Can Bariatric Surgery be Considered Standard Therapy to Treat Type 2 Diabetes?

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Abstract

With the rapid increase in obesity there has been a pronounced increase in obesity-related metabolic disorders including type 2 diabetes, cardiovascular disease, dyslipidaemia and hypertension. Bariatric surgery is a highly effective treatment for achieving long-term weight loss and is increasingly recognised to have benefits in diabetes treatment and cause improvement in other metabolic factors. Recent small randomised trials reported better glycaemic control after surgical intervention compared to pharmacological therapy. Physiological studies suggest a surgery-specific, weight-independent effect on glucose homeostasis. Long-term efficacy is to be proven. Consensus on definition of diabetes and diabetes remission must be achieved. Larger multicentre, randomised trials need to be done to clarify the place of metabolic surgery in diabetes treatment algorithms.

Keywords

Bariatric surgery, type 2 diabetes, body mass index, remission of diabetes, gastric bypass

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Obesity has become an increasingly important health problem. According to estimations of the World Health Organization, the worldwide prevalence of obesity has more than doubled between 1980 and 2008. In 2008, 10 % of men and 14 % of women in the world were obese (body mass index [BMI] ≥30 kg/m^2), compared with 5 % of men and 8 % of women in 1980.[1]

With the rapid increase in obesity there has been a pronounced increase in obesity-related metabolic disorders including type 2 diabetes, cardiovascular disease, dyslipidaemia and hypertension.[2]

Type 2 diabetes is a multi-factorial disorder and obesity is considered the most important risk factor. The prevalence of obesity among adults with diagnosed diabetes is over 50 %, and the prevalence of overweight is over 80 %.[3] It has been estimated that the risk of developing type 2 diabetes is increased 93-fold in women and 42-fold in men who are severely obese (BMI ≥ 35 kg/m^2) rather than of healthy weight.[4,5]

Given this information, weight loss is one of the most important treatment strategies to obtain good glycaemic control (glycated haemoglobin [HbA_{1c}] <7 %). Intentional weight loss of at least 5 % to 10 % of body weight has repeatedly been shown to improve glycaemic control and cardiovascular risk profiles in obese subjects with type 2 diabetes.[6–8]

Type 2 diabetes is usually a progressive disease characterised by both a loss of insulin secretory capacity of the pancreatic ß-cells over time and insulin resistance, resulting in progressive hyperglycaemia and subsequent micro- and macrovascular complications. This natural course requires a continuous monitoring and intensification of the therapy with adding new pharmacological agents. Unfortunately, a number of hypoglycaemic agents, including insulin, sulphonylurea and thiazolidinediones exacerbate weight gain.

In the long term, all conservative medical and lifestyle treatments of obesity often fail to achieve sufficient blood glucose control in morbidly obese patients. The mean maintenance weight loss after conservative interventions for obesity is <25 % after 2 years.[9]

Bariatric surgery is a highly effective treatment for achieving long-term weight loss in adults with obesity.[10] Moreover, bariatric surgery is increasingly recognised to have benefits in diabetes treatment and can also be associated with improvements or normalisation in blood pressure, lipid profile, quality of life and obstructive sleep apnoea syndrome.[11]

Types of Bariatric Surgery and Indications

The disappointing results of medical treatments, along with the growing incidence of obesity and its related life-threatening complications, has led to the widespread use of bariatric surgery.

In the past, different possible surgical procedures were developed to achieve weight loss. The most commonly used bariatric procedure worldwide in 2011 was Roux-en-Y gastric bypass (RYGB) (46.6 %). Sleeve gastrectomy accounted for 4.5 % of the bariatric procedures in 2008, while the number of this type of bariatric procedure increased to 27.8 % in 2011. Adjustable gastric banding (AGB) was performed in 17.8 %,

which means a decline of 24.5 % compared with 2008. Nowadays, the biliopancreatic diversion/duodenal switch is less used (2.2% in 2011).[12]

