ZAHRAE SANDOUK, MD
Clinical Assistant Professor, Division of Metabolism, Endocrinology & Diabetes, Department of Internal Medicine, University of Michigan, Ann Arbor

M. CECILIA LANSANG, MD, MPH
Associate Professor of Medicine, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH; Director, Inpatient Diabetes Services, Department of Endocrinology, Diabetes, and Metabolism, Cleveland Clinic

Diabetes with obesity—Is there an ideal diet?

ABSTRACT

For individuals who are overweight or obese, weight loss is effective in preventing and improving the management of type 2 diabetes. Together with other lifestyle factors like exercise and behavior modification, diet plays a central role in achieving weight loss. Diets vary based on the type and amount of carbohydrate, fat, and protein consumed to meet daily caloric intake goals. A number of popular diets are reviewed as well as studies evaluating the effect of various diets on weight loss, diabetes, and cardiovascular risk factors. Current trends favor the low-carbohydrate, low-glycemic index, Mediterranean, and very-low-calorie diets. However, no optimal dietary strategy exists for patients with obesity and diabetes, and more research is needed. Given the wide range of dietary choices, the best diet is one that achieves the best adherence based on the patient's dietary preferences, energy needs, and health status.

KEY POINTS

Weight loss in individuals who are obese has been shown to be effective in the prevention and management of type 2 diabetes.

Diets vary based on the type and amount of carbohydrate, fat, and protein consumed to meet daily caloric intake goals.

Diets of equal caloric intake result in similar weight loss and glucose control regardless of the macronutrient content.

The metabolic status of the patient based on lipid profiles and renal and liver function is the main determinant for the macronutient composition of the diet.

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According to National Health and Nutrition Examination Survey data, more than one-third of adults in the United States are obese and more than two-thirds of adults with type 2 diabetes mellitus (DM) are obese.[1] In light of overall increased life expectancy, the Centers for Disease Control and Prevention estimates that adults in the United States have a 40% lifetime risk of developing diabetes, as diabetes and obesity remain at epidemic levels.[2]

Weight loss in individuals who are overweight or obese is effective in preventing type 2 DM and improving management of the disease.[3,4] Dietary changes play a central role in achieving weight loss, as do other important lifestyle interventions such as exercise, behavior modification, and pharmacotherapy. Achieving glycemic goals with diet alone is difficult, and for patients with DM who are also obese, it may be even more challenging.

Medical nutrition therapy, a term coined by the American Dietetic Association, describes an approach to treating medical conditions using specific diets. As developed and monitored by a physician and registered dietitian, diet can result in beneficial outcomes and is a front-line approach for patients with noninsulin-dependent diabetes.[5] Medical nutrition therapy for patients with type 2 DM is most effective when used within 1 year of diagnosis and is associated with a 0.5% to 2% decrease in hemoglobin A1c (HbA1c) levels.[6] This article reviews the role of diet in managing patients with both type 2 DM and obesity. Several diets are presented including what is known about their effect on weight loss, glycemic control, and cardiovascular risk prevention in patients with diabetes and obesity.

WEIGHT LOSS AND DIET FOR PATIENTS WITH OBESITY AND DIABETES

A person is overweight or obese if he or she weighs more than the ideal weight for their height as calculated by the body mass index (BMI; weight in kg/height in meters squared). A BMI of 25 to 30 is overweight and a BMI of 30 or greater is obese.[7] The recommended daily caloric intake for adults is based

on sex, age, and daily activity level and ranges from 1,600 to 2,000 calories per day for women and 2,000 to 2,600 calories per day for men. The lower end of the range is for sedentary adults, and the higher end is for active adults (walking 1.5 to 3 miles per day at 3 to 4 miles per hour, in addition to independent living).[8]

According to the American Diabetes Association (ADA), weight loss requires reducing dietary intake by 500 to 750 calories per day, or roughly 1,200 to 1,500 kcal/day for women and 1,500 to 1,800 kcal/day for men.[3] For patients with obesity and type 2 DM, sustained, modest weight loss of 5% of initial body weight improves glycemic control and reduces the need for diabetes medications.[9] Weight loss of greater than 5% body weight also improves lipid and blood pressure status in patients with obesity and diabetes, though ideally, patients are encouraged to achieve weight reduction of 7% or greater.[10]

Evidence of benefits from lifestyle and dietary modifications

The fact that patients with obesity and type 2 DM have increased risk of cardiovascular morbidity and mortality is well established.[11] Multiple studies considered the effects of weight loss on cardiovascular morbidity and mortality. Our article focuses on dietary modifications, though most large, multicenter trials used both diet and increased physical activity to achieve weight loss. It is difficult to determine if diet or physical activity had the most effect on outcomes; however, results show that weight loss from dietary and other lifestyle interventions leads to change in outcomes.

