Obesity and Diabetes

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published online 2020

Bibliography

Exp Clin Endocrinol Diabetes

DOI 10.1055/a-1284-6050

ISSN 0947-7349

Georg Thieme Verlag KG, Rüdigerstraße 14,
70469 Stuttgart, Germany

German Diabetes Association: Clinical Practice Guidelines

This is a translation of the DDG clinical practice guideline published in Diabetologie 2020; 15 (Suppl 1): S139-S147. DOI 10.1055/a-1179-2778.

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Weight reduction is an integral part of the therapy of many patients with type 2 diabetes. The effectiveness of weight reduction in the treatment and prevention of type 2 diabetes has been proven by many studies. In the "Finnish Diabetes Prevention Study", the conversion of prediabetes to type 2 diabetes was reduced by 58 % through lifestyle intervention [1]. Similar results were obtained in the "Diabetes Prevention Program" [2]. An English study showed that for every 1 kg of weight lost in the first year after diagnosis of type 2 diabetes, life expectancy increases by 3 – 4 months [3], and Williamson et al. [4] showed that a weight reduction of 10 kg reduces overall mortality in people with type 2 diabetes by 25 %. In addition, weight reduction not only improves blood glucose levels, but also virtually all comorbidities of diabetes simultaneously (hypertension, fatty liver disease, depression, obstructive sleep apnea syndrome [OSAS], etc.). However, these effects appear to be particularly strong when a weight reduction of at least 5 % can be achieved [5]. Weight gain in type 2 diabetes treatment worsens cardiovascular risk factors and is associated with an increase in cardiovascular events and mortality [6].

From the 2018 consensus report of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) and the 2019 update [7], it is clear that self-managed lifestyle intervention with weight reduction is of major importance in the treatment of type 2 diabetes. As a general treatment goal, patients with obesity and diabetes should aim for weight stabilization in the range of the normal weight (BMI 18.5 – 24.9 kg/m^2).

Since both an increased abdominal subcutaneous and visceral fat mass are associated with insulin resistance, measurement of waist circumference also serves as a good indicator of metabolic and cardiovascular risk and helps in the assessment of effective weight loss [8]. The BMI is also considered an independent predictor of cardiovascular events. However, waist circumference seems to be a better indicator of cardiovascular risk than BMI [9]. Women with a waist circumference ≥ 80 cm and men with ≥ 94 cm should not gain any further weight (▶ **Table 1**).

If the waist circumference is already at ≥ 88 cm for women and at ≥ 102 cm for men, the body weight should be reduced [9].

People with diabetes and a BMI of ≥ 25 kg/m^2 should aim to lose weight. At least 5 % of the initial body weight should be lost within 6 – 12 months. This reduction of 5 % already leads to a significant improvement in blood glucose levels. In people with diabetes and a BMI ≥ 35 kg/m^2, the goal of weight reduction should be at least 10 % of the starting weight. Once the weight reduction goals have been achieved, the treatment aims at long-term weight stabilization.

▶ **Table 1** General therapy goals for long-term weight stabilization.

Indicator	General therapy goal
BMI	18.5 – 24.9 kg/m²
Waist circumference for women	≤ 80 cm
Waist circumference for men	≤ 94 cm

Nutritional Therapy

The nutritional recommendations for obesity and type 2 diabetes are identical in the essential points and can be combined very well.

In order to properly structure a nutrition therapy, standardized action processes are necessary. The German-Nutrition Care Process (G-NCP) offers a very good basis for this.

Dietetic action competence is the central core of the G-NCP; it must be comprehensible and evaluable. The nutritional diagnosis according to a corresponding Problem-Etiology-Sign-Resources (PESR) system with reference to corresponding Nutrition-Care-Indicators (data from assessment) is the core of the planning of interventions and the corresponding nutrition therapy.

In the therapy of people with obesity and type 2 diabetes, the first step should be to implement the nutritional guidelines in the sense of a health-promoting diet.

The German Nutrition Society (Deutsche Gesellschaft für Ernährung - DGE) has been formulating guidelines to promote healthy eating since 1956. The "10 rules of the DGE" were last updated in August 2017 and offer sufficient individual leeway, as they do not define classic and rigid regulations or prohibitions. Instead, they can provide a basic framework for intervention planning and implementation in therapy.

