 ± 1.2 % vs. − 0.2 ± 0.8 %; P < 0.0001). There was also a reduction in weight (TeLiPro − 6.2 ± 4.6 kg vs. control − 1.0 ± 3.4 kg, BMI (− 2.1 ± 1.5 kg/m^2 vs. − 0.3 ± 1.1 kg/m^2). Furthermore, the intervention group reported a generally better quality of life as well as a better nutritional status [30].

Strategies for weight reduction and weight maintenance

RECOMMENDATION

- Weight reduction must be clearly indicated before it is recommended. Higher age is a risk factor for sarcopenia and cardiometabolic disadvantages from hypocaloric diets.
- Close follow-up with dietary counseling is necessary to facilitate good long-term adherence.
- The weight loss strategy should match the preferences of the overweight person (individualized nutrition therapy).
- The strategy for sustainable stabilization of a reduced body weight should be coordinated on an individual basis with the affected person.
- To date, no dietary pattern is clearly superior to other dietary patterns in weight reduction.

Comment

Various forms of hypocaloric dietary modification - ranging from long-term useful procedures to procedures limited to short interventions - lead to a reduction in body weight in T2Dm patients and often also to an improvement in metabolic status and other cardiovascular risk factors. However, only a few patients succeed in achieving significant long-term weight loss, both with complex lifestyle intervention and with formula diets. Thus, to date, the true goal – diabetes remission, as well as reduction in actual long-term risk for cardiovascular morbidity and mortality – remains achievable at best for subgroups that are difficult to define [13, 31]. Bariatric procedures are also successful in diabetes remission, but are also subject to strict criteria for indication [32].

Numerous strategies have evolved for weight loss, differing in approach in terms of daily energy intake (low-calorie diet [LCD]/VLCD), nutrient ratio (low-fat/low-carb), consistency (common foods/formula drinks), preference for an omnivorous or vegetarian/vegan diet, as well as the limiting of fasting and eating times (intermittent fasting).

The effects of these respective approaches are continually published and championed. However, there is no strategy that is fundamentally superior to another. It depends on personal preference as to which method (or combination of methods) the person wanting to lose weight prefers and which method motivates him or her to implement it sustainably in everyday life [2, 3].

In most studies, it has not been conclusively clarified as to how the targeted, and ultimately achieved, weight reduction is actually decisive or necessary for the obtaining results [33]. Dietary modifications *without* weight reduction also sometimes achieve dramatic improvements. A systematic head-to-head comparison of hypo- and isocaloric diets with the *same* macronutrient ratio is rarely described in literature. Meta-analyses find little long-term metabolic benefit for a primary weight loss intervention compared with standard therapy, albeit with considerable heterogeneity among studies [34].

Maintenance of long-term weight loss is strongly influenced by the ability to adhere to the diet program. Behavioral support can significantly improve outcomes. There are individual differences in response to each diet that are greater than the difference in mean weight loss between comparison diets.

Interaction between diet and physical activity

RECOMMENDATION

- A high level of low-intensity physical activity (e. g., brisk walking) after meals improves body weight regulation and is beneficial for glycemic control.

Comment

While inactivity or a predominantly sedentary lifestyle pose a risk for excessive caloric intake and thus for the development of obesity [35–37], a high level of physical activity even at a low intensity (e. g., fast walking) ensures a better adaptation of appetite to energy demand [38, 39] and thus improves the regulation of body weight even independently of a higher caloric expenditure [38].

Additionally, exercise type, intensity, and timing (fasting or postprandial) have an impact on glycemic regulation [40]. In this regard, the intensity of physical activity correlates positively with the improvement of insulin sensitivity, and the best results are obtained by a combination of strength and endurance training [40]. There is evidence that high-intensity exercise (e. g., high-intensity interval training-HIIT) best improves glycemic control when fasting (i. e., when substrate availability is low) [40]. However, the effectiveness and safety of this method in patients with T2Dm need further investigation. In contrast, low-intensity physical activity is safe and effective in improving glycemia in patients with T2Dm, especially when substrate availability is high. Accordingly, fast walking after eating has a beneficial effect on postprandial glycemia by improving insulin-independent glucose uptake [41–46].

Reducing carbohydrates (low-carb)

RECOMMENDATION

- For weight reduction, a moderate reduction in carbohydrates is recommended as a possible method, especially in the short term (e. g., traditional Mediterranean, plant-based).
- Carbohydrates should preferably be consumed in the form of whole grains, legumes, and nuts.
- For weight maintenance, low-carb are probably on par with low-fat diets and should be chosen according to individual preference.
- Low-carb diets in particular can only be implemented in individuals with insulin therapy under close therapy monitoring.

Comment

Carbohydrates account for an average of about 45 % of energy intake in the diet of Germans, including about 90 grams of sugar (= 18 energy percent [E %]) and often mainly rapidly metabolized polysaccharides. Epidemiologically, there is increased mortality with carbohydrate intakes greater than and less than 50 % (the latter only with animal-emphasized protein sources) [47]. Reducing carbohydrates as part of a dietary intervention almost invariably leads to weight loss and metabolic changes. The scientific literature mostly considers low-carbohydrate diets in juxtaposition to low-fat diets. Carbohydrate reduction can be classified as moderate-carb, low-carb, or very-low carb, depending on the intensity; according to this, the traditional Mediterranean diet is also a low-carbohydrate diet [42].

American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD) classify low-carb as a dietary therapeutic option, but classify the Mediterranean diet as superior [48]. This consensus reflects the state of knowledge from recent meta-analyses: among all dietary models defined in terms of food *quality* examined in randomized controlled trials (RCTs), the traditional Mediterranean diet performs best for fasting glucose and lipid profile, and is among the top 3 diets for HbA_{1c} levels, blood pressure, and weight reduction, respectively. Low-carb is the most effective method for reducing HbA_{1c} levels and body weight; in reducing fasting glucose, blood pressure, and blood lipids, this diet is also very successful and more effective than low-fat [49–51]. However, with prolonged use, low-carb and low-fat converge in their effect; whether this is due to waning adherence or a failure of the metabolic response cannot be answered at present [52].

A very recent meta-analysis also highlights that low-carb (< 26 E % or < 130 g carbohydrate [carbs]/day) may be superior to low-fat in diabetes remission. After 6 months, significantly more patients achieve HbA_{1c} levels below 6.5 % with low-carb; the differences are not significant when the additional criterion of no medication or longer intervention is applied [53].

Looking at the effect of specific food groups on the overall metabolic picture of all cardiovascular risk parameters, among 66 food categories, nuts, legumes, and whole grains (all of which are carbohydrate carriers) performed best [50]. Isocaloric replacement alone of different digestible carbohydrates with each other produces only relatively small effects on fasting glucose and low-density lipoprotein (LDL) cholesterol (sugar replaced with starch), as well as homeostasis model assessment-insulin resistance (HOMA-IR) and uric acid (fructose replaced with glucose). The evidence of these results is, however, considered to be low [54]. Effects on inflammatory parameters are not observed [55].

Overall, the traditional Mediterranean diet is to be regarded as a specific representative of "low-carb" as an optimal dietary form. More generally, "low-carb" and "low-fat" are metabolically equivalent after a few months of intervention at the latest [55]. According to current knowledge, there is no clear long-term optimum for the energy content of carbohydrates. Patients whose personal preference strongly leans toward one of these dietary variants can use it. However, depending on the intensity and dynamics, additional intermediate metabolic controls are recommended to detect an individually unpredictable derailment of glycemia and insulin resistance, lipid metabolism or uric acid levels at an early stage [50].

Reducing fats (low-fat)

RECOMMENDATION

- A low-fat diet cannot be recommended to individuals with T2Dm as a generalization.

Comment

As described in the section on carbohydrate reduction, reducing dietary fats alone is associated with inferior outcomes compared with all low-carbohydrate diets for weight reduction, blood pressure reduction, and optimization of triglycerides and glycemic parameters [48, 51, 52, 56]. Compared to diabetes prevention by complex lifestyle intervention and a low-fat approach has been consistently shown [24], the chance of diabetes remission by low-fat dietary change as a sole intervention is comparatively small [26, 57].

RECOMMENDATION

- Industrially-produced trans fats should continue to be avoided; natural trans fats are probably not problematic.

Comment

The quality of the fat also has a relevant influence on the glycemic metabolic state. In observational studies, industrially-produced trans fats have been shown to increase mortality, in particular by increasing the risk of CHD. An increased risk of diabetes is not described [58].

Natural trans fats, such as those found in beef and dairy products, are associated with decreased diabetes risk in epidemiological studies and do not affect the risk of cardiovascular mortality or morbidity [58].

Saturated fats

RECOMMENDATION

- Foods with a natural saturated fat content are safe if consumed in moderation. Highly processed products with added saturated fats should be avoided.

Comment

The discourse on saturated fats has not reached a definitive conclusion even in 2021. The criticism of saturated fats (sometimes even erroneously all fats) fueled by the Seven Countries Study and many epidemiological follow-up surveys is no longer justified in recent meta-analyses on cohort studies [58]. The evidence regarding a potential for harm from saturated fat is insufficient [59]. Even butter, as a typical food with very high levels of saturated and total fat, epidemiologically only increases mortality minimally, but does not affect cardiovascular risk and is more associated with lower diabetes risk [60]. Other high-fat or low-fat dairy products also have little adverse effect on metabolic outcomes [61].

RCTs on low-fat diets show a mean slight reduction in body weight, BMI, body fat percentage, and waist circumference [62], but no effect on CHD, cardiovascular mortality, or all-cause mortality [63]. A reduction in saturated fat consistently has a beneficial effect on the inflammatory phenotype [31, 64]. It has also been shown to lower LDL levels but worsen HDL and triglyceride levels [65].

Unsaturated fats

RECOMMENDATION

- High levels of unsaturated fatty acids should be targeted in patients with T2Dm, regardless of total fat, through intake of natural foods but not supplements.

Comment

Observational studies describe clear diabetes- and cardioprotective associations for monounsaturated and polyunsaturated fatty acids, especially for linoleic acid and alpha-linolenic acid [66–68].

In intervention studies, evidence of cardio-protection and mortality reduction is lacking for polyunsaturated fatty acids (PUFAs) omega-6 fatty acids and non-long-chain plant omega-3 PUFAs [69, 70]. Moreover, in meta-analyses of randomized controlled trials, no glycemic benefit is seen for unsaturated fatty acids when compared against saturated fatty acids [71]. Compared with carbohydrates, monounsaturated fatty acids (MUFAs) are beneficial in all metabolic axes except for blood pressure [72, 73]. Compared to saturated fats or placebos, there is a benefit in waist circumfer-

ence, inflammation, triglyceride levels, platelet aggregation, and probably fatty liver (omega-3 fatty acids) [74–78]. A high omega-3/omega-6 fatty acid ratio may play a beneficial role in people with diabetes and during prolonged intervention, particularly in lowering insulin but not glucose levels [79, 80]. Women appear to benefit more markedly than men [81]. There is no clear interventional benefit for alpha-linolenic acid with respect to diabetic metabolic status [82].

Intermittent fasting/interval fasting

RECOMMENDATION

- Intermittent fasting can be used as a means of weight reduction under medical supervision.
- No general recommendation can be made for any form of interval fasting.

Comment

In addition to the qualitative adjustment of the diet through a modified nutrient profile or targeted redistribution of food groups, meal frequency is also considered a starting point for weight reduction and metabolic improvement.