Look AHEAD (Action for Health in Diabetes) trial. This large, multicenter, randomized controlled trial evaluated the effect of weight loss on cardiovascular morbidity and mortality in overweight or obese adults with type 2 DM. The 5,145 participants were assigned either to a long-term weight reduction intensive lifestyle intervention of diet, physical activity, and behavior modification or to usual care of support and education. At 1 year, the lifestyle intervention group had greater weight loss, improved fitness, decreased number of diabetes medications, decreased blood pressure, and improved biomarkers of glucose and lipid control compared with the usual care group.[12] No significant reductions in cardiovascular morbidity and mortality were found, though an observational post hoc analysis of the Look AHEAD data suggested an association between the magnitude of weight loss and the incidence of cardiovascular disease.[13]

The diet portion of the intensive lifestyle intervention consisted of self-selected, conventional foods while recording dietary intake during week 1. In week 2, patients weighing less than 114 kg (250 lbs) restricted their intake to 1,200 to 1,500 kcal/day, and patients weighing 114 kg or more restricted their intake to 1,500 to 1,800 kcal/day. Fewer than 30% of calories were from fat, with less than 10% from saturated fat. During week 3 through week 9, meal replacement options and conventional foods were used to reach caloric goals. Participants then decreased the use of meal replacement and increased the use of conventional foods during week 20 through week 22.[14]

The mean weight loss for participants in the intensive lifestyle intervention group was 8.6% compared with 0.7% in the support and education group ($P < .001$). HbA1c decreased by 0.7% in the intervention group compared with 0.1% the support and education group ($P < .001$).[12]

Finnish Diabetes Prevention Study. This study evaluated lifestyle changes in diet and physical activity in the prevention of type 2 DM in participants with impaired glucose intolerance. Participants (N = 552) were randomly assigned to the control group or the intervention group where detailed instruction was provided to achieve weight loss of greater than 5%.[15] The dietary goals included fewer than 30% of total calories from fat, with fewer than 10% from saturated fat, increased fiber consumption (15 g per 1,000 kcal), and physical activity of 30 minutes daily.[15] During the trial (mean duration of follow-up 3.2 years), the risk of type 2 DM was reduced by 58% in the intervention group compared with the control group.[15]

Diabetes Prevention Program Research Group. A landmark study by the Diabetes Prevention Program Research Group randomized 3,234 participates with elevated plasma glucose levels to placebo, metformin, and lifestyle intervention arms.[4] Those in the lifestyle intervention arm were educated about ways to achieve and maintain a 7% or greater reduction in body weight using a low-calorie, low-fat diet and moderate physical activity. Results based on a mean follow-up of 2.8 years found a 58% reduction in the incidence of diabetes for those in the lifestyle intervention arm.[4]

DIETS AND THEIR EFFECTS ON OBESITY, DIABETES, AND CARDIOVASCULAR RISK

When patients seek consultation about diet, they frequently ask about specific types of popular diets, not the very controlled diets employed in research studies. Dietary preferences are personal, so patients may have researched a particular diet or feel that they will

Summary: low-carbohydrate diet

Allows 50 to 100 g/day; < 40% calories from carbohydrates[18,20]

- Foods: higher in protein (meat, poultry, fish, shellfish, eggs, cheese, nuts, seeds); higher in fat (oils, butter, olives, avocados); low-carbohydrate vegetables (green salad, cucumber, broccoli, squash)
- Avoid: rice, pasta, bread
- Weight loss: rapid, 11.4 kg over 6 months reported[24–27]
- Hemoglobin A1c: reduced 1.4% in 6 months, or 0% to 2.2%[18,24]
- Cardiovascular: lower triglyceride, higher high-density lipoprotein cholesterol[18]
- Weight regain: rapid, 6 months
- Challenges: limits important nutrients; monitor lipids, renal function, protein intake

be more adherent if only 1 or 2 components of their meals are changed. There is no single optimal dietary strategy for patients with both obesity and type 2 DM. In general, diets are categorized based on the 3 basic macronutrients: carbohydrate, fat, and protein. We will review several popular diets, delineating content, effects on weight loss, glycemic control, and cardiovascular factors.

LOW-CARBOHYDRATE DIET

Carbohydrates are organic compounds in food that include sugars and starches and are a source of energy for cells in the body and the brain in particular. The US Department of Agriculture Recommended Dietary Allowance of carbohydrate is 130 g per day minimum or 45% to 65% of total daily caloric intake.[16] For a 1,700-calorie diet, 130 g of carbohydrate is 30% of the total caloric intake; in a 1,200-calorie diet, it is 43%.[17]

In practice, the median intake of carbohydrates for US adults is much higher, at 220 to 330 g per day for men and 180 to 230 g per day for women.[16] The ADA recommends that all Americans consume fewer refined carbohydrates and added sugars in favor of whole grains, legumes, vegetables, and fruit.[18]

Low-carbohydrate diets focus on reducing carbohydrate intake with the thought that fewer carbohydrates are better. However, the definition of a low-carbohydrate diet varies. In most studies, carbohydrate intake was limited to less than 20 g to 120 g daily or fewer than 4% to 45% of the total calories consumed.[17,19] Intake of fat and total calories is unlimited, though unsaturated fats are preferred over saturated or trans fats.