The 10 Rules of the DGE [10]

1. Enjoy a variety of foods
2. Vegetables and fruits – have 5 a day
3. Select whole grains
4. Supplement the selection above with animal products
5. Use healthy oils and fats
6. Reduce sugar and salt
7. Drink water
8. Cook with care
9. Eat mindfully and enjoy your meal
10. Mind your weight and stay active

The nutritional recommendations should lead to a daily energy deficit of 500 kcal, in individual cases even higher. To achieve such an energy deficit, various strategies are recommended [11]:

- Reduction of fat consumption preferred
- Reduction of carbohydrate intake preferred
- Combined reduction of fat and carbohydrate consumption

Carbohydrates play a central role in the nutritional therapy of patients with obesity and diabetes. The quality of the selected carbohydrate foods - ideally rich in fiber, vitamins and minerals and low in added sugars, fats and sodium - should be considered in the individual nutritional planning.

For patients with type 2 diabetes who do not achieve their blood glucose therapy goals or who want to avoid an escalation of drug-based diabetes therapy, reducing the total carbohydrate intake with low-carbohydrate or very low-carbohydrate diets may therefore be a viable approach [12].

An increase in dietary fiber intake, preferably through food (vegetables, legumes [beans, peas and lentils], fruits and intact whole grain products) or through dietary supplements, can help to lower the HbA1c level. Based on recent meta-analyses, an increase in daily fiber intake by 15 g or up to 35 g/day may be a reasonable goal to reduce the risk of mortality in adult diabetes patients [13].

Nutritional therapy can include formula diets as a meal replacement strategy or alone, temporarily and with medical supervision. However, crash diets or very one-sided forms of nutrition can be dangerous [11]. When using formula diets, the focus is on weight loss. Unfortunately, patients do not learn anything about their eating habits during this time, nor is there any reference to food or portion sizes. Therefore, the use of formula diets should be discussed on an interdisciplinary basis in the context of therapy planning. There is no ideal percentage of calories from carbohydrates, proteins and fat for every person with diabetes or at risk of diabetes. Therefore, the distribution of macronutrients should be based on an individual assessment of current eating habits, preferences and metabolic goals.

When advising patients with diabetes, a key strategy for achieving blood glucose targets should include an assessment of the current food intake, which requires keeping a dietary journal. This should be followed by individual guidance on self-monitoring the carbohydrate intake to optimize meal timing and food choices, and recommendations for medication and physical activity.

In all the therapy efforts, it is important for the patient to maintain his or her enjoyment of food. It is equally important for the patient to receive encouragement, for example about the choice of food, and practical tools for daily food planning. The motivation for a healthy, balanced diet should always be framed by the guidelines of diabetes and obesity nutrition therapy. The focus on maintaining the quality of life and positive self-esteem can be aided by nutritional behavior (portion sizes, meal frequency, fast food available and eating behaviors), food selection (fatty foods, confectionery and snacks) in addition to the recommendations of limited sucrose intake (WHO recommendation < 25 g/d) [14].

Multimodal therapy approach

Large intervention studies on conservative weight loss measures, such as the Counter-Balance study (COUNTERacting BetA cell failure by Long term Action to Normalize Calorie intakE) or the DiRECT study, showed that people with obesity and type 2 diabetes were able to achieve type 2 diabetes remission through weight loss and long-term weight stabilization [15, 16]. Longer-term data from the Look-AHEAD study also show that mean weight gain and glucose metabolism parameters were also better with intensified lifestyle modification compared to standard 3 – 4 consultations per year, but this was not reflected in a difference in the primary cardiovascular endpoint [17]. Interestingly, however, even the control group with 3 – 4 standard consultations per year showed some weight loss over the course of the study and not, as would be epidemiologically expected, further weight gain. It can be concluded from this that a successful treatment strategy for weight reduction in people with