The outcome on weight loss and other metabolic parameters and the short- and long-term risks depends on the type of surgical procedure. A meta-analysis of Buchwald et al. in 2004 including 22,094 patients reported a mean percentage of excess weight loss of 61.2 % for all types of bariatric surgical procedures. It was less for AGB (47.5 %) compared with gastric bypass (61.6 %), gastroplasty (68.2 %) and biliopancreatic diversion or duodenal switch (70.1 %).[13]

The 2009 Cochrane review analysed the results of 26 studies including patients with and without diabetes. They concluded that bariatric surgery resulted in greater weight loss than conventional treatment in individuals with moderate obesity (BMI >30 kg/m²) as well as in patients with severe obesity. Reductions in co-morbidities, such as diabetes and hypertension, as well as improvements in health-related quality of life were noted.[11] The large prospective Swedish Obesity Study (SOS) reported that, after 10 years, weight loss of 25 % of body weight had been successfully maintained in surgical objects, compared with 1.5 % in non-surgical patients.[14]

According to the 1991 National Institutes of Health Consensus Conference Guidelines, patients are considered as surgical candidates only if their BMI ≥ 40 kg/m² or if their BMI is ≥ 35 and they suffer from obesity-related co-morbidities, such as hypertension, cardiovascular disease, sleep apnoea and type 2 diabetes.[15] Nowadays, there is a growing appreciation for the role of bariatric surgery as a tool in diabetic management. There are indications that patients with poorly controlled type 2 diabetes and a BMI lower than 35 kg/m² may also benefit from bariatric surgery. However, further evidence is needed to support these recommendations.

Effects of Bariatric Surgery on Diabetes

Several observational data have shown a markedly improved and sustained glycaemic control in type 2 diabetes patients with obesity following bariatric surgery. Comparison between the different studies is difficult because of the use of different types of surgical procedures, different criteria for diabetes remission and different reporting of duration and severity of type 2 diabetes.

The meta-analysis by Buchwald et al. in 2009 reported a complete remission of type 2 diabetes in 76.8 % of patients treated with bariatric surgery and resolution or improvement in 86.0 %. At 2-year follow-up, 62 % remained in remission.[16] This review was significantly limited by the fact that remission was largely based on clinical reporting and not on HbA_{1c} or other biochemical outcomes. In addition, follow-up of most cohorts was poorly described. The more rigorous Cochrane review reported a percentage remission of diabetes ranging from 57 % for a banding procedure to 95 % for the biliopancreatic diversion procedure.[11]

However, it is important to note that all of these studies used less strict criteria for diabetes remission than those proposed by a consensus statement in 2009.[17]

The panel of experts defined remission of type 2 diabetes as achieving glycaemia below the diabetic range of at least one year's duration in the absence of pharmacological or surgical therapy. Partial remission was defined as sub-diabetic hyperglycaemia (HbA_{1c} < 6.5 %, fasting glucose 100–125 mg/dl or 5.6–6.9 mmol/l), complete remission was defined as a return to normal measures of glucose metabolism (normal HbA_{1c} fasting glucose < 100 mg/dl or 5.6 mmol/l) for the same duration.

According to this new definition, Pournaras et al. reported only a 34.4 % complete remission after a median of 23 (range 12–75) months in 209 patients with type 2 diabetes who underwent bariatric surgery (40.6 % after gastric bypass, 26 % after sleeve gastrectomy and 7 % after AGB). These data indicate that an improved glycaemic control rather than remission could be expected after this type of surgery.[18]

Until recently, no randomised trials were performed to evaluate whether glycaemic control improved more in patients undergoing bariatric surgery compared with intensive medical therapy.