Limiting the intake of disaccharide sugar in the form of sucrose and high-fructose corn syrup is endorsed because of concerns that these sugars are rapidly digested, absorbed, and fully metabolized. However, several randomized trials showed that substituting sucrose for equal amounts of other types of carbohydrates in individuals with type 2 DM showed no difference in glycemic response.[20] The resulting conclusion is that the postprandial glycemic response is mainly driven by the amount rather than the type of carbohydrates. The consumption of sugar-sweetened beverages is associated with obesity and an increased risk of diabetes, attributed to the high caloric intake and decreased insulin sensitivity associated with these beverages.[21]

Of the 2 monosaccharides, glucose and fructose, that make up sucrose, fructose is metabolized in the liver. The rapid metabolism of fructose may lead to alterations in lipid metabolism and affect insulin sensitivity.[22] While the ADA does not advise against consuming fructose, it does advise limiting its use due to the caloric density of many foods containing fructose.

Multiple studies have investigated the effect of a low-carbohydrate diet on weight loss, glucose control, and cardiovascular risk, but comparing the results is difficult due to the varying definitions of a low-carbohydrate diet.

Low-carbohydrate diets are associated with rapid weight loss. A 6-month study of 31 patients with obesity and type 2 DM found a mean weight change of −11.4 kg (± 4 kg) in the low-carbohydrate group compared with −1.8 kg (± 3.8 kg) in the high-carbohydrate control group, a loss maintained up to 1 year.[23] Another study of 88 patients with type 2 DM who consumed less than 40 g/day of carbohydrate had a weight loss of 7.2 kg over 12 months.[24] Samaha et al[25] compared a low-carbohydrate diet with a low-fat diet in 132 participants with obesity (mean BMI 43), of which 39% had diabetes and 43% had metabolic syndrome. Those in the low-carbohydrate diet group had significantly more weight loss over a period of 6 months (−5.8 kg mean, ± 8.6 kg standard deviation [SD] vs −1.9 kg mean ± 4.2 kg SD, P = .002). However, at 1 year, there was no significant difference in weight loss between groups. At 36 months, weight regain was 2.2 kg (SD 12.3 kg) less than baseline in the low-carbohydrate group compared with 4.3 kg (SD 12.2 kg) less than baseline in the low-fat group

(P = .071).[25,26] On the other hand, a meta-analysis of 23 randomized trials involving 2,788 participants found no difference in weight loss at 6 months between those on a low-carbohydrate diet and those on a low-fat diet.[19]

With respect to glucose control, low-carbohydrate diets have been associated with a 1.4% (SD ± 1.1%) decrease in HbA1c during a 6-month period in 31 patients with obesity and type 2 DM.[23] Another 6-month study of 206 patients with obesity and diabetes comparing a low-carbohydrate diet with a low-calorie diet found no significant difference in HbA1c (−.48% vs −.24%, respectively) and a weight loss of 1.34 kg vs 3.77 kg, respectively (P < .001).[27] The change in glycemic control did not persist over time, perhaps due to the weight regain associated with this diet. A meta-analysis concluded that HbA1c was reduced more in patients with type 2 DM randomized to a lower-carbohydrate diet compared with a higher-carbohydrate diet (mean change from baseline 0% to −2.2%).[17]

No studies of the effects of a low-carbohydrate diet on overall cardiovascular morbidity or mortality exist. However, Kirk et al[17] reported results of a low-carbohydrate diet on cardiovascular risk factors such as lipid profiles and showed a significant reduction in triglyceride levels but no effect on total cholesterol, high-density lipoprotein cholesterol (HDL-C), or low-density lipoprotein cholesterol (LDL-C) levels.

The ADA has reported that low-carbohydrate diets may be effective in the management of type 2 DM in the short term. Caution is warranted because they could eliminate important sources of energy, fiber, vitamins, and minerals. It is also important to monitor lipid profile, renal function, and protein intake in certain patients, especially those with renal dysfunction.[6]

LOW-GLYCEMIC DIET

The glycemic index (GI) is a measure of the rise in plasma glucose 2 hours after ingesting carbohydrate in food compared with a reference food such as glucose that contains an equivalent amount of carbohydrate. The GI measures the postprandial response of different carbohydrates: high-GI foods raise blood glucose more than medium- or low-GI foods.

Various factors affect the GI including the type of carbohydrate, fat content, protein content, and acidity of the food consumed, as well as the rate of intestinal reaction to the food. The faster the digestion of a food, the higher the GI. High-GI foods (> 70), such as those highly processed and with high starch content, produce higher peak glucose levels when compared with low-GI foods (< 55). Low-GI foods include lentils, beans, oats, and nonstarchy vegetables.