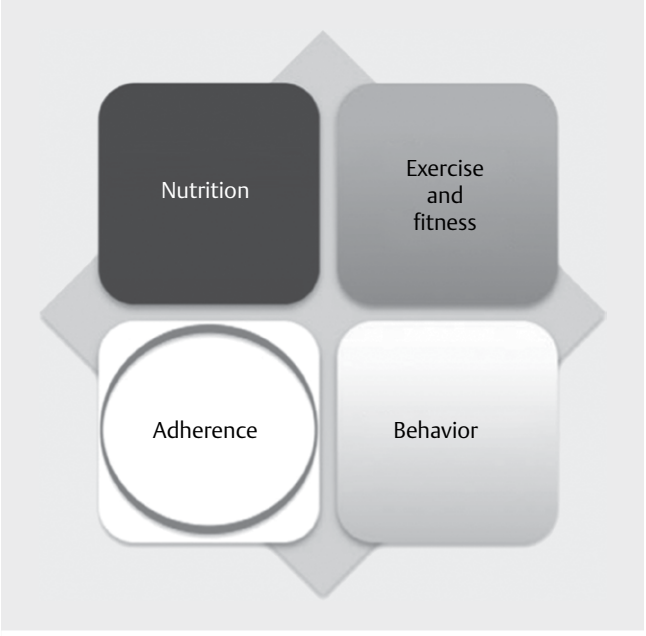
type 2 diabetes should always start early and, above all, in the long term, at least 3 – 4 lifestyle consultations per year.

Specific treatment objectives

Therapy goals should be individually tailored to the patient and, in particular, take into account comorbidities and cardiovascular risk factors. For people with obesity and type 2 diabetes without other concomitant diseases and without cognitive impairment, the recommendations of the National Healthcare Guidelines [18] can be used.

Components of the multimodal therapy approach

Conservative measures of lifestyle modification form the basis of obesity therapy. The coordinated implementation of nutritional, exercise and behavioral therapeutic interventions in an interdisciplinary team is crucial (▶ **Fig. 1**). As part of a nutritional medical intervention, eating behavior is first evaluated and then the aim is to reduce the ingested calories in a controlled manner and to optimize the composition of the food against the background of concomitant diseases (see section "Nutritional Therapy"). In addition to traditional training sessions, grocery shopping together and cooking courses are also held with the patients. Within the framework of behavioral therapy support, a structured analysis of possible factors (stress, emotions, psychiatric pre-existing conditions, concomitant diseases, etc.) that have a negative impact on eating behavior, i. e. hyperalimentation, takes place first. In the course of further treatment, these factors are then specifically addressed by behavioral therapy (e. g. learning coping strategies, stimulus control, learning of flexibly-structured vs. rigid eating/activity behavior, etc.). A sufficient and long-term adherence of the patient is crucial for the therapeutic success of multimodal obesity therapy.



▶ **Fig. 1** Components of a multimodal therapy concept for people with obesity and diabetes.

Standardized, partly commercial, weight loss programs follow exactly this multimodal approach and should therefore be actively offered and recommended to patients with obesity and diabetes.

Physical Activity

Regular physical exercise helps to prevent weight gain. Several studies have shown that people with an active lifestyle and sufficient physical activity can more easily achieve weight stabilization [19]. The duration and type of physical activity should be determined individually. The new U.S. Physical Activity Guidelines state that adults achieve the maximum benefit from physical activity if they regularly spend 150–300 min per week on moderate activity or 75–150 min per week on intensive activity, or an equivalent combination of moderate and vigorous aerobic activity [20]. These guidelines emphasize the benefits of aerobic activity in particular, as well as shorter periods of physical activity. Patients should therefore be encouraged to be physically active. In particular, patients with chronic co-morbidities who have maintained the capacity to exercise should engage in aerobic physical activity to reduce cardiovascular risk. In addition, it is recommended that muscle-strengthening activities be performed on 2 or more days, which also promotes bone stability. Elderly people should also be encouraged and supported to perform exercises to improve balance and reduce the risk of falls in the long term. Coordination and dexterity exercises have also been shown to be beneficial in old age.

Drug therapy for Patients with Diabetes and Obesity

The ADA/EASD Consensus Report on Pharmacotherapy of Type 2 Diabetes, published at the end of 2018, classifies according to therapeutic goals. If the focus is on promoting weight loss, GLP-1 receptor agonists and SGLT2 inhibitors are stated as equivalent combination partners in addition to metformin as a first-choice therapeutic [7]. Triple therapy with metformin, a GLP-1 analogue and an SGLT2 inhibitor, possibly with the addition of basal insulin, is also recommended if the HbA1c target corridor is not reached [7].