Randomized trials of daily meal frequency show a small benefit in favor of less frequent meals (1–2 vs. 6–8) with respect to body weight, fat mass, and waist circumference. However, these effects are of low overall evidence [82].

Less frequent food intake prolongs lifespan in some animal models. Observational studies in humans (e. g., in the context of Ramadan) see only relatively small metabolic changes in healthy individuals, and moreover, these changes are transitory [83–85]. In diabetics, metabolic deterioration is also described. Further cohort studies describe a less frequent occurrence of coronary heart disease and [86, 87].

Targeted, long-term, regular skipping of meals according to a fixed chronological pattern (interval fasting) comprises different variants: alternate day fasting, 5:2 fasting, and time-restricted eating (e. g., 16:8 fasting). These are sometimes compared in literature together with continuous caloric restriction or even unchanged control diets.

In all meta-analyses on interval fasting (8 meta-analyses on over 40 RCTs), no superiority of interval fasting over continuous calorie restriction is found. Compared with an unchanged control diet, there is a significantly greater reduction in body weight, waist circumference, blood pressure and triglycerides, but not in LDL cholesterol, fasting glucose or HbA_{1c}[88–92]. RCTs with T2Dm patients are scarce. These show the same pattern of desired outcomes as in the aforementioned meta-analyses, but an increased risk of hypoglycemia [93–97].

Meal replacements/formula diets (with/without multimodal program)

RECOMMENDATION

- Low-calorie formula diets allow clinically-relevant weight loss in people with T2Dm, associated with significant improvement in glucose and lipid metabolism and reduction in other cardiovascular risk factors.

Comment

Replacing meals with low-calorie formulary diets is a safe and effective weight loss intervention in overweight and obese individuals with T2Dm compared with conventional calorie-restricted diets. In addition to favorably affecting anthropometric parameters such as waist circumference and body fat mass, formula diets also improve other cardiometabolic risk parameters such as blood pressure, fasting glucose, HbA_{1c} level, and lipid metabolism [98–101]. In weight loss programs, the use of formula diets results in pronounced weight loss similar to that seen after bariatric surgery, associated with sustained diabetes remission. However, only 25 % achieve a weight reduction of > 15 % at which remission is very likely to occur [13, 102].

Scientific background

Obesity is one of the most important risk factors for the development of T2Dm [103]. Overweight or obesity exists in 60–90 % of patients with T2Dm [104, 105]. In contrast, weight loss leads to an improvement in glucose and lipid metabolism and a decrease in elevated blood pressure levels. Thus, weight loss in patients with T2Dm represents one of the most important therapeutic measures [105]. However, weight loss, already challenging for people without diabetes, is often further complicated in people with T2Dm because of genetic and metabolic differences, fear of hypoglycemia, glucose-lowering therapies that promote weight gain, decreased physical activity, and diet fatigue. Low-calorie diets have the potential to result in weight loss similar to bariatric surgery in people with T2Dm. A meta-analysis of 9 studies examining the effects of very-low-energy diets (VLED) in a total of 192 obese people with T2Dm found that participants had lost 9.6 % of baseline weight after 6 weeks and fasting glucose had reduced by 50 % after only 2 weeks [106]. However, many people with T2Dm find it difficult to make longer-term lifestyle changes aimed at weight loss, and motivation may be rapidly lost in the absence of short-term intervention success. Low-calorie formula diets have now been shown in numerous studies to be a safe and effective treatment option to improve cardiometabolic endpoints such as waist circumference, body fat mass, blood pressure, and HbA_{1c} levels in obese patients with T2Dm [98–101]. A meta-analysis including 4 studies with a total of more than 500 study participants found that weight loss resulting from low-calorie formula diets, providing between 300 and 1000 kcal of energy per day, was similar for both people with T2Dm and without diabetes, with a mean weight loss between 8 and 21 % of baseline weight after a treatment period of 4–52 weeks. There was also no difference in the rate of weight loss between people with

(− 0.6 kg per week) and without T2Dm (− 0.5 kg per week) [107]. In another study, there was also no difference in weight loss after starting a low-calorie formula diet between patients with and without diabetes. One fifth of the participants achieved a weight loss of more than 15 kg after 12 months. Among participants who continued the weight management program beyond one year, nearly 40 % had a weight loss of at least 15 kg after 24 months [108]. Weight loss resulting from temporary use of a low-calorie formula diet is associated with longer-term improvement in glucose and lipid metabolism and blood pressure [109]. Also, in patients with inadequate metabolic control, meal replacement with a formula diet can lead to a clinically-relevant decrease in HbA_{1c} and a substantial reduction in insulin doses in patients on intensified conventional insulin therapy [110, 111]. Diabetes remission also appears possible as a result of strict caloric restriction, as suggested by the results of the Diabetes Remission Clinical Trial (DiRECT) [112]. Nearly half of the overweight and obese patients with T2Dm who initially received only a formula diet of 825 to 853 kcal per day for 3–5 months achieved diabetes remission in contrast to only 4 % of patients who received only standard therapy from their primary care physician [13]. After 12 months, one quarter of the intervention group had achieved the stated goal of losing 15 kg or more and no participant in the control group. Diabetes remission was very closely associated with weight loss. While remission did not occur in any of the patients who gained weight, the remission rate was 86 % in participants who lost at least 15 kg. Two years after the intervention, more than one-third of patients with T2Dm were still in remission. In participants who had lost more than 10 %, the remission rate was as high as 64 % [102]. Even in people with an increased risk of diabetes due to overweight or obesity and at least one other metabolic syndrome comorbidity, additional meal replacement with a decreasing frequency formula diet over the study period was superior to lifestyle intervention alone in terms of weight loss and improvement of cardiometabolic risk factors [113]. In addition, conversion from prediabetes to normoglycemia was achieved in half of the participants who also received a formula diet, whereas this was the case in less than one-third of the participants treated with lifestyle intervention alone [114].

Additional aspects of weight reduction in insulin-treated T2Dm

RECOMMENDATION

- Insulin therapy should be limited to what is necessary due to the anabolic effect of the hormone. Weight loss under insulin therapy is more difficult.

Comment

In addition, insulin therapy often leads to weight gain in patients with diabetes, most of whom are already overweight: the United Kingdom Prospective Diabetes Study (UKPDS), in which T2Dm patients treated with insulin were randomized, showed an average weight gain of 6.5 kilograms [115]. Despite insulin therapy, lifestyle intervention remains a very important therapeutic component [116].

However, another study showed that the higher the baseline BMI of the patients, the lower the weight gain. When the HbA_{1c} value decreased by one percentage point, weight increased by an average of 1.24 kg in those with normal weight (BMI less than 25 kg/m^2), but weight decreased by as much as 0.32 kg in those with severe obesity (BMI greater than 40 kg/m^2) [117].

Summary evaluation and outlook

There are a number of methods to choose from for weight reduction or weight stabilization. There is more or less good evidence for each of these methods. In our view, the focus must be placed on the individual preferences of the patients, which strengthen adherence to the respective therapy method regardless of the outcome.

Dietary patterns

RECOMMENDATION

- For diabetes management and reduction of the risk of cardiovascular complications in individuals with T2Dm, a variety of dietary patterns is acceptable, such as a Mediterranean, vegetarian, or vegan diet.
- There is currently insufficient evidence to recommend the DASH diet, the Nordic dietary pattern, and the Paleo diet specifically for the treatment of T2Dm.
- Until additional evidence is available on the superiority of a specific dietary pattern related to diabetes therapy target parameters, individuals with T2Dm should be guided by the commonalities of the dietary patterns mentioned: choosing non-starchy vegetables and low-processed foods and avoiding refined sugars and highly-processed grains.

Comment

Based on current evidence, there is no dietary pattern that could be universally recommended for all affected individuals with T2Dm. Instead, according to the recommendations of professional societies, different dietary patterns such as the Mediterranean diet or a vegetarian or vegan diet are suitable to achieve the target parameters of diabetes therapy [2, 118–120]. While the evidence for the effects of the Mediterranean diet in individuals with T2Dm is primarily based on RCTs (including several larger trials and longitudinal studies) and their systematic reviews and meta-analyses [121], the RCTs on vegetarian and vegan diets mostly have small case numbers and short study durations [121–124]. The currently-available evidence on the DASH diet, the Nordic dietary pattern [125–127], the Paleo diet [2], and the macrobiotic diet [124, 128] in individuals with T2Dm is small and partly contradictory, so that further studies are needed to support observed beneficial effects of these dietary patterns for diabetes management in T2Dm.

In individuals with newly-diagnosed T2Dm, the Mediterranean diet achieved a weight loss of ≥ 5 %, which was considered clinically relevant [129]. Similarly, further meta-analyses from RCTs in individuals with T2Dm found significantly greater weight loss for the

Mediterranean diet compared with the respective control diets [130–132]. Adherence to a vegetarian or vegan diet also resulted in weight loss in individuals with and without T2Dm [133–136].

Based on a network meta-analysis of 56 RCTs and 9 dietary patterns [136] and evidence from several meta-analyses of RCTs [131, 132, 137], the Mediterranean diet is superior to the respective control diets in reducing HbA_{1c} and most effective after low-carb diets in reducing HbA_{1c} and fasting blood glucose, followed by the Paleo diet and vegetarian diet [49, 131, 132, 137]. Other systematic reviews and meta-analyses confirmed the positive effects of vegetarian and vegan diets on glycemic control in individuals with and without T2D [123]. However, all other diets studied in the network meta-analysis also significantly reduced HbA_{1c} and fasting blood glucose in individuals with T2Dm compared with control diets, and the overall results were rated with very low to moderate credibility and strength of evidence because of significant inconsistencies [49]. Thus, superiority of one dietary regimen over the others in terms of glucose parameter reduction cannot be inferred at this time [138]. In addition, further studies are needed to confirm the effects of dietary patterns on glycemic control in individuals with T2Dm independent of weight loss [120, 122, 138, 139] and which examine differences between vegetarian and vegan dietary patterns [122, 123].

In addition to positive effects on weight loss and glycemic control, dietary patterns could also reduce the incidence and mortality of various cardiovascular outcomes and improve individual cardiometabolic risk factors such as dyslipidemia and arterial hypertension in individuals with and without T2Dm [122, 123, 131, 132, 140]. The available evidence on this is low to moderate for the Mediterranean diet and very low to low (incidence and mortality) and low to moderate (risk factors) for the vegetarian/vegan diet and the Dietary Approaches to Stop Hypertension (DASH) diet, respectively. For the Nordic dietary pattern, only a preliminary study assessment is available to date, indicating very low evidence for reduction in incidence and mortality from coronary heart disease [123, 140]. A meta-analysis based on 52 RCTs and 9 dietary patterns concluded that, with low to moderate evidence, the Mediterranean diet was most effective in increasing HDL cholesterol and reducing triglycerides compared with control diets, whereas the vegetarian diet was most effective in reducing LDL cholesterol compared with control diets [51]. For effects of the Mediterranean, vegan, and vegetarian diets on microvascular complications associated with T2Dm, the evidence is limited to a few studies with small subject numbers. Based on surrogate parameters, improvements are suggested for nephropathy and retinopathy with adherence to the above dietary patterns, whereas the evidence for risk of microvascular complications is insufficient and results for neuropathy are inconsistent [122]. Overall, based on the available evidence, it is thus difficult to draw solid conclusions for the effects of dietary patterns on microvascular and macrovascular complications in individuals with T2Dm [122].