Summary: low-glycemic diet

Foods with glycemic index < 55

- Foods: whole wheat, rye, pita breads; oats, brown rice, couscous; muesli, bulgur; most fruits; nonstarchy vegatables
- Weight loss: none; −0.32 kg[30]
- Hemoglobin A1c: reduced 0.5%[29]
- Cardiovascular: undetermined
- Weight regain: undetermined
- Challenges: limits important nutrients; glycemic index varies with preparation and among individuals

Low-GI foods curb the large and rapid rise of blood glucose, insulin response, and glucagon inhibition that occur with high-GI foods. Many low-GI foods have high amounts of fiber, which prolongs distention of the gastrointestinal tract, increases secretion of cholecystokinin and incretins, and extends statiety.[28]

In a meta-analysis of 19 randomized trials of overweight or obese patients (BMI > 25), a low-glycemic diet did not show weight loss when compared with an isocaloric control diet (mean difference −0.32 kg; 95% confidence interval [CI] −0.86 kg, 0.23 kg).[29] On the other hand, the effect on glycemic control is more pronounced. Another meta-analysis that included 11 studies of patients with DM who followed a low-glycemic diet for less than 3 months to over 6 months showed that those who followed a low-glycemic diet had a significant reduction of HbA1c (6 studies had HbA1c as the primary outcome, HbA1c weighted mean difference −0.5%; 95% CI, −0.8 to −0.2; P = .001). Five studies reported on parameters related to insulin action, and 1 showed increased sensitivity measured by euglycemic-hyperinsulinemic clamp in a low-glycemic diet (glucose disposal 7.0 ± 1.3 mg glucose/kg/min) vs a high-glycemic diet (4.8 mg glucose/kg/min ± 0.9, P < .001).[28]

There are no large trials of cardiovascular mortality or morbidity of low-glycemic diets, but some studies have included cardiovascular parameters. A randomized study of 210 patients with type 2 DM evaluated cardiovascular risk factors after 6 months of a low-glycemic diet and high-glycemic diet. The low-glycemic diet group had an increase in HDL-C compared with the high-glycemic diet group (1.7 mg/dL; 95% CI, 0.8

Summary: low-fat diet

Allows < 30% calories from fat

- Foods: whole wheat, rye, pita breads; oats, brown rice, couscous; muesli, bulgur; most fruits; nonstarchy vegatables
- Avoid: saturated and trans fats
- Weight loss: 5.3 kg in 6 months,[37] 11% in 1 year[38]
- Hemoglobin A1c: minimal to none
- Cardiovascular: lower low-density lipoprotein cholesterol and triglyceride, higher high-density lipoprotein cholesterol[37]
- Weight regain: 4% at 2 years[38]
- Challenges: differentiating types of fat, avoiding saturated and trans fats

to 2.6 mg/dL vs −0.2 mg/dL; 95% CI, −0.9 to –0.5 mg/dL, P = .005).[30] Another crossover study of 20 patients with type 2 DM on a low-glycemic diet over 2 consecutive 24-day periods revealed a 53% reduction of the activity of plasminogen activator inhibitor-1, a thrombolytic factor that increases plaque formation.[31] Most studies were of short duration; thus, weight regain was not clearly established.

The GI of low-GI foods differs based on the cooking method, presence of other macronutrients, and metabolic variations among individuals. Low-glycemic diets can reduce the intake of important dietary nutrients. The ADA notes that low-glycemic diets may provide only modest benefit in controlling postprandial hyperglycemia.[32]

LOW-FAT DIET

Low-fat diets have 30% or fewer calories from fat, approximately 50 g of fat for a 1,500 kcal/day. The intake of dietary fat and free fatty acids reduces insulin sensitivity and enhances hepatic glucose production contributing to hyperglycemia.[33] The mechanisms by which dietary fat and fatty acids reduce insulin sensitivity include modifications of the cell membrane composition, gene expression, and enzyme activity. Fatty acids also promote inflammatory cytokines and induce endothelial dysfunction. The type of fat rather than its total amount plays a role in glycemic control and cardiovascular disease risk.[32]

Different types of fats have different effects on metabolism. LDL-C is mostly derived from saturated fats.[34] Consuming 2% of energy intake from trans fat substantially increases the risk of coronary heart disease.[35] Though the ideal total amount of fat for people with diabetes is unknown, the amount consumed still has important consequences, especially since patients with type 2 DM are at risk for coronary artery disease. The Institute of Medicine states that fat intake of 20% to 35% of energy is acceptable for all adults.[16]

Low-fat diets along with reduced caloric intake induce weight loss, but this cannot compete with the rapid weight loss that patients experience with the low-carbohydrate diet. This was shown in multiple studies including a meta-analysis of 5 randomized clinical trials of 447 patients with obesity who lost less weight in the low-fat diet group compared with low-carbohydrate diet group (weighted mean difference −3.3 kg; 95% CI, −5.3 to −1.4 kg) at 6 months.[36] Interestingly, the difference between diets was nonexistent after 12 months (weighted mean difference −1.0 kg; 95% CI, −3.5 to 1.5 kg), which may be due to weight regain in the low-carbohydrate diet group.[36]