Metformin

The data on weight loss with metformin over the longest period of time was obtained from the Diabetes Prevention Program. In the first 3 years of this double-blind, randomized study, patients on metformin lost an average of 2.9 kg (placebo 0.4 kg). The effects lasted up to 15 years. In a direct comparison of metformin with 2nd or 3rd generation sulfonylureas, a meta-analysis showed a mean difference in weight of − 3.86 kg ([95 %-CI − 5.18; − 2.53 kg], n = 3185, 4 studies, I 2 = 69 %) in favor of metformin therapy [24]. In studies in untreated patients with type 2 diabetes, weight change in the metformin study arms was + 1.5 to − 2.9 kg [24]. Weight loss was also reported in 3 studies compared to DPP-4 inhibitors (mean difference in weight between − 0.7 and − 2.2 kg). The 3 individual studies involving 3 different active ingredients were not combined into a meta-analysis.

GLP-1 receptor agonists

GLP-1 receptor agonists lower body weight primarily through central nervous effects and a reduction in appetite. Inhibition of gastric emptying may play an additional but subordinate role [21]. In various clinical studies in patients with type 2 diabetes, the mean weight reduction under GLP-1 receptor agonist therapy was about 3 kg. Semaglutide once a week is the most effective GLP-1 receptor agonist in terms of weight loss. In the Phase 3 study program SUSTAIN, the weight reduction was 3.5 – 4.6 kg with semaglutide 0.5 mg and 4.5 – 6.5 kg with 1 mg semaglutide (▶ **Table 2**).

Currently, liraglutide is the only GLP-1 receptor agonist approved at a dose of 3 mg/d for the treatment of obesity (BMI ≥ 27 kg/m^2 with concomitant disease or BMI ≥ 30 kg/m^2). The approval is based on data from the SCALE study program. Mean weight loss with 3 mg liraglutide was approximately 8.4 kg at 56 weeks compared to 2.8 kg with placebo [22, 23]. In a 3-year study involving 2254 overweight or obese patients with pre-diabetes, treatment with 3.0 mg liraglutide daily reduced the likelihood of manifestation of type 2 diabetes during the treatment period by 79 % compared to placebo.

▶ **Table 2** Weight reducing effects of GLP-1 receptor agonists and SGLT2 inhibitors.

GLP-1 receptor agonist	Mode of action	Dose	Weight	Reference
Dulaglutide delay of action	by binding to IgG4 molecule	sc 0.75 – 1.5 mg per week	– 0.8 to – 2.9	Dungan KM, Povedano ST, Forest T, et al. Once-weekly dulaglutide versus once-daily liraglutide in metformin- treated patients with type 2 diabetes (AWARD-6): a randomised, open-label, phase 3, non-inferiority trial. Lancet 2014; 384: 1349 – 1357
Exenatid39	AS Peptid	5 – 10 µg bd	– 1.4 to – 4.0	Buse JB, printer DJ, Taylor KL, et al. DURATION-1: exenatide once weekly produces sustained glycemic control and weight loss over 52 weeks. Diabetes Care 2010; 33: 1255 – 1261
Exenatide LAR	Delayed effect due to encapsulation in microspheres	2 mg per week	– 1.6 to – 2.7	Buse JB, Rosenstock J, Sesti G, et al. Liraglutide once a day versus exenatide twice a day for type 2 diabetes: a 26-week randomised, parallel-group, multinational, open-label trial (LEAD-6). Lancet 2009; 374: 39 – 47
Liraglutide 1.8 mg	Delay of action by C16 fatty acid	1.2 – 1.8 mg	– 2 to – 5	Buse JB, Rosenstock J, Sesti G, et al. Liraglutide once a day versus exenatide twice a day for type 2 diabetes: a 26-week randomised, parallel-group, multinational, open-label trial (LEAD-6). Lancet 2009; 374: 39 – 47
Liraglutide	3mg	3 mg	– 6	4Efficacy of Liraglutide for Weight Loss Among Patients With Type 2 Diabetes The SCALE Diabetes Randomized Clinical Trial JAMA 2015; 314: 687–699
Lixisenatide	AS Peptide	10 – 20 µg/d	– 1.3 to – 3	Buse JB, Rosenstock J, Sesti G, et al. Liraglutide once a day versus exenatide twice a day for type 2 diabetes: a 26-week randomised, parallel-group, multinational, open-label trial (LEAD-6). Lancet 2009; 374: 39 – 47
Semaglutide	Delay of action by C20 fatty acid	0.5 – 1 mg per week	– 3.43 to – 4.54	Canters S, Wilkinson L, Vrazic H et al. Comparative efficacy of once-weekly semaglutide versus SGLT-2 inhibitors in patients inadequately controlled with one to two oral antidiabetic drugs: a systematic literature review and network meta-analysis. BMJ Open 2019; 9: e023 458
SGLT2 inhibitor	**SGLT2:SGLT1 selectivity**	**Dose**	**Weight**	**Reference**
Canagliflozin	200	100 – 300 mg/d	– 2.5 to – 4	Stenlöf K, Cefalu WT, Kim KA, et al Efficacy and safety of canagliflozin monotherapy in subjects with type 2 diabetes mellitus inadequately controlled with diet and exercise. Diabetes Obes Metab 2013; 15: 372 – 382
Dapagliflozine	1200	5 – 10 mg/d	– 2.65 to – 3.2	Ferrannini E, Ramos SJ, Salsali A, et al Dapagliflozine monotherapy in type 2 diabetic patients with inadequate glycemic control by diet and exercise: a randomized, double-blind, placebo-controlled, phase 3 trial. Diabetes Care 2010; 33: 2217 – 2224
Empagliflozine	2500	10 – 25 mg/d	– 2.08 to – 2.5	Haring HU, Merker L, Seewaldt-Becker E, et al. Empagliflozin as add- on to metformin in patients with type 2 diabetes: a 24-week, randomized, double-blind, placebo-controlled trial. Diabetes Care 2014; 37:1650–1659
Ertugliflozine	223	55-15 mg/d	– 2.5 to – 3.5	Rosenstock J, Frias J, Pall D, et al Effect of ertugliflozine on glucose control, body weight, blood pressure and bone density in type 2 diabetes mellitus inadequately controlled on metformin monotherapy (VERTIS MET). Diabetes Obes Metab 2018; 20: 520 – 529