Based on the available evidence, because no dietary pattern is superior to others, individualized meal planning focusing on dietary patterns rather than individual nutrients or individual foods (or the factors common to dietary patterns) is recommended [2, 3, 118].

Singular effects of individual nutrients

Protein

Effect on glycemia

RECOMMENDATIONS

- We recommend a protein intake of 10–25 % of dietary energy (%E) for patients with T2Dm younger than 60 years and 15–25 % for those older than 60 years with intact renal function (glomerular filtration rate [GFR] > 60 ml/min/m²) and a constant weight.
- In impaired renal function of any stage, protein reduction to less than 0.8 g/kg body weight is unlikely to be beneficial and should be avoided because of the risk for malnutrition, especially in higher-grade renal failure.

Comment

A detailed AWMF S3 guideline on protein intake in T2Dm can be found at the following Internet address: [141]. A meta-analysis has been published and is freely available [142].

Protein is required as a supplier of amino acids in a minimum amount of about 0.8 g/kg body weight or 10 E % to avoid malnutrition and sarcopenia. The lower limit of 0.8 g/kg/day may be insufficient for the elderly because of decreasing efficiency of protein synthesis [143], so a higher protein intake of at least 1 g/kg body weight/day is recommended [144].

The importance of a higher protein intake is controversial. Arguments for higher protein intake include better satiety and higher energy expenditure through postprandial thermogenesis, which may counteract weight gain. Protein metabolism requires considerably less insulin than carbohydrates, which facilitates blood glucose control and may simplify insulin dosing. However, a certain amount of insulin is required because of the protein-induced release of glucagon [145]. Elderly people often experience significant muscle loss due to disease, glucocorticoid therapy, immobility, or loss of appetite, which is why geriatricians also recommend a higher protein intake [146].

Arguments against higher protein intake arise from observational epidemiological studies describing higher mortality [143, 147] and diabetes incidence [148] with higher protein intake. Because they do not adequately account for lifestyles and other variables, the conclusions of these observational studies have been called into doubt in Cochrane meta-analyses [148, 149]. Intervention studies consistently show positive effects of higher protein intake in overweight individuals without diabetes [150, 151]. High protein intake above 20 E % versus below 20 E %, for example, approximately 1.2–1.6 g/kg body weight, did not increase the risk of diabetes or other diseases in prediabetes patients in a large European-Australian prospective randomized intervention trial over 3 years [150].

Recommendation for chronic renal insufficiency Historically, low-protein dietary plans have been recommended to reduce albuminuria and prevent progression of (diabetic) nephropathy.

Recent meta-analyses are available on the issue of protein intake in individuals with diabetes mellitus and chronic renal failure,

showing that protein restriction to 0.6–0.8 g/kg body weight does not provide a demonstrable improvement in renal function [152]. Currently, it is still recommended by nephrology societies [153], but not in the consensus paper of the Nutrition Working Group of the American Diabetes Association [2].

Substantial protein restriction to 0.3–0.4 g/kg body weight showed a significant but small reduction in end-stage renal disease (ESRD) but no effect on mortality in the Cochrane analysis [154, 155]. Carrying out such a dietary regimen is exceptionally difficult, leads to a significant deterioration in quality of life, and carries a high risk of malnutrition and sarcopenia, which are associated with increased mortality in stages of ESRD [156]. In addition, the amino acid preparations (keto analogues) to be used as supplements for this extreme form of nutrition cannot be prescribed in Germany.

The consensus paper of the Nutrition Working Group of the American Diabetes Association also does not recommend restricting protein intake in renal insufficiency [2].

Recommendation for weight reduction

RECOMMENDATION

- In the context of weight reduction diets of up to 12 months duration, the protein content can be increased to 23–32 % of the total energy intake.

Comment

Hypocaloric weight reduction diets usually contain a relatively high protein content. Because of the overall reduction in calories, it is usually in the normal range of 0.9–1.2 g/kg body weight, i. e., in the normal to slightly higher range. Numerous comparative studies of higher and lower protein content are available for these diets. Overall, moderate differences in cardiometabolic risk factors due to higher versus lower protein levels have been shown in previous meta-analyses [130, 142, 157]. Although higher protein diets only modestly enhance weight loss, they moderately improve fasting blood glucose levels and systolic blood pressure. Overall, the higher protein diets perform slightly better and show no disadvantages [142].

Quality of carbohydrates, glycemic index, sugars in highly-processed foods

RECOMMENDATION

- Selecting low glycemic index (GI) carbohydrates contributes to an improvement of health risks in patients with T2Dm.
- The influence of GI or glycemic load (GL) in this context is proportionally independent of glycemic regulation and also results in, for example, improved plasma lipids and a higher intake of healthy content such as fiber, micronutrients, and secondary phytochemicals, with lower consumption of detrimental content from highly processed foods with high GI/GL.

Comment

The glycemic index (GI) and the glycemic load (GL) describe the influence of carbohydrate-rich foods on glycemia. The GI indicates how quickly the carbohydrates of a food are digested, absorbed and thus become effective as blood glucose, while the GL adjusts the GI for the amount of carbohydrate consumed. Thus, the blood glucose response of a food depends primarily on characteristics of the food itself (e. g., degree of processing and fat content) [158]. Phenotype characteristics of patients such as the composition of the intestinal microbiome are thought to play a minor role [159, 160] although individual influences have also been observed [161]. A dietary GI ≤ 40 or ≤ 55 is considered low and a GI ≥ 70 is considered high [162]. Prospective observational studies find a positive influence of a low GI/GL diet on the prevention of T2Dm [163, 164]. In patients with T2Dm, a high consumption of low GI foods such as legumes and oats can improve glycemic control, increase insulin sensitivity, and thus reduce insulin requirements [165]. These effects are now explained partly by a positive influence of poorly digestible carbohydrates on the microbiome [166]. To date, the extent to which the benefits of a low-GI diet are explained by its higher fiber content remains controversial. A 6-month intervention with a low-GI diet was slightly better at reducing HbA_{1c} compared with a diet rich in grain fiber (0.5 vs. 0.18 %) [167]. However, this study had significant weaknesses because the high-fiber group was asked to avoid high-GI foods, and the low-GI group ultimately had higher fiber consumption than the high-fiber group. In fact, a 12-week substitution of high glycemic carbohydrates with isomaltulose (low-GI) resulted in a reduction in HbA_{1c} and HOMA index in patients with T2Dm [168], indicating an influence of GI independent of dietary fiber content.

Despite convincing evidence on diabetes prevention from observational studies and plausible mechanistic explanations, systematic reviews based on randomized controlled trials on the influence of GI/GL of the diet in patients with T2Dm come to contradictory results. They show both positive [169, 170] and no effects [171, 172] on relevant outcome parameters such as HbA_{1c} level and fasting blood glucose level.

In turn, the result of prospective cohort studies investigating the influence of GI/GL on complications of diabetes is clearer. The risk of CHD showed a clear and dose-dependent relationship with dietary GL or GI [164]. In the group of overweight subjects, the risk for cardiovascular events or mortality due to a high GI is particularly high in this regard [173]. These findings fit with previous results showing a higher risk of fatal and nonfatal cardiovascular events with increasing postprandial glycemia [174, 175]. Characteristic of the dyslipidemia associated with T2Dm are high triglyceride levels, low HDL cholesterol levels, and a high proportion of small dense LDL particles. This lipid pattern can be positively influenced not only by reducing carbohydrate consumption but also by lowering GI/GL [176].

The discrepancy between the results from observational and intervention studies is proportionally explained by the fact that the health assessment of foods based on the GI is inadequate. Carbohydrate quality using GI correlates not only with fiber content, but also with micronutrient content and phytochemical content. At the same time, high carbohydrate quality is associated with lower consumption of highly-processed foods and thus, for example, a lower

intake of sugars and saturated fats. High carbohydrate quality therefore has long-term effects on the prevention of diabetes and its complications, independent of the regulation of glycemia.

Dietary fiber

Dietary fiber, in general

RECOMMENDATION

- Various dietary fibers from natural sources should be consumed daily.
- Although there is little evidence to date to support the recommendation of 30 g of dietary fiber per day (15 g/1000 kcal), this represents a valid target for nutritional counseling.

Comment

In cohort studies, high intakes of insoluble dietary fiber, particularly grains, are associated with decreased risk of T2Dm, CHD, cancer, and other diseases [51, 177–179]. Patients with T2Dm also show a dose-dependent reduction in mortality risk [180]. Thus, for T2Dm, whole grain products (bread, rice, pasta) in particular represent a protective food group. Meta-analyses show significant benefits of a higher fiber diet or fiber supplements for body weight, glycemia and insulin resistance, lipid profile and inflammatory status [181], sometimes also for blood pressure [182] even under isocaloric conditions. Even though dietary fiber lowers the glycemic index, it appears to be too imprecise an indicator of recommended foods [181]. Emphasizing "whole grains," or even better the actual fiber intake, is the most effective and meaningful. Based on an average dietary pattern with 20 grams of fiber, an increase of 15 grams to 35 grams per day is targeted [181].

However, due to the heterogeneity of the studies, resulting among others from the variety of dietary fibers, fiber-containing foods, cohorts and interventions (whole grains, non-grain products, fortified foods, supplements, etc.), a further differentiation of these results is necessary [51, 181].

Insoluble dietary fiber

RECOMMENDATION

- Carbohydrates should preferably be obtained from high-fiber foods, especially whole-grain products. The benefit of supplementation has not yet been proven.

Comment

Intervention studies with whole grain products show a glycemic benefit at minimum for rice, but not for wheat and rye products [183]. Apart from a small effect on body weight, no cardiometabolic benefits that can be clearly attributed to whole grain products have been described in meta-analyses [184]. Studies explicitly examining insoluble dietary fiber in an intervention setting are few [185–187], but none, to date, in patients with T2Dm. Previous data suggests that the tighter the metabolic restriction, the more pronounced the efficacy of dietary fiber [187, 188].

Soluble dietary fiber

RECOMMENDATION

- High-fiber foods, especially whole grains, but also vegetables, legumes, and low-sugar fruits are recommended in T2Dm and are likely metabolically beneficial. The long-term benefit of supplementation is not established despite consistent short-term effects for glycemia, lipid status, and possibly blood pressure.

Comment

For soluble fiber, there is insufficient epidemiological evidence for long-term benefit, both in terms of morbidity and mortality.

In contrast to insoluble fiber, however, research on soluble fiber is much more advanced, particularly in the form of supplementation studies. For beta-glucans and psyllium, a minimum of a short- to medium-term (weeks to months) benefit on blood glucose and insulin resistance has been demonstrated; however, long-term data is lacking [189]. Beneficial effects on glycemia and insulinemia have also been systematically described for inulin (specific fructans), especially for women and obese people with T2Dm [190, 191]. However, such studies of a duration of more than 3 months intervention duration are scarce.

The glycemic benefits of inulin and psyllium are probably due to fermentation to short-chain fatty acids, not weight reduction [192]. A mixed effect may be present for beta-glucans [193].

Psyllium, konjac glucomannan, and also beta-glucans also moderately lower LDL cholesterol and triglyceride levels and may therefore provide secondary benefits in T2Dm [194–197]. No clear metabolic benefits have been demonstrated for other soluble fibers (guar, pectin) [198].

Antihypertensive effects have been described on average for all viscous fibers, but are most expected for psyllium. The effect of 2 mmHg systolic and 0.5 mmHg diastolic is hardly clinically relevant [199].