Foster et al[37] studied 307 participants with obesity assigned to a low-fat or low-carbohydrate diet. Both groups lost 11% in 1 year, and with regain, lost 7% from baseline at 2 years. There was no statistically significant difference between groups during the 2 years, but there was a trend for more weight loss in the low-carbohydrate group in the first 3 months (P = .019).[37]

The low-fat diet has no to minimal improvement in glycemic control in patients with diabetes and obesity, regardless of the weight loss achieved. However, a low-fat diet is associated with some beneficial effects on cardiovascular risks. Nordmann et al[36] found no difference in blood pressure between low-carbohydrate and low-fat diets. The low-fat diet was associated with lower total cholesterol and LDL-C levels (weighted mean difference 5.4 mg/dL [0.14 mmol/L]; 95% CI, 1.2 mg/dL to 10.1 mg/dL [0.03–0.26 mmol/L]).[36] Triglyceride and HDL-C levels were more favorably changed in the low-carbohydrate diet (for triglycerides, weighted mean difference −22.1 mg/dL [−0.25 mmol/L]; 95% CI, −38.1 to −5.3 mg/dL [−0.43 to −0.06 mmol/L]; and for HDL-C, weighted mean difference 4.6 mg/dL [0.12 mmol/L]; 95% CI, 1.5 mg/dL to 8.1 mg/dL [0.04–0.21 mmol/L]).[36]

VERY-LOW-CALORIE DIET

Very-low-calorie diets provide 400 to 800 calories per day of high-quality protein and carbohydrate fortified with vitamins, minerals, and trace elements.[38] Very-low-calorie diets promote quick weight loss and use commercial formulas, liquid shakes, and soups to replace all regular meals. This type of diet results

in rapid weight loss without leading to electrolyte imbalances associated with starvation. It was widely promoted in the 1970s, but then lost some of its popularity due to concerns for patients' safety and even death.[39] For these reasons, individuals on very-low-calorie diets should be closely monitored by a team of health professionals.

Saris et al[38] reported results from 8 randomized clinical trials ranging from 10 to 32 patients with obesity comparing very-low-calorie diets with a low-calorie diet of 800 to 1,200 calories a day. Over the first 4 to 6 weeks, weight loss was between 1.4 kg and 2.5 kg per week and was higher with the very-low-calorie diet when compared with the low-calorie diet though not statistically significant. Interestingly, when followed for 16 to 26 weeks, the difference in weight loss was again not statistically significant with no trend for more weight loss in the very-low-calorie diet group. Another meta-analysis looking at 6 randomized clinical trials in patients with obesity showed that weight loss with very-low-calorie diets was statistically significant when compared with low-calorie diets (16.1% ± 1.6% vs 9.7% ± 2.4% weight loss over a period of 12.7 ± 6.4 weeks).[39]

In general, it is believed that when individuals lose a large amount of weight in a short period, a larger weight regain will occur, resulting in a higher weight than before the initial loss. This was refuted by Tsai et al,[39] who found that long-term data (1 to 5 years) showed the percentage of weight regained is higher with a very-low-calorie diet (62%) vs a low-calorie diet (41%) but the overall weight lost remains superior with the very-low-calorie diet, though not statistically significant (6.3% ± 3.2% and 5.0% ± 4.0% loss of initial weight, respectively).

Toubro et al[40] looked at 43 obese individuals who followed the very-low-calorie diet for 8 weeks compared with 17 weeks of a conventional diet (1,200 kcal/day) followed by a year of unrestricted calories, low-fat, high-carbohydrate diet or fixed calorie group (1,800 kcal/day). The very-low-calorie diet group lost weight at a more rapid rate, but the rate had no effect on weight maintenance after 6 or 12 months. Interestingly, the group that followed the "unrestricted calories, low-fat, high-carbohydrate diet" for a year maintained 13.2 kg (8.1 kg to 18.3 kg) of the initial 13.8 kg (11.8 kg to 15.7 kg) weight loss, while the fixed-calorie group maintained less weight loss (9.7 kg [6.1 kg to 13.3 kg]). Saris[38] concluded that the rapid weight loss by very-low-calorie diet has better long-term results when followed up with a program that includes nutritional education, behavioral therapy, and increased physical activity.