The time to a diagnosis of type 2 diabetes was thus 2.7 times longer in patients treated with 3.0 mg liraglutide compared to placebo and the difference in body weight reduction was − 4.3 % (http://dx.doi.org/10.1016/S0140-6736(17)30069-7).

In the Scale Diabetes study, patients with type 2 diabetes and BMI ≥ 27 kg/m^2 could benefit from a therapy with liraglutide 3.0 mg daily. The observed weight reduction from baseline body weight was − 6.0 % (vs. 2.0 % with placebo) and the proportion of patients with weight reduction of more than 5 % was 54.3 % with liraglutide compared to 21.4 % with placebo [22].

The Scale Insulin study examined the effect of 3.0 mg liraglutide daily for weight reduction in patients with obesity and insulin-dependent type 2 diabetes. Compared to placebo, patients on liraglutide therapy achieved greater weight loss (ETD − 4.3 %), greater HbA1c reduction and had lower insulin requirements at the end of the study (week 56) (Diabetes Care 2020; 43: 1085 – 1093 | https://doi.org/10.2337/dc19-1745).

Initial Phase 3 study data is available for the substance semaglutide. In the STEP 3 study, at a dose of 2.4 mg once a week weight loss was − 16 % in 611 patients after one year (placebo group − 5.7 %). Semaglutide has, however, not been approved for the indication obesity [25].

SGLT2 inhibitors

SGLT2 inhibitors inhibit sodium-glucose cotransporter-2 (SGLT2) in the proximal renal tubule, through which 90 % of glomerular-filtered glucose is reabsorbed, thereby increasing renal glucose excretion. This results in an energy loss of approximately 250 – 300 kcal per day and allows weight reduction. However, weight reduction is limited by possible compensation mechanisms. As further mechanisms of weight loss, an increased rate of lipolysis or an activation of energy-consuming gluconeogenesis by glucagon release stimulated by SGLT2 inhibitors have been discussed. In insulin-treated patients, insulin dose reduction on comedication with SGLT2 inhibitors also contributes to weight loss. The SGLT2 inhibitors approved for antidiabetic therapy cause a dose-dependent moderate weight loss in the order of 1.5 – 2 kg (placebo-adjusted) (▶ **Table 2**). The weight loss is initially more pronounced and usually ends on a new plateau after about 26 weeks.