In 2008, Dixon et al. published the first unblinded randomised controlled trial to compare laparoscopic gastric banding (LABG) versus a lifestyle and pharmacotherapy intervention in 60 obese patients (BMI 30–40 kg/m²) with recently diagnosed type 2 diabetes (< 2 years). Remission was defined by a HbA_{1c} < 6.2 % and a fasting glucose level < 125 mg/dl in the absence of antidiabetic medication. At 2-year follow-up, 73 % of the patients in the surgical group achieved remission of type 2 diabetes versus 13 % of the patients in the conventional therapy group. Remission of type 2 diabetes was related to weight loss and lower baseline HbA_{1c} levels.[19]

Recently, two other randomised trials comparing the effect of pharmacological therapy versus surgical interventions on glycaemic control were published. Schauer et al. randomised 150 obese type 2 diabetes patients with an average HbA_{1c} of 9.2 ± 1.5 % to medical therapy alone versus medical therapy plus RYGB or sleeve gastrectomy. The primary endpoint (HbA_{1c} ≤ 6.0 % after one year) was achieved in 42 % of the gastric bypass group and 37 % of the sleeve-gastrectomy group versus 12 % of the medical-therapy group.[20] Very recently, the results of 2-year follow-up of 60 patients of the initial study were published. At 24 months, the proportion of patients with HbA_{1c} ≤ 6.0 % decreased in the sleeve gastrectomy group from 26 % to 11 % but persisted in the RYBG group (from 44 % to 33 %). Despite similar weight loss, the absolute reduction in percent truncal fat was greater in gastric bypass versus sleeve gastrectomy group. In gastric bypass patients, normal glucose tolerance and pancreatic ß-cell function were restored in contrast with sleeve gastrectomy where insulin sensitivity was only partially restored and pancreatic ß-cell function did not improve.[21]

In a second recent randomised trial involving 60 obese patients with a history of at least 5 years of diabetes, Mingrone et al. reported no diabetes remission at 2 years in the medical-therapy group versus 75 % in the gastric-bypass group and 95 % in the biliopancreatic diversion group. Diabetes remission was defined as a fasting glucose < 100 mg/dl and HbA_{1c} < 6.5 % while taking no antidiabetic medications.[22]

All three studies are too small and the duration of follow-up is to short to draw conclusions on long-term efficacy of bariatric surgery on diabetes related morbidity and mortality compared with conventional medical therapy.

Recent results from the SOS, a large prospective non-randomised intervention trial, indicate that bariatric surgery also may be effective in diabetes prevention. There was an incidence rate of developing type 2 diabetes of 6.8 cases per 1,000 person-years in the bariatric surgery

Table 1: Studies Describing Remission and Relapse of Diabetes after Bariatric Surgery

Study	Design	Number of Patients with Type 2 Diabetes	BMI (kg/m²)	Procedure	Definition of Remission	Proportion with Remission	Proportion with Relapse of Type 2 Diabetes	Time at Relapse
Chikunguwo et al.[26]	Retrospective case-control	177	> 35	RYGB	No diet or hypoglycaemic drugs	89 %	43 %	Within 5 years
DiGiorgi et al.[33]	Retrospective case-control	42	> 40	RYGB	Not defined	64 %	24 %	≥ 3 years
Sjöstrom et al.[34]	Prospective case-control	342	> 35	RYGB, AGB, vertical banded gastroplasty	FPG < 7 mmol/l and no hypoglycaemic drugs	72 %	50 %	10 years
Arterburn et al.[35]	Retrospective case-control	4,434	Not reported	RYGB	FPG < 100 mg/dl and/or HbA_{1c} < 6 % and no hypoglycaemic drugs	68 %	35 %	Within 5 years
Kim and Richards[36]	Retrospective case-control	219	> 35	RYGB	HbA_{1c} < 7 % and no hypoglycaemic drugs	71 %	3 %	2 to 5 years

AGB = adjustable gastric banding; BMI = body mass index; FPG = fasting plasma glucose; RYGB = Roux-en-Y gastric bypass.

group compared to 28.4 cases per 1,000 person-years in the control group. The greatest reduction in risk of incident diabetes was seen in those with higher fasting glucose at baseline.[23]

Predictors of Remission of Diabetes

A few studies have attempted to identify predictive factors for the remission of diabetes. Hamza et al. observed that the percentage of excess weight loss and younger age were independent predictors of remission of type 2 diabetes in 487 patients who underwent a gastric bypass procedure or a LAGB.[24]

Kadera et al. also reported that a greater excess weight loss was associated with remission of type 2 diabetes in 71 patients who underwent a RYGB.[25] However, this finding is not helpful in a preoperative setting with regard to patient selection.