Summary: very-low-calorie diet

Provides 400 to 800 calories daily with meal replacements[39]

- Foods: meal replacements such as Optifast, SlimFast shakes
- Weight loss: 1.4 to 2.5 kg/week[39]; 16.1% over 12.7 weeks[40]
- Hemoglobin A1c: reduced 0.9% over 12 weeks[41]
- Cardiovascular: little effect[42]
- Weight regain: 62% at 5 years[40]
- Challenges: close monitoring by professionals required; requires meal replacements; low adherence rate

Very-low-calorie diets achieve glycemic control by reducing hepatic glucose output, increasing insulin action in the liver and peripheral tissues, and enhancing insulin secretion. These benefits occur soon after starting the diet, which suggests that caloric restriction plays a critical role. A study at the University of Michigan showed that the use of very-low-calorie diets in addition to moderate-intensity exercise resulted in a reduction of HbA1c from 7.4% (± 1.3%) to 6.5% (± 1.2%) in 66 patients with established type 2 DM.[41] HbA1c of less than 7% occurred in 76% of patients with established diabetes and 100% of patients with newly diagnosed diabetes.[41] Improvement in HbA1c over 12 weeks was associated with higher baseline HbA1c and greater reduction in BMI.[41]

Long-term cardiovascular risk reduction of very-low-calorie diets is small. One study showed that serum total cholesterol decreased at 2 weeks but did not differ at 3 months from baseline.[42] A large reduction was observed in serum triglycerides at 3 months (4.57 mmol/L ± 1.0 mmol/L vs 2.18 mmol/L ± .26 mmol/L, P = .012) while HDL-C increased (0.96 mmol/L ± .06 mmol/L vs 1.11 mmol/L ± .05 mmol/L, P = .009).[42] Blood pressure was also reduced in both systolic pressure (152 mm Hg ± 6 mm Hg vs 133 mm Hg ± 3 mm Hg, P = .004) and diastolic pressure (92 mm Hg ± 3 mm Hg vs 81 mm Hg ± 3 mm Hg, P = .007).[42]

Challenges with this diet include significant weight regain and safety concerns for patients with obesity and type 2 DM, especially those who are taking insulin, since this diet will lead to significant rapid lowering of insulin levels.[38] Finally, very-low-calorie diets require a multidisciplinary approach with frequent health professional visits.

Summary: Mediterranean diet

Focuses on 30% to 40% calories from monounsaturated fats

- Foods: olive oil, fresh fruits and vegetables, cereals, beans, nuts, seeds, limited dairy, limited eggs and red meat, wine moderately with meals
- Weight loss: 7.4 kg in 1 year[43]
- Hemoglobin A1c: reduced 0.4% to 0.6%[43,47]; lower incidence type 2 diabetes[46]
- Cardiovascular: systolic blood pressure reduced 7.1 mm Hg; reduced high-density lipoprotein cholesterol ration of .2645
- Weight regain: less, 0.5 kg over 2 years[44]
- Challenges: slower weight loss but higher adherence rate

MEDITERRANEAN DIET

The Mediterranean diet focuses on the moderate ingestion of monounsaturated fats such as olive oil (30% to 40% of daily energy intake), legumes, fruits, vegetables, nuts, whole grains, fish, and moderate ingestion of wine. A study of 259 overweight (mean BMI 31.4) patients with diabetes found a mean weight loss of as much as 7.4 kg at a steady state after 12 months.[43] A systematic review of 5 randomized clinical trials of obese adults (N = 998) showed that sustained weight loss (up to 12 months) was greater in the Mediterranean diet compared with a low-fat diet (range of mean values: −4.1 to −10.1 kg vs 2.9 to −5.0 kg), but similar to a low-carbohydrate diet (4.1 to −10.1 kg vs −4.7 to −7.7 kg).[44]

This diet also has a positive impact on glycemic control and has been shown to reduce the incidence of diabetes. Estruch et al[45] conducted a randomized controlled trial on 772 adults at high risk for cardiovascular disease, of which 421 had type 2 DM, assigned to Mediterranean diet supplemented either with extra-virgin olive oil or mixed nuts compared with a control group receiving advice on a low-fat diet. Their primary prevention trial, PREDIMED, looked mainly at the rate of total cardiovascular events (stroke, myocardial infarction, cardiovascular death); however, a subgroup analysis showed that the incidence of new-onset diabetes was reduced by 52% with the Mediterranean diet compared with the control group after 4 years of follow-up. Multivariate-adjusted hazard ratios of diabetes were 0.49 (0.25–0.97) and 0.48 (0.24–0.96) in the Mediterranean diet supplemented with olive oil and nuts groups, respectively, compared with the control group. Intuitively, they also showed that the higher the adherence, the lower the incidence rate.[46] This occurred despite no difference in weight loss between the groups and may indicate that the components of the diet itself could have anti-inflammatory and antioxidative effects. Esposito et al[47] showed that after 1 year of intervention in 215 patients with type 2 DM, HbA1c was lower in those assigned to the Mediterranean diet vs those assigned to a low-fat diet (difference: −0.6%; 95% CI, −0.9 to −0.3). Similarly, in a 12-month trial, Elhayany et al[43] found a significant difference in the reduction in HbA1c in those on the Mediterranean diet compared with a low-fat diet (0.4%, P = .02).