Incretin co-agonists

Results from several studies to date confirm the potential of the dual glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 incretin agonist tirzepatide to reduce HbA1c and body weight in people with type 2 diabetes. In the randomized, double-blind, phase 2 study on the efficiency and effectiveness of tirzepatide, 318 participants were randomized to one of 6 treatment groups. In the 4 intervention arms, the co-agonist was administered subcutaneously once a week at doses of 1 mg, 5 mg, 10 mg or 15 mg and compared with placebo and subcutaneous dulaglutide 1.5 mg (once a week) [26].

By activating both incretin receptors, tirzepatide led to a dose-dependent weight reduction of up to 11.3 kg at 26 weeks with an initial BMI of 32 kg/m^2 and a HbA1c reduction of 2.4 % compared to 2.7 kg and 1.1 % with 1.5 mg dulaglutide once weekly. Gastrointestinal side effects, which occurred mainly at the beginning of treatment, should be lessened by dose escalation while maintaining efficacy. Initial results of the Phase 3 SURMOUNT study program for overweight and obese patients (without type 2 diabetes), which was initiated at the end of 2019, are expected in 2022.

Diabetes Surgery and Interventional Diabetes Therapy

For people with type 2 diabetes, especially if they are obese, surgical therapy can be a useful supplement to conservative therapy. For the treatment of type 1 diabetes or other forms of diabetes, diabetes surgery is not recommended because there is insufficient data on efficacy and safety. The therapeutic principle of diabetes surgery, interventional diabetes therapy or even metabolic surgery has only developed in recent years on the basis of randomized studies in which surgical therapy of type 2 diabetes was superior to conservative strategies in terms of weight reduction, diabetes remission and improvements in glucose metabolism.

Value

Diabetic surgery refers to surgical procedures from the field of obesity surgery, whose indication is not exclusively weight-dependent, but also the treatment of type 2 diabetes. The main goal of surgical therapy is to improve the glycemic metabolic control. For other obesity-associated diseases such as arterial hypertension, lipid metabolism disorders or non-alcoholic fatty liver disease, there is currently insufficient data to establish the indication for metabolic intervention primarily because of these diseases. For most people with type 2 diabetes, diabetes surgery will not be the first choice in therapy concept escalation. This is mainly due to the fact that modern antidiabetic drugs and modified insulin therapies offer a safe and long-term effective diabetes therapy with a good quality of life. At the same time, however, patients with type 2 diabetes, who can particularly benefit from surgical treatment of diabetes, should be informed about this therapeutic option. The benefits of timely metabolic surgery should always be weighed against the risks.

Indication

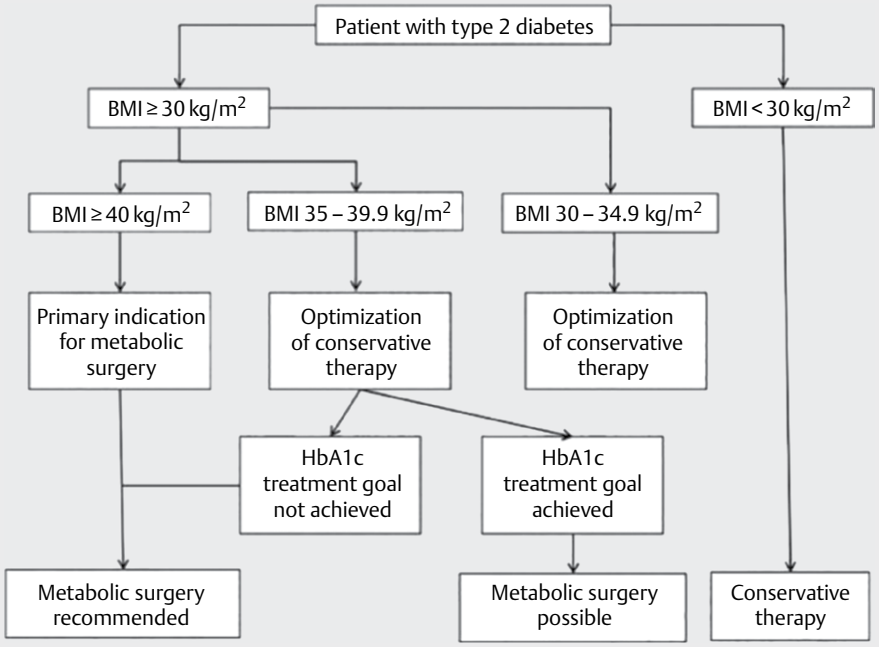
At the 2nd "Diabetes Surgery Summit Consensus Conference", experts from surgery and diabetology proposed a therapy algorithm for people with type 2 diabetes (▶ **Fig. 2**) [27].