Another factor associated with a higher rate of diabetes remission is less severe disease. Several studies have reported that persons who were treated preoperatively with oral antidiabetic agents alone had higher remission rates than patients treated with insulin.[25–27] In accordance with this finding, shorter duration of diabetes has also been associated with higher remission chances.[24,28,29]

In 2011, Hayes et al. published six mathematical models to identify which patients would experience remission of their type 2 diabetes after one-year follow-up. They used 13 preoperative parameters and included 130 patients. The major predictive variables included preoperative BMI, HbA_{1c}, fasting plasma glucose, the presence of hypertension and diabetic status (unrecognised, diet controlled, tablet controlled or insulin controlled).[30]

Other studies[25] have found no significant association between HbA_{1c} and diabetes remission. A recent small study including 126 patients reported that a preoperative fasting plasma C-peptide < 1.0 nmol/l in severely obese type 2 diabetes patients (indicating ß-cell failure) is associated with markedly reduced chance of complete remission of type 2 diabetes after RYGB. They propose to measure C-peptide levels in all diabetic patients up for bariatric surgery to improve the prediction of outcome.[31] Recently, another small study reported that a preoperative inflammatory profile with high levels of pro-inflammatory adipocytokines and low values of adiponectin are associated with smaller improvements in biochemical-metabolic factors of glucose homeostasis and lipid profile in morbidly obese women at 12 months after surgery.[32]

Duration of Remission

Durability of control and remission of diabetes remains uncertain. Mid- to long-term follow-up studies report relapse rates of type 2 diabetes up to 50 % (see *Table 1*).[26,33–36] Chikunguwo et al. reported a recurrence rate of 43.1 % at five-year follow-up in 157 patients with type 2 diabetes who had undergone a RYGB. Durable remission correlated most closely with an early disease stage at gastric bypass. Weight regain was only a weak predictor of type 2 diabetes recurrence.[26]

A smaller study by DiGiorgi et al. reported a recurrence or worsening beyond three years after RYGB in 24 % of patients with initial resolution or improvement of glycaemic control.[33]

In the SOS study, 72 % of patients had an early remission of type 2 diabetes two years after bariatric surgery. However, after 10 years this was reduced to 36 % of patients.[34]

Arterburn et al. reported an initial complete diabetes remission rate of 68.2 % after RYGB in 4,434 type 2 diabetes patients. Among these, 35.1 % redeveloped diabetes within 5 years.[35] Significant predictors of complete remission and relapse were poor preoperative glycaemic control, insulin use and longer diabetes duration.

Nevertheless, it is possible that a period of remission of diabetes has a positive effect on long-term morbidity and mortality. Large randomised prospective trials with long-term follow-up are necessary to clarify these questions.

Possible Mechanisms Responsible for Improvement in Glycaemic Control

Depending on the type of surgical procedure, improvement of glucose control can be observed within days after bariatric surgery, before there is any substantial weight loss. The physiological mechanisms by which glucose homeostasis is influenced are not well understood yet, but it seems that there is a surgery-specific, weight-independent effect.

Restrictive procedures such as gastric banding seem to have an antidiabetic effect purely mediated by caloric restriction, followed by

gradual weight loss. Acute changes in the secretion of glucoregulatory gut hormones are not reported so far.[37]

Different potential mechanisms by which RYGB directly improves glucose homeostasis have been suggested. The foregut hypothesis proposes that the exclusion of the proximal bowel prevents secretion of an unidentified signal that promotes insulin resistance and type 2 diabetes.[38]

By contrast, the hindgut hypothesis suggests that the rapid stimulation of the distal ileum by nutrients (as a result of the shortened length of the small bowel) improves glycaemia through the enhanced secretion of gut peptides such as glucagon-like peptide-1 (GLP-1), which augments glucose-dependent insulin secretion.[39,40]

Vertical sleeve gastrectomy, a procedure that does not result in shunting of the duodenum, does not favour the duodenal exclusion hypothesis. This procedure results in an increase in gut hormones similar to that seen in RYGB.[41]