Many studies have shown a beneficial effect of the Mediterranean diet on cardiovascular health. Estruch et al[45] showed that 772 patients (143 with type 2 DM) at high risk of cardiovascular disease who followed a Mediterranean diet with nuts for 3 months had a reduced systolic blood pressure of −7.1 mm Hg (CI, −10.0 mm Hg to −4.1 mm Hg) and reduced HDL-C ratio of −0.26 (CI, −0.42 to −0.10) compared with a low-fat diet. There was also a reduction in fasting plasma glucose of −.30 mmol/L (CI, −.58 mmol/L to −.01 mmol/L).[45]

PROTEIN-SPARING MODIFIED FAST

The protein-sparing modified fast combines a very-low-carbohydrate ketogenic diet and a very-low-calorie diet. The initial 6-month phase consists of fewer than 800 calories a day followed by a gradual increase in calories over 6 months. Carbohydrate is restricted to 20 to 50 g/day during the initial phase, with protein intake of 1.2 to 1.5 g/kg of ideal body weight per day.[48]

One of the earlier studies on protein-sparing modified fast showed that weight loss was as high as 21 kg ± 13 kg during the initial phase and 19 kg ± 13 kg during the refeeding phase.[49] Weight regain is high: in the protein-sparing modified fast, most patients return to their baseline weight in 5 years.[50]

A study comparing 6 patients who were put on a protein-sparing modified fast diet with 6 patients who underwent gastric bypass surgery showed that the mean steady-state plasma glucose fell from 377 mg/dL to 208 mg/dL (P < .008) and mean fasting insulin values fell from 31.0 to 17.0 μU/mL (P < .004).[51] There were also changes in cardiovascular risk factors: mean HDL-C values increased from 33.8 mg/dL to 40.5 mg/dL (P < .008), and factor VIII coagulant activity decreased from 194% to 140% (P < .005).[51] Total

Summary: protein-sparing modified fast diet

Combines a very-low-carbohydrate ketogenic diet with a very-low-calorie diet

- Foods: low in carbohydrate, high-to-moderate protein intake, minimal fat, includes shakes and meal replacement for low-calorie portion
- Weight loss: 21 kg (± 13 kg) initially, 19 kg (± 13 kg) refeeding[49]
- Hemoglobin A1c: mean plasma glucose from 377 to 208 mg/dL; mean fasting glucose from 31 to 17 µU/mL[51]
- Cardiovascular: higher high-density lipoprotein cholesterol, lower low-density lipoprotein cholesterol and cholesterol; not maintained at 1 year[51,52]
- Weight regain: most return to baseline by 5 years[50]
- Challenges: close monitoring by professionals required; requires meal replacements; lower adherence rate

cholesterol and LDL-C levels were also improved, but these changes were not always maintained at follow-up visits.[52]

VEGETARIAN AND VEGAN DIETS

A vegetarian diet consists primarily of cereals, fruits, vegetables, legumes, and nuts and generally excludes animal foods and dairy products. Less restrictive vegetarian diets may include eggs and dairy products. A vegan diet is one of the most restrictive diets and excludes all types of animal products, including honey and processed foods.

In 2013, Mishra et al[53] conducted a randomized clinical trial of employees with obesity and type 2 DM (N = 291) assigned to a low-fat vegan diet or no intervention for 18 weeks. Weight decreased in the low-fat vegan diet group compared with the control group (2.9 kg vs 0.06 kg, respectively, $P < .001$). Statistically significant reductions in total cholesterol (8 mg/dL vs 0.01 mg/dL, $P < .01$), LDL-C (8.1 mg/dL vs 0.9 mg/dL, $P < .01$), and HbA1c (0.6% vs 0.08%, $P < .01$) occurred in the intervention group compared with the control group.[53]

Many studies of vegetarian and vegan diets have been of short duration and used a combination of low-fat and vegetarian or vegan diets on people that were not all considered obese. Research is limited for vegan and vegetarian diets, and not enough information exists about the effects on glycemic control and cardiovascular risk. Vegan and vegetarian diets may reduce the intake of many essential nutrients. Vegans who exclude dairy products, for example, have low bone mineral density and higher risk of fractures due to inadequate intake of calcium.

Summary: vegetarian and vegan diets

- Foods: fruits, vegetables, cereals, legumes, whole grains, nuts, soy, fiber; vegan excludes all animal-derived products including dairy, eggs, honey, processed foods
- Weight loss: 2.9-kg decrease[53]
- Hemoglobin A1c: reduced 0.6% (not statistically significant)[53]
- Cardiovascular: minimal impact, if any[53]
- Weight regain: unknown
- Challenges: may lack important nutrients

HIGH-PROTEIN DIET

Amino acids contribute to glucose synthesis through gluconeogenesis and play a role in recycling of glucose carbon via the glucose-alanine cycle. High-protein diets include more than 30% of total energy intake from protein (112 g/day assuming 1,500 kcal/day).

Parker et al[54] reported a weight loss of 5.2 kg ± 1.8 kg in 12 weeks in 54 patients with obesity and type 2 DM irrespective of a diet with high or low protein content. Women on a high-protein diet lost more total fat and abdominal fat compared with women on a low-protein diet. Total lean mass decreased in all patients irrespective of diet.