According to the current S3 Guideline, the indication for metabolic surgery in people with type 2 diabetes and a BMI ≥ 35 kg/m^2 can be given in Germany if diabetes-specific individual target values cannot be achieved [28]. A BMI ≥ of 40 kg/m^2 and above can be used as a primary indication for metabolic surgery in people with type 2 diabetes, even if the parameters of blood glucose control and the complexity of drug therapy for diabetes are not taken into account.

The indication for a metabolic intervention should be determined jointly by diabetologists and surgeons (especially if the BMI is < 40 kg/m^2). It is also recommended to perform metabolic interventions only at a center with special expertise.

Surgical methods

In diabetic surgery, procedures from obesity surgery are used (e. g. laparoscopic Roux-en-Y gastric bypass or sleeve gastrectomy), although there are no general recommendations for a standard sur-



▶ **Fig. 2** Algorithm for therapy decision for metabolic surgery in people with type 2 diabetes. The decision tree is based on the proposal of the 2nd Diabetes Surgery Summit Consensus between different disciplines [27].

▶ **Table 3** Advantages and disadvantages of various procedures in diabetes surgery. Data according to [27].

Procedure	Advantages	Disadvantages
▪ Sleeve gastrectomy	▪ Good risk-benefit ratio ▪ Also possible in the very high BMI range (e. g. as two-stage concept)	▪ Inferior to RYGB in terms of long-term weight control, reflux control and diabetes remission
▪ Proximal Roux-en-Y gastric bypass (RYGB)	▪ Good control of reflux disease ▪ Superior to the sleeve gastrectomy in terms of type 2 diabetes remission	▪ Increased morbidity compared to the sleeve gastrectomy with the same mortality ▪ Risk of dumping syndrome, ulcers and internal hernias ▪ Risk of malabsorption
▪ Mini gastric bypass (MGB)	▪ Lower perioperative morbidity than RYGB, since only one anastomosis	▪ Increased risk of malabsorption with long biliopancreatic diversions ▪ Risk of dumping syndrome and internal hernias ▪ Potential bile reflux in the stomach pouch

gical procedure. When making individual therapy decisions, the advantages and disadvantages of surgical therapy procedures must be considered in order to achieve the therapeutic goals and avoid complications (▶ **Table 3**). The choice of procedure is individualized according to S3 Guidelines and takes into account the patient's initial weight, concomitant diseases, the patient's wishes, the technical feasibility of the procedure and others [27].

Side effects and risks of diabetes surgery

The well-established therapeutic benefit of metabolic surgery must be weighed against the risks of this therapy when making individual therapy decisions. It should be borne in mind that, in contrast to conservative obesity management, there are very effective and safe drug therapies for the treatment of type 2 diabetes, although these options are not always consistently exhausted. The main side effects of antidiabetics include gastrointestinal complaints (e. g. metformin, GLP-1 receptor agonists), weight gain and an increased risk of hypoglycemia (sulfonylureas, insulin). However, these adverse effects of pharmacotherapy are very rarely life-threatening, while the perioperative mortality of metabolic surgery is about 0.1 – 0.3 % [28, 29]. In addition to acute surgery complications (e. g. pulmonary embolism, fistulas of the staple suture, bleeding, anastomosis insufficiency), metabolic surgery can also increase the risk of micronutrient deficiency, skin wrinkles, weight gain, addiction, suicidal tendencies and suicides in the long term [28, 29]. International consortia such as the Longitudinal Assessment of Bariatric Surgery (LABS) [29] or others with case numbers of more than 15 000 surgically-treated obese people with type 2 diabetes have found a 30-day mortality rate of 0.1 – 0.3 % and severe complications in 2.3 – 4.3 % associated with the procedures [29, 30]. The main risk factors for the occurrence of serious adverse events are a history of leg vein thrombosis and pulmonary embolism, obstructive sleep apnea syndrome and

extremely high body weight [29]. The decisive measure to reduce the risk of long-term adverse effects of metabolic surgery is structured, long-term follow-ups of patients.