Improved hepatic insulin sensitivity is noted immediately after RYGB due to energy restriction. Peripheral insulin sensitivity is improved later in response to the postoperative weight loss.[42,43] Insulin secretion in response to an oral stimulus is significantly altered after RYGB, the postprandial rise in insulin concentration is earlier and reaches a higher peak level.[37,44,45] Insulin secretion after RYGB in response to an intravenous stimulus also changes, and a gradual increase in first phase insulin secretion is noted.[37,46,47]

Other factors possibly contributing to improved glucose homeostasis have been described. A reduced secretion of ghrelin, a hormone that stimulates appetite and inhibits insulin is reported after RYGB.[48,49] Other mechanisms implicated in glycaemic improvement could be changes in the rate of eating, gastric emptying, intestinal transit time, nutrient absorption and sensing. Alterations in the bile acid metabolism have also been described.[50]

Bariatric Surgery for Patients with Type 2 Diabetes and a Body Mass Index < 35 kg/m²

Following the beneficial results on glycaemic control in type 2 diabetes patients with BMI ≥ 35 kg/m², the question has to be asked whether bariatric surgery should be considered as a primary treatment for type 2 diabetes patients with a BMI < 35 kg/m². Several recent publications have reported on the glycaemic benefits of bariatric surgery in patients with type 2 diabetes and a BMI < 35 kg/m².

In 2010, a literature review analysed the results of 16 studies including 343 patients with a BMI less than 35 kg/m² undergoing bariatric surgery. Follow-up ranged from 6 to 216 months. Patients lost a meaningful, but not excessive, amount of their preoperative weight, resulting in a BMI within the upper end of the normal weight category. At 6 months, 85.3 % of patients were off antidiabetic medication, with an $HbA_{1c} \leq 6$ % and slightly above normal fasting plasma glucose. Relatively low complications were noted with a very low operative mortality (0.29 %). There was a trend towards a greater reduction in weight and diabetes remission in the lowest subset of patients studied (BMI 25.0–29.9) relative to those with BMI 30–35. Malabsorptive/restrictive procedures were also associated with a greater reduction in BMI and diabetes remission.[51]

A more recent review, published in 2012, reported on the results of 18 studies including 477 type 2 diabetes patients with mean BMI < 35 kg/m² who underwent metabolic surgery. The follow-up period ranged from 6 months to 18 years. Prior to the surgical procedure, 30 % of the patients had been treated with insulin. Mean BMI decreased from 30.4 to 24.8 kg/m².

Remission of type 2 diabetes (fasting plasma glucose < 126 mg/dl and $HbA_{1c} < 6.5$ % without the use of diabetes medications) was achieved in 64.7 %. In patients with a short history (≤ 8 years) of type 2 diabetes, the remission rate was 66.0 % compared with 52.9 % in patients with a long history (> 8 years). Postoperative complication rate was 10.3 % with a mortality rate of 0 %.[52]

Recently, Cohen et al. published a large single-centre study with a long follow-up examining RYGB for 66 type 2 diabetes patients with a BMI between 30 and 35 kg/m². Participants had poorly controlled (HbA_{1c} 9.7 ± 1.5 %) long-standing diabetes (12.5 ± 7.4 years) despite the usage of antidiabetic medication in everyone. During 6 years of follow-up, durable remission ($HbA_{1c} < 6.5$ % without diabetes medication) was reported in 88 % of patients, with glycaemic improvement in an additional 11 %. The majority of patients were off diabetes medication. Mean HbA_{1c} lowered to 5.9 ± 0.1 %. There was no correlation between weight loss and several measures of improved glucose homeostasis, which is consistent with weight-independent antidiabetic mechanisms of RYGB. There was also an improvement in hypertension and dyslipidaemia in, respectively, 58 % and 64 % of patients. The rate of minor surgical complications was 15 %, and there were no major complications or mortality.[53] A limitation of this study is that the definition of remission does not exactly follow that recommended by a consensus statement in 2009 ($HbA_{1c} < 6$ %).[17]

Until now, no practical guidelines can be recommended for surgical approaches to diabetes in patients with a BMI < 35 kg/m².[54] The heterogeneity of studies is too large to draw good conclusions. Long-term studies and large randomised controlled trials need to be performed. There needs to be a clear consensus on the definition of type 2 diabetes and the definition of remission. It also needs to be made clear whether the extent of sustained remission of type 2 diabetes is influenced by the extent of sustained weight loss, duration of diabetes, presurgery antidiabetic medications and the type of bariatric surgery.