Nutritional aspects of special populations

Geriatric patients

RECOMMENDATION

- The nutrition therapy goals for geriatric patients should focus on maintaining independence and avoiding malnutrition and hypoglycemia.
- Obesity is associated with reduced mortality in this group of individuals and should not be reduced.

Comment

In principle, the nutritional recommendations for elderly people with T2Dm do not differ from those for older metabolically-healthy

people or younger people with T2Dm. At the same time, the general nutritional recommendations for this patient group apply to geriatric patients with T2Dm. The consequences of malnutrition in old age, especially in functionally-dependent patients, are severe and should also be in focus for patients with T2Dm. For example, the loss of muscle mass associated with weight loss exacerbates age-related sarcopenia and frailty, thereby promoting disability and loss of independence.

The S2k guideline "Diagnosis, Therapy and Follow-up of Diabetes in the Elderly" (Diagnostik, Therapie und Verlaufskontrolle des Diabetes im Alter) contains very detailed recommendations also on nutritional therapy for older persons with diabetes. It makes clear that therapy goals - also with regard to nutrition - can often change in elderly and especially geriatric patients, but do not have to. Functionality and maintenance of independence are paramount.

Although an improvement in insulin sensitivity could also be achieved in the elderly through intentional weight reduction [200], strict dietary prescriptions should be avoided in the elderly with excess weight or obesity because of the risk of malnutrition. Dietary restrictions that may limit food intake are potentially harmful and should be avoided. If weight loss is considered, dietary measures should be combined with physical activity whenever possible and should focus on meeting protein intake requirements. A significant increase in mortality was found in those over 65 years of age only above a BMI of 30 kg/m^2 [200]. Restrictions on the consumption of familiar and favorite foods lead to a reduction in the subjectively perceived quality of life. This aspect is of decisive importance, especially for people of advanced age.

The risk of potential malnutrition is present when there is a persistent reduced food intake (approximately < 50 % of requirements for more than 3 days) or when several risk factors are present simultaneously that either reduce the amount of food eaten or significantly increase energy and nutrient requirements. The risk of malnutrition can be assessed, for example, using the Mini Nutritional Assessment (MNA) or the corresponding short form (SF-MNA); both screening methods are well evaluated [201, 202]. In underweight patients, the causes should be clarified and corrected if possible.

Nutritional therapy should also focus on the prevention of hypoglycemia, with initial emphasis on medication adjustment for this purpose.

For further discussion, especially for persons with diabetes in nursing homes and when artificial nutrition is required, reference is made to the S2k guideline "Diagnosis, Therapy and Follow-up of Diabetes Mellitus in Older Adults" and the S3 guideline "Clinical Nutrition in Geriatrics" [203–205].

Due to the complexity of geriatric patients, who are often multimorbid, the planning and implementation of disease-specific diets should, if necessary, be carried out by a multi-professional team including nutrition-specific expertise.

Migrants

RECOMMENDATION

- Medical professionals should ensure that patients have understood the dietary instructions and that their nuclear families are included in the therapy.
- Medical professionals should ascertain and take into account the individual nutritional concept of the patient and his or her environment (for example, religious aspects, cultural beliefs, the fasting month of Ramadan, pregnancy).

Comment

Reference is made to the specific therapy and nutritional aspects of migrants in the DDG Clinical Practice Guideline *Diabetes and Migration*[206].

There are some very individual eating habits in the context of different cultures and regions. Eating culture is shaped by geographic, historical, sociological, economic, and psychological characteristics of a society and is shared by the members of a given community. Culture represents a fundamental determinant to "what we eat" [207]. Migrants often have different dietary behaviors than natives. They sometimes prefer different foods, often eat more carbohydrates, have different meal concepts, a different understanding of portions, and different food preparation methods and food combinations. Their dietary concepts are usually based on their own traditional cuisine, personal habits, and they also adopt the eating habits of the native population, often resulting in a new "mixed cuisine" [208]. It is not uncommon for special foods to be obtained from the home countries. Migrants from some cultures may have little use for the weights in local recipes when cooking. People have a highly variable postprandial glucose response to identical foods. Individualized culturally sensitive counseling improves adherence [209]. In this context, fasting during Ramadan - food choices and fasting rules influenced by religion - pregnancy, and shift work play a special role. In everyday practice, knowledge of the main sources of carbohydrates and in what form and when carbohydrates are eaten is vital. The practice tool on nutritional patterns [206, 210] of migrants, which was created by the Diabetes und Migration Working Group of the DDG, is intended to provide initial information and assistance. A pragmatic regional breakdown with information on common cuisine forms the basis. In addition to the type (hot/cold) and number of meals, the main sources of carbohydrates and other regional characteristics are presented. Cuisines are quite diverse around the world, and there are further great diversities regionally. It should be taken into account that many beverages have, in the meantime, made their way into many food cultures worldwide, for example soft drinks, energy drinks, various sweetener-enriched beverages and some types of beer.

Possible language barriers and culturally-sensitive communication should be considered when providing nutritional counseling [206]. Individualized, culturally-sensitive counseling therefore improves compliance and treatment success.

Nutritional aspects of special foods and food supplements

Beverages

RECOMMENDATION

- Individuals with T2Dm should minimize their intake of sugar-sweetened beverages.

Comment

Current evidence-based guidelines from the American and British Diabetes Societies generally recommend a reduction in the consumption of sugar-sweetened beverages for individuals with diabetes to control blood glucose levels and body weight and reduce the risk of cardiovascular disease and fatty liver (Levels of Evidence B and 2, respectively) [2, 118, 119]. Reducing the consumption of sugar-sweetened beverages is also generally desirable, as it contributes to increased micronutrient density, a reduction in the intake of added sugars, and thus a more balanced diet overall [211].

However, the evidence for the association between sugar-sweetened beverage consumption, glycemic control, and insulin sensitivity/resistance is deemed insufficient for adults (regardless of diabetes status) based on cohort studies and RCTs, so that no robust conclusions can be drawn [212]. A meta-analysis of 11 cohort studies shows an association between higher sugar-sweetened beverage intake and higher fasting blood glucose and insulin concentrations after adjustment for potential confounders for individuals without diabetes [213]. Two systematic reviews and meta-analyses specific to the effects of sugar-sweetened beverages containing fructose on glycemic control and serum lipid concentrations examined the effects of isocaloric substitution of glucose or sucrose with fructose in beverages and solid foods. Both short-term and long-term (study duration 2–10 weeks) substitution showed no adverse effects of fructose on either the maximum postprandial blood glucose, insulin or triglyceride concentrations, or the fasting blood glucose, insulin or triglyceride concentrations in subjects with normoglycemia, prediabetes, and T2Dm [214, 215]. However, when interpreting these results, it should be noted that a subgroup analysis was only performed for short-term substitution in normoglycemic individuals for the effect of sugar-sweetened beverages vs. sugar-sweetened foods [215], and the subgroup analyses for individuals with T2Dm in both studies were based on only a very small number of trials [214, 215].

The evidence for the association between sugar-sweetened beverage consumption and diabetes-associated macrovascular complications such as coronary events, stroke, hypertension, and dyslipidemia is also generally rated as insufficient for adults [212]. Systematic reviews (and meta-analyses) based on 4–11 prospective cohort studies indicate associations between sugar-sweetened beverage consumption and vascular risk factors (hypertension, hyperlipidemia), coronary heart disease, stroke, and mitral valve regurgitation [216–218]. To note, however, is that the results are not specific to individuals with T2Dm [216–218]. For the association between sugar-sweetened beverages and coronary heart disease, no significant effects were observed in the two studies of individuals with diabetes [217], and analyses for diabetes as a mediator for the association between sugar-sweetened beverages and vascular risk factors yielded inconsistent results [216].

With regards to diabetes-associated microvascular disease, another meta-analysis based on 5 study populations (also not exclusively individuals with T2Dm) found a significant association between chronic consumption of sugar-sweetened beverages and chronic kidney disease. However, the included studies were very heterogeneous, and evidence for publication bias was present [219].

Two systematic reviews and meta-analyses based on 4 and 12 cohort studies (including some individuals with T2Dm) on the association between sugar-sweetened beverage consumption and nonalcoholic fatty liver showed a significantly higher risk of nonalcoholic fatty liver disease (NAFLD) for the highest vs. lowest intake category of sugar-sweetened beverages [220, 221]. Even the lowest intake of < 1 glass/week was associated with a 14 % increase in the relative risk for NAFLD, and consumption of sugar-sweetened beverages showed a dose-dependent effect on the risk for NAFLD [220].

In conclusion, in line with the recommendation for the general population, a reduction in sugar-sweetened beverage intake should be targeted as part of a balanced diet for individuals with T2Dm to reduce the risk of cardiometabolic comorbidities [2, 118, 119, 211–212]

Scientific background

When interpreting the data on the effects of sugar-sweetened beverages on individual diabetes-related target parameters, the following points should be considered: 1) the majority of studies do not exclusively examine individuals with T2Dm, so further studies in this patient group are needed to confirm the transferability of the results; 2) most associations for sugar-sweetened beverages are significant only for the comparison of extreme consumption categories, but not for moderate intake levels, which, however, roughly correspond to the mean estimated global intake of sugar-sweetened beverages [222]. On the one hand, the effects of additional sugar consumption on target parameters seem to depend on the energy balance and, on the other hand, on the sugar source as sugar-sweetened beverages providing excess energy seem to have a particularly negative effect on, for example, fasting blood glucose and insulin concentrations [223]. Furthermore, the direct association between the consumption of beverages containing fructose and sugar-sweetened beverages with the increased risk of, for example, the incidence of metabolic syndrome and other cardiometabolic risk factors and events seems to be limited to sugar-sweetened beverages and not transferable to the consumption of sugars from other sources (e. g., fruit, yogurt, fruit juices) [222, 224]. Possible explanations for this observation are that 1) the effect of sugar-sweetened beverages appears to be strongly mediated by the additional energy intake and resulting weight gain; that 2) other sources of fructose or sugar contain additional potentially health-promoting ingredients (which is not true of sugar-sweetened beverages) and that 3) sugar-sweetened beverages represent a marker of an overall unhealthier lifestyle [222].

Whole grains

RECOMMENDATIONS

- In overweight patients with T2Dm, a diet rich in whole grains can help reduce the total energy intake and thus support targeted weight loss.
- Consumption of low-processed whole grain products with a high proportion of whole grains results in a less pronounced postprandial blood glucose response, which may be a nonpharmacologic treatment option, particularly for people with T2Dm without insulin resistance.
- Patients with T2Dm on insulin treatment should primarily consider consumption of whole grain products in terms of quantity according to carbohydrate content and additionally according to glycemic index, and adjust it to their insulin therapy.
- Highly processed whole grain products show no additional beneficial effects on postprandial blood glucose response

Comment

For the general population, choosing whole grain products is recommended [225]. This is justified by their higher content of vitamins, minerals, and secondary phytochemicals, as well as beneficial effects on digestion and intestinal health due to the associated higher fiber intake. In addition, long-term cohort studies [226, 227] and numerous meta-analyses/reviews of cohort studies show associations between a significantly increased whole grain consumption and an up to 20 % reduced risk of cardiovascular disease and mortality [228–234]. This results in recommendations by authors that even "moderate increases in whole grain consumption could reduce the risk of premature death" [232]. However, a causal relationship has not yet been established. In studies, the underlying dietary data is often based on only one survey (3-day protocol or Food Frequency Questionnaire at beginning of the cohort study), and classifications of foods as "whole grain foods" are inconsistent.