Scope of aftercare

Bariatric operations require lifelong aftercare. According to the S3 Guideline, post-operative care for surgery for obesity and metabolic diseases includes [28]:

- Control of the weight development
- Adjustment of medication for concomitant diseases
- Assessment of eating habits and appropriate advice
- Encouragement of sporting activity
- Check for implementation of a supplement for the prophylaxis of
- Deficiency symptoms due to malnutrition or malabsorption
- Laboratory controls
- Screening for mental illnesses
- Recognizing complications and initiating appropriate interventions or Indication of necessary/recommended further operations
- Encouragement to participate in self-help groups
- Information on avoiding pregnancy in premenopausal women in the first 2 years

Antidiabetic medication

Diabetic metabolic control is significantly improved upon completion of the operation. It is therefore important to ensure that the antidiabetic medication is adjusted. Medications with a risk of hypoglycemia should be paused (sulfonylureas) or significantly reduced (insulin).

Insulin

The insulin requirement decreases with increasing insulin sensitivity. In practice, reducing the insulin doses by about 20 – 50 % (basal insulin, carbohydrate unit factor) has been proven. Close blood glucose monitoring is necessary. The insulin doses should be titrated so that the fasting blood glucose value is 80 – 110 mg/dL. If the basal insulin dose in patients with type 2 diabetes falls below 0.1 – 0.2 U/kg body weight, this therapy can be discontinued. Should the use of prandial insulin in type 2 diabetes patients also be necessary postoperatively, the altered kinetics of glucose absorption argues for the use of short-acting insulin analogues. It is imperative to continue insulin therapy in patients with type 1 diabetes.

15 – 20 % of insulin-treated patients with type 2 or type 1 diabetes develop diabetic ketoacidosis within the first 48 h to 2 months postoperatively. In most cases, this is caused by inadequate insulin administration. Continued basal insulin administration is therefore particularly important in type 1 diabetes.

Metformin and SGLT2 inhibitors

In the first 6 months after bariatric surgery there is a significant increase in ketogenesis [30]. The risk of lactate acidosis or ketoacidosis is thus increased. To date, there are no studies on the frequency of lactate acidosis with metformin or euglycemic ketoacidosis with SGLT2 inhibitors after bariatric surgery. Nevertheless, according to the current information on both drugs, a pause in the first 6 – 12 weeks is recommended [31].

Since SGLT2 inhibitors lead to osmotic diuresis, the risk of dehydration is increased postoperatively.

GLP-1 receptor agonists and DPP-4 inhibitors

For both drug classes, structured studies in post-bariatric patients are lacking. However, small studies indicate that the efficacy of GLP-1 receptor agonists is not significantly reduced despite elevated endogenous GLP-1 levels. The use of DPP4-inhibitors is especially useful early postoperatively due to the low side effect spectrum.

Summary

Weight reduction strategies are part of the basic therapy for people with obesity or type 2 diabetes. People with type 2 diabetes should be motivated to eat a healthy and balanced diet and increase physical activity. Targeted weight reduction is also an escalation step in therapy for patients with type 2 diabetes. When choosing drug therapy for type 2 diabetes, preference should be given to active ingredients (metformin, GLP-1 receptor agonists, SGLT2 inhibitors) that enable weight reduction. Since weight reduction for people with obesity or type 2 diabetes is difficult to achieve through conservative therapeutic strategies, metabolic surgery has developed into the therapy alternative for patients with type 2 diabetes and a BMI > 35 kg/m² in recent years. Compared to conservative type 2 diabetes therapy, metabolic surgery is significantly more effective in terms of weight reduction, long-term weight stability and blood glucose reduction, but is also associated with higher acute and long-term risks.

Conflict of interest

Jens Aberle states fees for lecturing and consulting activities for Astra Zeneca, Boehringer Ingelheim, Lilly Germany and Novo Nordisk. Anne Lautenbach states the following conflicts of interest: Travel support: Eli Lilly and Novo Nordisk; Research support: Astra Zeneca; Advisory Board activity: Novo Nordisk. Matthias Blüher received honorariums for lecturing and consulting work from Amgen, Astra Zeneca, Boehringer-Ingelheim, Daiichi-Sankyo, Lilly, Novartis, Novo Nordisk and Sanofi. Lars Selig, Svenja Meyhöfer and Sebastian M. Schmid have no conflicts of interest.

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