Studies have shown that high-protein diets can improve glucose control. Ajala et al[55] reviewed 20 clinical trials of patients with type 2 DM randomized to various diets for more than 6 months. In the trials that used a high-protein diet as an intervention, HbA1c levels decreased as much as 0.28% compared with the control diets ($P < .001$). A small study of 8 men with untreated type 2 DM compared a high-protein low-carbohydrate diet (nonketogenic, protein 30%, carbohydrate content 20%, fat 50%) with a control diet (protein 15%, carbohydrate 55%, fat 30%).[56] The high-protein low-carbohydrate diet group had lower HbA1c levels (7.6 mg/dL ± 0.3 mg/dL vs 9.8 mg/dL ± 0.5 mg/dL) and mean 24-hour integrated serum glucose (126 mg/dL vs 198 mg/dL) compared with the control diet. Most of the studies

Summary: high-protein diet

Includes > 30% calories from protein sources

- Foods: low-fat cottage cheese, cheese, tofu, red meat, chicken, peanut butter, fish, lentils
- Weight loss: 5.2 kg (±1.8 kg) in 12 weeks[54]
- Hemoglobin A1c: reduced 0.28%[55]
- Cardiovascular: lower low-density lipoprotein cholesterol, reduction in abdominal fat, no change in high-density lipoprotein cholesterol[54]
- Weight regain: unknown
- Challenges: must be individualized diet accounting for cardiometabolic risk and renal profile

of high-protein diets have been small and of short duration, and have used a combination of macronutrients (high protein and low carbohydrate), limiting the ability to identify the dietary component that had the most effect.

There are no studies evaluating cardiovascular outcomes, but some studies have included cardiovascular risk factors such as LDL-C levels and body fat composition. Parker et al[54] showed that women on a high-protein diet lost more total fat (5.3 kg vs 2.8 kg, $P = .009$) and abdominal fat (1.3 kg vs 0.7 kg, $P = .006$) compared with a low-protein diet. Interestingly, no difference in total fat and abdominal fat was found in men. LDL-C reduction was greater in a high-protein diet compared with a low-protein diet (5.7% vs 2.7%, $P < .01$).[54] In a review by Ajala et al,[55] the high-protein diet was the only diet that did not show a rise in HDL-C levels after interventions of more than 6 months.

The ADA does not recommend high-protein diets as a method for weight loss because the long-term effects are unknown. ADA recommendations include an individualized approach based on a patient's cardiometabolic risk and renal profiles. Protein content should be 0.8 g/kg to 1.0 g/kg of weight per day in patients with early chronic kidney disease, and 0.8 g/kg of weight per day in patients with advanced kidney disease.[6]

COMPARISONS AMONG DIETS

Studies comparing diets have reached varying conclusions and have been limited by inconsistent diet definitions, small sample sizes, and high participant dropout rates. A meta-analysis conducted by Ajala et al[55] included 20 randomized controlled trials that lasted 6 months or more with 3,073 individuals in the analysis. Low-carbohydrate, vegetarian, vegan, low-glycemic, high-fiber, Mediterranean, and high-protein diets were compared with low-fat, high-glycemic, ADA, European Association for the Study of Diabetes, and low-protein diets as controls. The greatest weight loss occurred with the low-carbohydrate (−0.69 kg, $P = .21$) and Mediterranean diets (−1.84 kg, $P < .001$). Compared with the control diets, the greatest reductions in HbA1c were with the low-carbohydrate (−0.12%, $P = .04$), low-glycemic (−0.14%, $P = .008$), Mediterranean (−0.47%, $P < .001$), and high-protein diets (−0.28%, $P < .001$). HDL-C levels increased in all the diets except the high-protein diet.[55]

CONCLUSION

The optimal macronutrient intake for patients with obesity and type 2 DM is unknown. Diets with equivalent caloric intakes result in similar weight loss and glucose control regardless of the macronutrient contents. It is important that total caloric intake be appropriate for weight management and glucose control goals. The metabolic status of the patient as determined by lipid profiles, and renal and liver function is the main driver for the macronutrient composition of the diet.

Current trends favor the low-carbohydrate, low-glycemic, Mediterranean, and low-caloric intake diets, though there is no evidence that one is best for weight loss and optimal glycemic control in patients with obesity and type 2 DM. Studies are limited by varying definitions, high dropout rates, and poor adherence. In addition, for many patients, weight regain often follows successful short-term weight loss, indicative of a low durability of results with many diet interventions. Medical nutrition therapy and a multidisciplinary lifestyle approach remain essential components in managing weight and type 2 DM. The ideal diet is one that achieves the best adherence when tailored to a patient's preferences, energy needs, and health status.

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Correspondence: *M. Cecilia Lansang, MD, MPH, Department of Endocrinology, Diabetes, and Metabolism, F20, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, OH 44195; lansanm@ccf.org*