With regard to diabetes management, the degree to which whole grain foods are processed is important. As early as 1988, Jenkins et al. published results on the postprandial blood glucose response after consumption of whole grain breads with varying ratios of whole grain flour and whole grain content. The blood glucose response is determined less by the overall whole grain property of a milled grain product (whole meal) than by the proportion of whole grains (whole grain) it contains [235]. The higher the proportion of whole grains, the lower the blood glucose response, because the fruit and seed hulls form a physical barrier to the action of amylase on the endosperm.

Thirty years later, these results regarding the influence of the degree of processing have recently been confirmed under experimental [236] as well as everyday conditions [237]. No positive effects on the diabetes treatment have been shown for the mere addition of wheat bran to the usual meals with the aim of increasing the dietary fiber content [238].

For people with T2Dm, the recommendations are differentiated for the different treatment situations and forms:

For overweight patients with T2Dm: a meta-analysis on fiber and whole grain consumption in diabetes management included 42 intervention studies. Increased fiber/whole grain consumption (compared to control groups) was shown to result in a ½ kg lower body weight and a resulting 0.2 % (2 mmol/mol) reduction in HbA_{1c}[180]. Shortcomings of this analysis are the heterogeneous designs of the included studies, including diabetes medication, study duration, diabetes diagnosis, and type of whole grain consumption.

In non-insulin-treated, normal-weight patients with T2Dm (without insulin resistance), consumption of minimally-processed whole grain products with a high proportion of whole grains may result in a less pronounced postprandial blood glucose response. Positive effects of such a dietary measure on the achievement of the therapeutic goal depend, among other things, on the patient's acceptance of this dietary form and, in the medium term, on the continuing existence of residual β-cell function.

Insulin-treated individuals with T2Dm should assess how their diets affect increases in blood glucose in order to adjust insulin dosage to match. Accordingly, they should primarily consider consumption of whole grain products in terms of quantity according to carbohydrate content and additionally according to glycemic index, and adjust it to their insulin therapy. Whole grain products can be consumed according to personal preference.

Highly processed whole grain products show no additional beneficial effects on postprandial blood glucose response.

Fruits and vegetables

RECOMMENDATION

- In the dietary planning for overweight patients with T2Dm, increased vegetable consumption in particular can support a targeted weight reduction.
- In the dietary planning for normal-weight patients with T2Dm, consumption of large portions of fruit (products) and starchy vegetables (potatoes, corn, rice, grains, etc.) should be avoided.
- Patients with T2Dm treated with insulin should consider the consumption of fruit in terms of quantity according to carbohydrate content and adjust it to their insulin therapy.
- Separation into recommended and non-recommended fruits is not considered useful.

Comment

For the general population, a daily intake of at least 3 servings of vegetables (400 g) and 2 servings of fruit (250 g) is recommended under the slogan "5 a day" [225]. Recent results from the PURE study [239] and meta-analyses/reviews of cohort studies [233, 240–242] show associations of increased fruit and vegetable consumption with a 5–20 % reduced risk with respect to cardiovascular disease and all-cause mortality. However, a cause-and-effect relationship has not yet been established, and data is inconsistent regarding effective fruit and vegetable varieties, minimum daily consumption levels, and the extent of clinical relevance with respect to specific diseases and mortalities. Beyond individual health,

comparable recommendations for vegetable and fruit consumption supplemented with approximately 100 g of legumes/soy products daily are provided by the EAT-Lancet Commission as part of a Planetary Health Diet for environmental and social reasons [243].

For people with T2Dm, the recommendation is differentiated for the different treatment situations and forms:

In overweight patients with T2Dm, fruit and vegetable consumption should be seen as a supportive component for weight reduction. When energy-dense foods are replaced by judicious consumption of fruits and increased consumption of vegetables, this can sustain weight reduction. Intervention studies on the singular effects of individual food (groups) on physical or blood parameters do not exist or do not allow causal statements to be made because of the many additional influencing factors. However, intervention studies in people with T2Dm on the effects of an overall plant-rich diet – rich in fruits and especially vegetables – have shown a significant reduction in body weight, with corresponding positive effects on glycemia [122, 244, 245].

In non-insulin-treated normal-weight patients with T2Dm, large amounts of carbohydrates at individual meals should be avoided to prevent strong postprandial blood glucose responses. Therefore, large amounts of fruit, fruit juices, and starchy vegetables are not recommended (clinical experience). For non-starchy vegetables, there is no limiting quantity recommendation for consumption.

Insulin-treated patients with T2Dm should assess how their diets affect increases in blood glucose in order to adjust insulin dosage to match. Accordingly, the consumption of fruits and starchy vegetables (potatoes, sweet potatoes) should be assessed for carbohydrate content according to carbohydrate units and the individual form of insulin therapy should be adjusted. Fruits and vegetables can be consumed according to personal preferences.

In general, it should be noted that large amounts of carbohydrates can be absorbed in a short time through fruit juices, smoothies, and dried fruit - compared to unprocessed fresh fruit.

Based on the data available, there is no evidence for a blanket separation into recommended and non-recommended types of fruit, which is repeatedly popularized in lay publications because of the different carbohydrate content.

Fish

RECOMMENDATION

- Oily fish may contribute to lowering blood lipids and the inflammatory phenotype and thus possibly the cardiovascular risk.
- Evidence to recommend fish oil supplements in T2Dm is insufficient.
- Sustainable fishing/fish farming should be considered when selecting fish meals [246].

Comment

Dietary patterns that include fish have been linked to a lower risk of diabetes in observational studies [247]. However, consumption of fish per se, as well as fish oils (long-chain omega-3 fatty acids such as docosahexaenoic acid [DHA] and eicosapentaenoic acid [EPA]), is inconsistently associated epidemiologically with diabetes risk. In Western regions (North America, Europe), there is a trend toward increased risk, whereas in the Pacific region, there is a trend toward decreased risk [248–251]. These associations are in discrepancy with cohort studies linking fish consumption in a dose-dependent manner to a significantly lower risk of visceral obesity [252] and indicating lower cardiovascular risk and cardiovascular and all-cause mortality [241, 253, 254]. There is no significant relationship to hypertension [50].

The benefit in terms of cardiovascular risk is also controversial. Meta-analyses of RCTs see slight or nonsignificant effects [255, 256]. A meta-analysis specific to T2Dm patients has not yet been published.

In intervention studies, the specific effects of fish consumption are poorly studied. Fish oils appear to improve insulin sensitivity in patients with metabolic syndrome–but not in healthy individuals [257]. This effect has been shown to be gender-specific in women, but data is lacking for men [81]. Data on diabetes incidence is not available. Glycemic parameters do not improve with supplementation [258].

Metabolic benefits from fish oil supplementation are most likely with respect to triglycerides and C-reactive protein (CRP) [75, 258]. For non-inflammatory benefits, a high EPA/DHA ratio is advantageous [258].

Meat

RECOMMENDATION

- In part, high-protein diets prove to be beneficial to possibly superior with regard to glycemia (see above). The replacement of carbohydrates with protein sources carried out in these diets can also be covered in part from animal sources, including meat of all kinds.
- From an environmental point of view (e. g., to reduce demands on land or greenhouse gas emissions), meat consumption should also be reduced to the recommended level of the German Nutrition Society (DGE) [246, 259]

Comment

A diet heavy in meat and thus generally low in carbohydrates is associated with increased (cardiovascular) mortality in observational studies [260]. Epidemiologically, there are also moderate associations with cancer, CHD, and T2Dm. These associations are particularly strong with red meat, especially processed red meat [149].

Intervention studies show improvement in numerous metabolic parameters when reducing the *amount* of meat consumed daily. Causality for the benefits of low meat diets is also unclear in RCTs because in these studies the reduction is either isocalorically compensated with other potentially beneficial foods (e. g., whole grains, vegetables, legumes, nuts) or a meat avoidance is implemented in a hypocaloric setting.

RCTs on meat exchanges (red vs. white meat) mostly present the same confounding variable (e. g., red meat = standard diet vs. white meat = Mediterranean diet). A relevant intervention effect on mortality and morbidity (including T2Dm incidence) is question-

able [260]. Only 6 RCTs have explicitly compared red and white meat and show no metabolic difference in the non-diabetic subjects studied [261–266].

Based on this data, in 2019, the NutriRECS Consortium concluded not to recommend meat reduction due to lack of evidence [267]. However, the NutriRECS Consortium's assessment of the available nutritional evidence reveals the common, although flawed, assumption that medical and nutritional research should be evaluated according to the same criteria. For example, less value is systematically placed on observational studies and RCTs are rated very highly. However, long-term RCTs with food, especially with blinding and placebo control, are very difficult to conduct in the nutrition field. Overall, the recommendation to avoid (red) meat is currently still much better justified from an ecological and animal ethics perspective than by metabolic research.

Cinnamon

RECOMMENDATION

- Consumption of cinnamon cannot be recommended to people with T2Dm as a component of successful diabetes therapy.

Comment

Over the past 15 years, numerous intervention studies have been published on the effects of cinnamon consumption on fasting blood glucose and HbA_{1c} levels in people with T2Dm. Despite inconsistent study results, beneficial effects of cinnamon consumption on treatment outcomes in T2Dm have been consistently disseminated. Two meta-analyses in 2011 and 2012 postulated positive effects for cinnamon on fasting blood glucose [268, 269], and HbA_{1c}[269] in their abstracts, while simultaneously concluding that the majority of the studies examined showed no relevant therapeutic effect on glycemia in people with T2Dm. Two meta-analyses in subsequent years have included the available studies up to early 2012 in their investigations, with the Cochrane paper [270] excluding studies of questionable quality from the analysis. Both studies found no significant effect of cinnamon consumption on HbA_{1c} levels. Allen et al. [271] showed positive treatment effects on fasting blood glucose, but put this into perspective due to clear methodological deficits in the studies examined. Two other recent reviews [272, 273] conclude that the use of cinnamon (as an adjuvant) in the treatment of T2Dm cannot be recommended in view of the current study situation. Methodological problems extraordinarily limit the validity and comparability of the studies: for example, although the daily cinnamon doses used in the intervention groups of the studies are always given (0.1 to 6.0 g/day), there are no, incomplete, or inconsistent details on the cinnamon variety investigated (C. cassia, C. aromaticum, C. zeylanium), the form of application (cinnamon powder, cinnamon extract, capsules, tablets), the amount of active cinnamon ingredient tested, the drop-out rate of the subject collective or the intention-to-treat analysis, and other influencing factors (body weight, diabetes medication) that may have affected the target glycemic parameters studied (especially fasting blood glucose and HbA_{1c} level) during the study period (4–18 weeks).

Artificial sweeteners

RECOMMENDATION

- The consumption of artificial sweeteners in T2Dm mellitus is harmless to health if the respective maximum amounts are observed and may be useful if used occasionally as part of diabetes therapy.
- In children and adolescents with T2Dm, the lower acceptable daily intake (ADI value) must be taken into account due to the lower body weight.

Comment

Artificial sweeteners are always the subject of controversial discussions in literature. According to one hypothesis, sweeteners could have an appetite-increasing effect due to their intense sweetness (e. g., [274]). However, when sweeteners were ingested (in the form of a beverage), compared with water, no appetite-increasing effect was found either in healthy, normal-weight subjects [275–277] or in metabolically healthy, overweight subjects. Sweeteners are said to have an orexigenic effect comparable to that of water [275].

The extent to which sweetener consumption affects glucose metabolism in patients diagnosed with T2Dm mellitus has been assessed in several clinical trials. No effect of sweetener consumption on the concentration of the parameters glucose, insulin or C-peptide, glucagon-like peptide-1 (GLP1), glucose-dependent insulinotropic peptide (GIP), peptide YY (PYY), glucagon, as well as HbA_{1c} could be detected [278–283]. Accordingly, the consumption of sweeteners does not seem to have a negative effect on glucose and insulin regulation in T2Dm.

The low cariogenic effect of sweeteners in contrast to conventional sugar is undisputed. In the case of saccharin, sucralose, aspartame as well as stevia, there is an additional bacteriostatic effect on oral flora [284, 285]. The extent to which sweeteners influence the intestinal microbiota has not yet been adequately clarified. In an intervention study, a change in the intestinal microbiota was observed in about half of the subjects (4/7) as a result of saccharin administration [286]. However, these results have not yet been confirmed.

The earlier reservation that sweeteners were carcinogenic has now been refuted. According to current knowledge, there is no evidence of a carcinogenic effect of sweeteners if the ADI value is not exceeded [287].

Scientific background

Sweeteners are synthetically produced or naturally-occurring compounds with high sweetness intensity, which are metabolized independently of insulin and are not cariogenic. Compared to sugar (sucrose), sweeteners have a sweetening power that is many times higher (30 to 20,000 times) and are therefore only used in very small quantities (milligram range), which are negligible in terms of calorie intake. As additives, sweeteners are subject to a health as-

sessment by the European Food Safety Authority (EFSA) prior to approval, which derives acceptable daily intakes (ADI). The ADI value indicates the amount of an additive that can be ingested daily per kilogram of body weight over a lifetime without posing health risks. After approval, sweeteners are reassessed if necessary and re-evaluated at regular intervals [288].

Probiotics

RECOMMENDATION

- Consumption of probiotics or synbiotics may have a beneficial effect on glucose regulation and lipid profile of T2Dm.
- A multi-strain preparation usually achieves a stronger effect than a single-strain preparation.
- Evidence is insufficient to date to recommend probiotic or synbiotic supplementation.

Comment

The effect of probiotic supplementation on T2Dm mellitus has been extensively studied. Various meta-analyses show a significant reduction in fasting blood glucose in T2Dm by probiotic supplementation, compared with placebo administration [289–294]. A significant reduction in insulin resistance (Homeostasis Model Assessment [HOMA]) index) was also observed in subjects with T2Dm as a result of probiotic administration, compared with the control group, in several meta-analyses [291, 295]. However, a long-term change, measured by the HbA_{1c} value, could not be detected by probiotic or synbiotic therapy (min. 12 weeks) [289, 290].

The results of meta-analyses regarding the effect of probiotic supplementation on lipid status in patients with T2Dm are heterogeneous. Two recent meta-analyses show, compared with placebo administration, a significant reduction in total cholesterol as well as triglyceride concentration (TG) in T2Dm as a result of 1 to 6 months of probiotic or synbiotic supplementation [289, 296]. In Mahboobi et al. (2018) [293], a significant improvement in TG, LDL, and HDL cholesterol concentrations was recorded as a result of synbiotic but not probiotic supplementation. Another meta-analysis did not find any association in this regard [297].

A recently-published randomized controlled intervention trial in a cross-over design by Palacios et al. (2020) [298] investigated the effect of probiotic administration as an adjunct to metformin therapy. After 12 weeks of administration of a multi-strain probiotic, improvement in glucose regulation (measured by fasting blood glucose concentration, HbA_{1c} level, and HOMA index) and gut barrier function (measured by zonulin), as well as increased plasma butyrate concentration, were observed compared with placebo administration.

There is the following to consider with probiotic supplementation: probiotics may have antibiotic resistance in mobile genes that can be transferred to other, potentially pathogenic bacteria through interbacterial exchange [299]. Examination of various commercially-available probiotics revealed that the probiotic bacteria tested were resistant to several broad-spectrum antibiotics [300].

Scientific background

In Germany, probiotics are defined as "living microorganisms that enter the intestine in sufficient quantities in an active form and thereby achieve positive health effects" [301]. Primarily, the genera *Lactobacillus* and *Bifidobacterium* are used for the formulation in probiotics. Furthermore, specific lactic acid-producing species of other genera, e. g. *Enterococcus faecalis, Streptococcus thermophilus* or probiotic yeasts (*Saccharomyces boulardii*) are used. The dose varies between 10^8 and 10^{11} colony-forming units, and the use of above genera or species is considered safe [302].

The gut microbiota can have a strong influence on glucose metabolism mainly by modulating insulin sensitivity [303] and insulin synthesis [304]. According to a postulated mechanism based on the mouse model, microbially-synthesized short-chain fatty acids (acetate, propionate, and butyrate) bind to G-protein-coupled receptors (GRP43), inducing the secretion of the peptide hormone GLP1 [305]. GLP1 stimulates insulin synthesis in both glucose-tolerant individuals and T2Dm patients [306].

Large-scale studies show that an altered gut microbiome (also called dysbiosis) is present in T2Dm sufferers [307–309]. However, because T2Dm medication, for example metformin, has been shown to modulate the gut microbiota [310–312], it is often unclear whether the change is due to the disease or the therapy. Therefore, it has not yet been possible to identify a characteristic T2Dm microbiome. However, some studies suggest that the microbiome in T2Dm is characterized by a lower proportion of butyrate-producing bacteria [307, 308, 312]. A loss of butyrate producers is discussed as a predictor of the transition of prediabetes to T2Dm [313], which is why supplementation by probiotics or synbiotics may be a relevant aspect.

Sucrose/fructose

RECOMMENDATION

- Fructose can be consumed in natural foods (e. g., fruit) as part of a balanced diet.
- Beverages sweetened with fructose should be avoided, especially if the daily recommended energy intake is exceeded.

Comment

According to the recommendations of the American and Canadian diabetes societies, the intake of mono- and disaccharides should not exceed 10 % and 12 % of the daily energy intake, respectively [314, 315]. Isocaloric replacement of carbohydrates such as starch and sucrose with fructose has no adverse effects on body weight [316], blood pressure [317], fasting triglycerides [318], postprandial triglycerides [319], fatty liver markers [320], or uric acid [321]. In people with diabetes, isocaloric replacement with fructose could lower fasting glucose and HbA_{1c} levels [322], especially when consumed in small amounts and in the form of fruit [323]. In contrast, fructose, especially in doses greater than 60 g per day or 10 E % of daily energy requirements, potentially causes mild triglyceride increases in people with T2Dm [318, 324]. Hypercaloric intake of

fructose further leads to weight gain [316], uric acid increase [321], hepatic insulin resistance, hepatic fatty acidosis, and transaminases increase [320, 325] with the excessive caloric intake as the presumed cause. For this reason, people with diabetes should minimize the consumption of sugar-sweetened beverages to prevent weight gain and improve the cardiometabolic risk profile [2].

Scientific background

High fructose corn syrup (HFCS) has been used to sweeten beverages since the 1970s in the USA and increasingly in other countries. Countries with higher HFCS consumption have 20 % higher diabetes prevalence compared with countries with lower HFCS consumption, independent of total sugar consumption and obesity prevalence [326].

Contrary to this epidemiologic association, prospective cohort studies of the effect of fructose on metabolism reached inconsistent results. For example, a meta-analysis of 15 prospective cohort studies did not indicate an association between fructose intake and increased risk of T2Dm that was independent of food type [327]. In a meta-analysis of 51 isocaloric studies and 8 hypercaloric studies, fructose only had unfavorable effects on lipid metabolism in terms of apolipoprotein B and triglyceride increases when offered as additional calories to an existing diet, whereas isocaloric replacement with fructose did not negatively affect lipid metabolism [318]. Consistent with this finding, fructose associated with increased energy intake, but not isocaloric fructose replacement, increased postprandial triglycerides in a meta-analysis of 14 isocaloric and 2 hypercaloric studies [328]. Similarly, in a meta-analysis of 24 controlled intervention studies, consumption of more than 100 g of fructose per day increased low-density lipoprotein (LDL) cholesterol and triglycerides, with no effect on serum lipids when fructose intake was less than 100 g per day [329]. A meta-analysis of 16 studies investigating isocaloric carbohydrate replacement with fructose in patients with T2Dm found heterogeneous effects on lipid metabolism with an increase in triglycerides and a decrease in total cholesterol without affecting LDL cholesterol [324].

Moreover, as shown in a meta-analysis of 21 studies, hypercaloric fructose consumption led to an increase in uric acid only in metabolically-healthy participants, whereas uric acid levels remained unchanged after isocaloric fructose intake in people both with and without diabetes [321]. A recent network meta-analysis indicated that replacement of fructose with starch resulted in decreased LDL cholesterol and replacement of fructose with glucose favorably affected insulin sensitivity and uric acid levels [330]. In contrast, in a meta-analysis of 18 studies in patients with T1Dm and T2Dm, isocaloric replacement with fructose resulted in a clinically-relevant decrease in HbA_{1c} of 0.53 % [322]. A similar HbA_{1c} value drop occurred in a meta-analysis of 6 controlled dietary intervention trials after consumption of up to 36 g fructose per day in the form of fruit, without affecting body weight or triglyceride, insulin, and uric acid levels [323]. Consistent with this finding, in patients with recently diagnosed T2Dm, consumption of fructose from sugary beverages, but not from fruit, had an unfavorable effect on peripheral and hepatic insulin sensitivity [331].

In a meta-analysis of 29 papers, short-term fructose consumption, both as an isocaloric exchange for other carbohydrates and as a hypercaloric supplement, led to the development of hepatic insulin resistance in normal-weight, overweight, and obese participants without affecting peripheral or muscle insulin sensitivity [332]. In a meta-analysis of 13 studies, isocaloric replacement with fructose did not favor the development of nonalcoholic fatty liver disease (NAFLD). In contrast, there was an increase in intrahepatocellular lipids and glutamate pyruvate transaminase as a result of increased fructose consumption [320]. Consistent with this finding, another meta-analysis of 6 observational studies and 21 intervention studies also found an increase in liver fat and glutamate oxaloacetate transaminase as a result of hypercaloric fructose intake [325].

In a meta-analysis of 31 isocaloric and 10 hypercaloric prospective cohort studies, fructose administration had no effect on body weight in the isocaloric studies, whereas, in contrast, intake of large amounts of fructose resulted in weight gain [316].

In summary, when assessing studies on the effect of fructose on metabolism, it is important to distinguish whether fructose was ingested isocalorically in exchange for other carbohydrates or hypercalorically as additional energy. Hypercaloric studies indicate the unfavorable effects of fructose on metabolism, which can probably be attributed to the intake of additional energy. Unfavorable effects of isocaloric fructose intake cannot be substantiated with the available studies. It is possible that fructose, consumed in small amounts and in the form of fruit, has beneficial effects on glucose metabolism.

Alcohol

RECOMMENDATION

- People with T2Dm should limit the amount of alcohol consumed to that recommended for the general population. Moderate, low-risk alcohol intake is consistent with good metabolic control and diabetes prognosis.
- People with diabetes with high-risk alcohol use or dependence need to be educated about the dangers of alcohol, specifically including worsened metabolic control, and the risk of secondary diseases.
- It must be pointed out in general that the risk of severe, especially nocturnal hypoglycemia under insulin therapy increases when larger amounts of alcohol are consumed and that this risk is reduced by consuming food during the period of alcohol consumption and raising the target blood glucose at night.

Comment

Differentiated content on the management of alcohol for people with diabetes mellitus can be found in the S2 guideline Psychosocial and Diabetes [333].

People with T2Dm should be counselled about the effects of alcohol consumption on blood glucose levels and, if alcohol is consumed, encouraged to consume at low risk levels. The Deutsche Hauptstelle für Suchtfragen (DHS) e. V. (German Centre for Addic-

tion Issues) defines 12 g of alcohol per day for women and 24 g of alcohol per day for men as thresholds for low-risk consumption. The World Health Organization (WHO) defines a consumption of 10 g of alcohol per day for women and 20 g of alcohol per day for men as low-risk. These amounts also apply to people with T2Dm.

Alcohol and glucose metabolism

In people with diabetes, a linear and inverse relationship is shown between regular alcohol consumption and HbA_{1c} levels [334] (level IIb). Consumption of one glass of wine per day (150 ml or 13 g alcohol) over a 3-month period resulted in a significant reduction in fasting glucose without increasing postprandial glucose levels compared with a control group consuming one glass of nonalcoholic beer per day. A positive effect on HbA_{1c} was greatest in the group with the higher baseline HbA_{1c}. In another controlled study, consumption of 1–2 glasses of wine per day (120–240 ml or 18 g of alcohol) over a 4-week period showed no negative effect on metabolic parameters (fasting glucose, lipids) but a significant positive effect on fasting serum insulin levels [335].

Alcohol consumption may impair blood glucose counterregulation and thus increase the risk of hypoglycemia under insulin therapy or insulinotropic oral antidiabetic agents [336–338].

Alcohol consumption is the cause of about one in 5 severe hypoglycemias leading to hospitalization [339]. However, the main effect of alcohol is likely to be the impairment of awareness, which leads to impaired perception of hypoglycemia and prevents affected individuals from responding appropriately [340].

Excessive consumption of alcohol interferes with diabetes management. Patients with excessive or risky alcohol consumption are less likely to implement therapy recommendations on exercise behavior, diet, medication intake, blood glucose self-monitoring or regular HbA_{1c} value monitoring. There is a linear relationship: the more alcohol consumed, the less frequently therapy recommendations implemented [341].

According to the S2k guideline Psychosocial and Diabetes, alcohol consumption should be assessed regularly - at least once a year - in people with diabetes, and help should be offered when risky alcohol consumption is an issue.

Nutritional supplements

RECOMMENDATION

- Individuals with T2Dm should meet their nutritional needs through a balanced diet. Routine micronutrient supplementation is not recommended.
- In patients with T2Dm and established vitamin D deficiency, vitamin D supplementation may improve insulin resistance.

Comment

The American, Canadian, and British Diabetes Societies summarize the evidence on supplementation in general for persons with diabetes as follows: there is no clear evidence that supplementation with vitamins, minerals (e. g., chromium or vitamin D), herbs, or spices (e. g., cinnamon or aloe vera) improves metabolic control in persons without underlying nutritional deficiencies, and they are not generally recommended to improve glycemic control [2, 118–120]. Routine supplementation with antioxidants (e. g., vitamins E, C, or carotene) is not recommended because of a lack of evidence of efficacy and concerns about long-term safety. However, multivitamin supplementation might be necessary in special groups, e. g., pregnant or lactating women, elderly persons, vegetarians, or persons with a very low-calorie or low-carbohydrate diet [2, 118]. Vitamin B12 deficiency may occur with metformin use, so regular testing of vitamin B12 levels should be considered in individuals with T2Dm and taking metformin, especially in the additional presence of anemia or peripheral neuropathy, and possible vitamin B12 deficiency could be compensated with supplementation [2, 118] (1, 4). In the case of supplement use, possible adverse side effects and drug interactions must be considered [2, 118, 342]. Rather than a general recommendation of routine nutritional supplementation, individuals with diabetes should be encouraged to meet their nutrient needs through a balanced diet [120]. It should be kept in mind that individuals with diabetes who do not achieve their metabolic goals may be at increased risk for micronutrient deficiencies, thus adherence to a balanced diet that provides the minimum daily recommended daily intake of nutrients, and micronutrients in particular, is essential [2].

Due to the large number of available nutritional supplements, the following *scientific background* will highlight a selection of substances – namely n-3 PUFAs, vitamin D, magnesium, chromium, zinc, antioxidants (vitamin C, E) and polyphenols – with regard to their potential efficacy in individuals with T2Dm. Criteria for the selection of these supplements were the relevance of the potential effects of supplementation on diabetes management and a relatively "good" data situation, primarily based on systematic reviews and meta-analyses.

Scientific background

Consumption of **n-3 PUFAs** is discussed in the context of positive effects on glycemic control and cardiovascular disease prevention in individuals with T2Dm [118]. A systematic review from the *Cochrane Library* (23 RCTs, n = 1075 T2Dm) showed a significant reduction in triglyceride (moderate effect) and VLDL concentrations (significant in subgroup analyses only for individuals with hypertriglyceridemia) and a significant increase in LDL cholesterol concentrations after supplementation with n-3 PUFAs vs. vegetable oils or placebo. Supplementation had no effects on total or HDL cholesterol concentrations, HbA_{1c} levels, fasting blood glucose or fasting insulin concentrations, or body weight compared with control [343]. An increase in LDL cholesterol concentration after supplementation with n-3 PUFAs vs. control was also confirmed in another systematic review and meta-analysis (24 RCTs, n = 1533 T2Dm) by Hartweg et al. [344]. However, supplementation did not show any change in LDL particle size, which characterizes diabetic dyslipoproteinemia along with changes in trigylceride and HDL cholesterol concentrations [344]. Furthermore, in both papers, the increase in LDL cholesterol concentrations by n-3 PUFA supplementation was not significant in the subgroup of individuals with

hypertriglyceridemia [343, 344]. A recent systematic review with meta-analysis (45 RCTs, n = 2674 T2Dm) confirmed the protective effects of n-3 PUFA supplementation vs. placebo on lipid metabolism and reported a significant reduction in LDL-cholesterol, VLDL-cholesterol, and triglyceride concentrations by supplementation with n-3 PUFAs vs. placebo [345]. Furthermore, O'Mahoney et al. showed a reduction in HbA_{1c} and no effects on fasting blood glucose, fasting insulin concentrations, and HOMA-IR by supplementation with n-3 PUFAs vs. placebo [345]. Brown et al. (83 RCTs, n = 121 070 with and without T2Dm) examined effects of higher vs. lower intakes of n-3, n-6, and total PUFA on diabetes risk, they also examined their effects on glycemic control and insulin resistance and found no effects of higher vs. lower n-3 PUFA intake on HbA_{1c}, fasting blood glucose, fasting insulin concentration, and HOMA-IR [71]. Furthermore, there is evidence that high-dose supplementation with long-chain n-3 PUFAs (> 4.4 g/d) may worsen glucose metabolism [71].

Overall, the American Diabetes Association summarizes the evidence on n-3 PUFAs for individuals with T2Dm with a recommendation of consumption of foods high in long-chain n-3 fatty acids from, for example, fish, nuts, and seeds for the prevention and treatment of cardiovascular disease (level of evidence B) [118]. However, benefits of routine n-3 PUFA supplementation are not supported based on current evidence (level of evidence A), as supplements do not appear to have the same beneficial effects as the corresponding whole foods on glycemic control and primary and secondary prevention of cardiovascular disease [118]. Furthermore, studies of n-3 PUFA supplementation with vascular events, cardiovascular disease, or mortality as an end point in individuals with T2Dm are lacking [343, 344].

Vitamin D deficiency is associated with alterations in glucose metabolism and insulin secretion [346]. However, evidence on effects of vitamin D supplementation on glycemic control is conflicting based on the systematic reviews and meta-analyses by Li et al. (20 RCTs, n = 2703 T2Dm) and Mirhosseini et al. (24 RCTs, n = 1528 T2Dm) [346, 347]. While both reviews confirmed a significant increase in serum 25-OH vitamin D levels and a reduction in HOMA-IR after supplementation with vitamin D compared with placebo [346, 347], a reduction in fasting blood glucose concentration and HbA_{1c} value after supplementation with vitamin D compared with placebo was significant only in Mirhosseini et al. [346, 347]. These positive effects on parameters of glycemic control and insulin resistance were particularly measurable with a high daily vitamin D dose (≥ 4000 IU/d) and a long intervention duration (7 months on average) [346]. According to Li et al., compared with placebo, vitamin D supplementation reduces fasting insulin concentrations only in nonobese subjects with T2Dm and fasting blood glucose concentrations only with short-term supplementation, doses > 2000 IU/d, and in subjects with vitamin D deficiency and good HbA_{1c} control at baseline [347]. Other systematic reviews and meta-analyses examined the effects of vitamin D supplementation compared with placebo on blood pressure, serum lipid concentrations, and chronic subclinical inflammation [348–351]. For blood pressure (15 RCTs, n = 1134 T2Dm), vitamin D supplementation vs. placebo showed a significant but small reduction in diastolic blood pressure and no change in systolic blood pressure [350]. Similarly, with respect to serum lipid concentrations (17 RCTS, n = 1365 T2Dm), vitamin D supplementation vs. placebo showed significant reductions in serum total, LDL, and HDL cholesterol concentrations, but these effects were small [348]. Furthermore, supplementation with vitamin D vs. placebo resulted in reductions in individual biomarkers of chronic subclinical inflammation such as CRP (20 RCTs, n = 1270 T2 D and 13 RCTs, n = 875 T2Dm) [349, 351]. While the recommendations for fracture prevention for individuals with T2Dm are identical to those for individuals in the general population and include supplementation with vitamin D [118], the quality of the evidence for the other outcomes considered, and the quality of the studies included in the reviews for them, have been found to be very heterogeneous by the authors. Further high-quality and long-term RCTs are thus needed to make a recommendation on vitamin D supplementation for individuals with T2Dm - beyond fracture prevention [346, 347, 349–351].

Magnesium, an essential mineral, is involved in intracellular carbohydrate metabolism, insulin secretion and signaling cascade, lipid metabolism, and regulation of blood pressure, among others [352]. Evidence on the effect of magnesium supplementation on glycemic control and blood pressure in individuals with T2Dm is conflicting [352–354]. After supplementation with magnesium vs. placebo (28 RCTs, n = 1694 T2Dm), there were significant improvements in fasting blood glucose concentration and systolic blood pressure, with more pronounced effects in individuals with hypomagnesemia at baseline, but no changes in fasting insulin concentration, HbA_{1c} value, and diastolic blood pressure [352]. In another systematic review with meta-analysis (21 RCTs, n = 1362 subjects with and without diabetes), supplementation with magnesium compared with control showed only a significant reduction in HOMA-IR in the overall population and stratified by diabetes status, but not in HbA_{1c} value or insulin concentration. Fasting blood glucose concentration was significantly reduced only with magnesium supplementation ≥ 4 months. In the stratified analysis by diabetes status, magnesium supplementation had no significant effects on fasting blood glucose, insulin concentration, or HbA_{1c} levels in subjects with diabetes compared with controls [353]. Asbaghi et al. examined the effects of magnesium supplementation (11 RCTs, n = 673 T2Dm) on blood pressure and anthropometric parameters [354]. Magnesium supplementation compared with placebo resulted in significant reductions in systolic and diastolic blood pressure, especially with supplementation > 12 weeks with ≥ 300 mg/d inorganic magnesium. However, there were no effects of magnesium supplementation vs. placebo on anthropometric parameters [354]. In addition to the effects of magnesium supplementation on glycemic control and blood pressure, Verma and Garg also investigated its effect on serum lipids and demonstrated a significant increase in HDL cholesterol concentration and a reduction in LDL cholesterol and triglyceride concentration compared with control [352]. Further long-term RCTs with good study quality in individuals with T2Dm are needed to make evidence-based recommendations on magnesium supplementation.

The essential trace element **chromium** plays an important role in carbohydrate and lipid metabolism [355]. Supplementation with chromium compared with placebo (23 RCTs, n = 1350 T2Dm and T1Dm [T1Dm included only in 1 RCT in addition to T2Dm]) result-

ed in significant reductions in fasting blood glucose and insulin concentrations, HbA_{1c} levels, and HOMA-IR. Based on subgroup analysis, these effects were more pronounced with longer-term supplementation of at least 12 weeks, but showed no dependence on the chromium dose used. All included studies were rated as good quality, but the meta-analysis did not stratify results according to the chromium formulation used (chromium picolinate, chromium chloride, chromium from brewer's yeast) [356]. Based on 2 previous systematic reviews and meta-analyses (22 RCTs, n = 1332 T2Dm and 14 RCTs, n = 875 T2Dm), the effects of chromium supplementation compared with placebo on fasting blood glucose concentrations were most pronounced when chromium picolinate was used or only significant when chromium from brewer's yeast was used [357, 358]. Increases in HDL cholesterol and reductions in triglyceride levels were also achieved, particularly with supplementation with chromium picolinate or chromium from brewer's yeast compared with placebo [358], so that further research is needed on the optimal formulation of chromium supplements for individuals with T2Dm.

The essential trace element **zinc** plays an important role in the synthesis, storage, and secretion of insulin [359]. The zinc deficiency and hyperglycemia observed in individuals with T2Dm may be interrelated [360]. Based on 11 observational studies, in individuals with T2Dm compared with metabolically healthy controls, whole blood zinc concentrations decreased with each additional year of diabetes. This inverse relationship was generally not explained by lower nutritive zinc intake, as only individuals with T2Dm and complications who were dependent on nutritional therapy (e. g., nephropathy) had significantly lower zinc intake [361]. A subgroup analysis of a systematic review with meta-analysis (32 RCTs and n = 1700 total, 19 RCTs with individuals with T2Dm) showed a significant reduction in fasting blood glucose concentration with supplementation with zinc vs. control for individuals with T2Dm. In the overall study population, which also included individuals at increased risk for T2Dm, supplementation with zinc additionally resulted in significant reductions in 2-h postprandial blood glucose concentration, fasting insulin concentration, HOMA-IR, HbA_{1c} level, and high-sensitivity (hs)CRP compared with control [362]. Furthermore, supplementation with zinc vs. placebo (9 RCTs, n = 424 T2Dm) reduced serum concentrations of triglycerides and total cholesterol. For LDL cholesterol concentrations, only positive effects of zinc supplementation compared with placebo were seen for stratified analyses by LDL cholesterol concentration and HbA_{1c} level at baseline and for an intervention duration < 12 weeks with dosing < 100 mg/d. An increase in HDL cholesterol concentration was shown only for individuals with HDL cholesterol concentrations in the normal range and elevated HbA_{1c} at baseline as well as stratified by intervention duration and zinc dosage [363]. Due to significant heterogeneity between the included studies and varying quality of the studies, further investigations are necessary before zinc supplementation can be recommended as an adjunctive therapy for T2Dm [362, 363].

Oxidative stress plays an important role in the pathogenesis of diabetes and its complications, so that supplementation with **antioxidants** could be expected to have beneficial effects on diabetes management [364]. In terms of glycemic control, a subgroup analysis of a systematic review and a meta-analysis based on 22 RCTs in individuals with and without T2Dm (n = 597 T2Dm) for supplementation with vitamin C compared with placebo showed a significant reduction in blood glucose concentrations, but not HbA_{1c} values and insulin concentrations for individuals with T2Dm, in older individuals and intervention duration ≥ 30 days [365]. A subgroup analysis of a systematic review with meta-analysis based on 14 RCTs in individuals with T2Dm (n = 714) showed significant reductions in HbA_{1c} and fasting blood glucose concentrations with vitamin E supplementation compared with control for individuals with low baseline vitamin E status and poor glycemic control [366]. Neither supplementation with vitamin C or vitamin E alone nor a combination of both antioxidants showed significant effects on HOMA-IR (14 RCTs, n = 735 T2Dm) [367]. Supplementation with the antioxidants vitamin C and vitamin E compared with placebo showed no overall effects on endothelial function in another study (10 RCTs, n = 296 T2Dm), but a significant improvement in endothelial function after intervention for nonobese individuals with T2Dm (BMI ≤ 29.45 kg/m^2) in a subgroup analysis [368]. Individuals with T2Dm and diabetic retinopathy compared with individuals with T2Dm without retinopathy had lower serum concentrations of antioxidants and higher concentrations of oxidative stress biomarkers based on 14 observational studies and 7 RCTs (n = 256 259). Due to strong methodological heterogeneity, only a qualitative synthesis of the included RCTs was performed, indicating beneficial effects of supplementation with antioxidants in diabetic retinopathy [369]. Overall, the reported effects of supplementation with antioxidants in individuals with T2Dm are primarily based on studies of low to moderate quality, so that the evidence for supplementation to improve metabolic control and endothelial function is currently insufficient [365–368].

Resveratrol or **polyphenols** in general are also antioxidants and thus could have positive effects on diabetes management [370]. Supplementation with polyphenols (36 RCTs, n = 1954 total, n = 1426 T2Dm) resulted in a significant reduction in HbA_{1c} compared with control (mean HbA_{1c} at baseline: 7.03 %). Subgroup analysis showed that this reduction was significant for individuals with T2Dm (mean HbA_{1c} value at baseline: 7.44 %), whereas no effects of supplementation were evident in individuals without diabetes and with prediabetes compared with controls [371]. In contrast, a systematic review from the *Cochrane Library* (3 RCTs, n = 50 T2Dm) showed no effects of supplementation with resveratrol on HbA_{1c} levels, fasting blood glucose concentrations, or insulin resistance. Overall, the available evidence from the included RCTs was rated as very low, so that the currently-available evidence on the safety and efficacy of supplementation with resveratrol was also rated as highly insufficient for it to be recommended for the treatment of T2Dm [370]. On systolic and diastolic blood pressure and mean arterial pressure or pulse pressure, supplementation with resveratrol showed no effects compared with control in the overall study population (17 RCTs, n = 681 total, n = 262 T2Dm). In subgroup analyses, resveratrol supplementation significantly reduced systolic blood pressure, mean arterial pressure, and pulse pressure in subjects with T2Dm compared with control [372].

Overall, due to, e. g., poor quality of included studies, heterogeneity in the method and results of the studies, an insufficient number of conducted studies or missing data on selected endpoints, long-term effects and long-term safety, there is still a need

for further research on all considered dietary supplements before they can be recommended as an adjunct to the therapy of T2Dm. Although for individual cases or specific groups of individuals with T2Dm, compensating for nutrient deficiency by taking a nutritional supplement may be considered on an individual basis, taking into account potential adverse side effects and drug interactions, in general, individuals with T2Dm should meet their nutrient needs through a balanced diet and routine supplementation with micronutrients is not recommended.

Particularity of inpatient therapy or special diets to reduce insulin requirements

RECOMMENDATION

- In the inpatient setting, 2-day oat or fiber days are highly recommended to break severe insulin resistance. These must be hypocaloric and contain a high fiber content. Oat days are very effective in this regard. Alternatively, other fiber diets may be chosen.
- Blood glucose levels do not rise as much after eating high-fiber oat products compared to other meals with a comparable amount of carbohydrates, and less insulin secretion is induced.

Comment

Multiple studies have shown that insulin resistance in people with T2Dm could be significantly reduced by a specific diet for several days. These diets have always been hypocaloric and high in fiber. Oat days performed best, with regard to the HOMA index. The amount of soluble fiber is particularly high in oats [373]. The special effect of oats is thought to lie in its composition. Oats contain β-glucan and, at about 7.8 %, the amount contained is particularly high [374]. In addition, an inhibitory effect of oat β-glucan on the expression of SGLT1 receptors as well as glucose transporter 2 (GLUT-2) in intestinal cells has been shown *in vitro*[375]. Furthermore, an inhibitory effect on dipeptidyl peptidase 4 (DDP4) was shown *in vitro* for certain oat proteins. This was somewhat stronger than the effect of buckwheat and barley [376]. It was also seen that oat β-glucan inhibited alpha-glucosidase [377].

Under inpatient conditions, a total of 14 patients were given oatmeal for 2 consecutive days, each with approximately 1100 calories per day. Mean blood glucose, adiponectin, and mean insulin dose were recorded before, 2 days after, and 4 weeks after the intervention. The mean insulin dose was reduced by 47 % and this effect could still be seen 4 weeks after the intervention. The authors hypothesized effects on the microbiome as a result of the oat days [378].

In the cross-over study "OatMeal And Insulin Resistance (OMA-IR)" in people with inadequately-controlled T2Dm, the insulin requirement on the 3rd and 4th day decreased very significantly as a result of 2 oat days compared to a diabetes-adapted diet only. At the same time, over the course of 4 weeks after the oat days, HbA_{1c} levels also decreased [379]. The study shows that oatβ-glucan is able to bind bile acids and lower blood cholesterol levels. Moreover, a close correlation was observed between the decrease in total bile acids as well as the decrease in proinsulin levels after oat days [380–386].

The European Food Safety Authority (EFSA) Panel on Dietetic Products, Nutrition and Allergies (NDA) considers it proven on the basis of studies that: the consumption of beta-glucan from oats […] leads to a reduction in the glucose rise after a meal [387]. Subsequently, the European Commission of the EU published the Health Claim: consumption of beta-glucans from oats […] as part of a meal contributes to the reduction of post-meal blood glucose levels [388].

In a meta-analysis of 103 comparative studies with 538 study participants, the addition of oat β-glucan to meals containing carbohydrates was shown to be associated with a reduced glucose and insulin response [389].

β-Glucan increases viscosity in the small intestine, delays gastric emptying and the release and absorption of food components, especially carbohydrates, thereby causing blood glucose to rise more slowly and resulting in a lower insulin response [390, 391].

Conflict of Interest

Thomas Skurk: has received lecture fees from Novo Nordisk. Diana Rubin: has received lecture fees from DGVS and Kaiserin-Friedrich-Stiftung. Anja Bosy-Westphal: none. Arthur Grünerbel: has received fees from Bavarian Medical Association, KV Bayern, Lilly, Novartis. Stefan Kabisch: has received fees and travel expenses from Sanofi, Berlin Chemie and Lilly; travel expenses and research support from J. Rettenmaier & Söhne, Holzmühle; further research support from Beneo Südzucker and California Walnut Commission. Peter Kronsbein: none. Karsten Müssig: none. Marie-Christine Simon: none. Astrid Tombek: none

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