Effects of Bariatric Surgery on Other Parameters

Bariatric surgery has also proven beneficial effects on other metabolic parameters. The meta-analysis of Buchwald et al. in 2004 reported a resolution of hypertension in 61.7 % of patients and an improvement of hyperlipidemia in 70 % or more patients. Obstructive sleep apnoea was resolved in 83.6 % of patients.[13]

The SOS study has reported that after 10 years a statistically significant greater proportion of people who had received surgery had recovered from hypertension, hypertriglyceridaemia, low high-density lipoprotein cholesterol and hyperuricaemia.[55,56] They reported also a reduced incidence of cancer and overall mortality in obese patients who underwent bariatric surgery as compared with conventional treatment.[14,57] Furthermore, they noted a reduced number of cardiovascular deaths. The number of total first time cardiovascular events (myocardial infarction or stroke) was lower in the surgery group than in the control group.[58]

Johnson et al. compared 2,580 adult obese patients with type 2 diabetes who underwent bariatric surgery with 2,580 controls in a retrospective

study. They found a 65 % reduction in macro- and microvascular events in moderately and severely obese patients with type 2 diabetes free of advanced cardiovascular and microvascular disease at baseline.[59]

Risks and Complications of Bariatric Surgery

The meta-analysis of Buchwald et al. reported a total mortality at < 30 days of 0.28 %, total mortality between 30 days and 2 years was 0.35 %[60]. Operative mortality is determined by several factors. This can be patient-related, surgeon-related or facility-related.[61,62] Preoperative variables that were found to be significant predictors of mortality in patients undergoing RYGB were a BMI > 50 kg/m², male sex, hypertension, known risk factors for pulmonary embolism and age > 45 years.[63]

Early postoperative morbidity is clearly related to the complexity of the surgical procedure. Over 57,000 procedures were reviewed by the US Bariatric Longitudinal Database. The one or more complication at 1-year rates were 4.6 %, 10.8 %, 14.9 % and 25.7 % following LAGB, sleeve gastrectomy, RYGB and biliopancreatic diversion, respectively.[64]

Bariatric surgery is most commonly complicated by anastomotic and staple-link leaks (3.1 %), wound infections (2.3 %), pulmonary events (2.2 %) and haemorrhage (1.7 %).[54] Late complications are mostly a consequence of disordered gastrointestinal tract function rather than failure of wound healing.

Nutritional deficiencies can result from poor oral intake due to anorexia, inadequate supplementation, prolonged vomiting or stricture formation or they can result from a failure of absorption.[65]

Consequently, postoperative patients need lifelong monitoring for micronutrient deficiencies as proposed by the clinical guidelines developed by the American Association of Clinical Endocrinologists, The Obesity Society and the American Society for Metabolic and Bariatric Surgery.[66]

Deficiencies in fat-soluble vitamins A, D and K and deficiencies in vitamins B12, B1, C and folate are most commonly observed after RYGB and other malabsorptive procedures,[67,68] which could lead to a variety of neurological complications.[69] Iron deficiency is reported in up to 50 % of premenopausal women who underwent a RYGB.[67] Calcium and vitamin D deficiency can lead to hyperparathyroidism and reduced bone density.[70,71] Protein malnutrition and deficiencies in selenium, zinc and copper are also observed.[68] Another possible long-term complication of RYGB is reactive hypoglycaemia. In a review of the Swedish Bariatric Surgery registry, incidence rates of hospitalisation for post-gastric bypass hypoglycaemia were less than 1 %.[72] Reactive hypoglycaemia is usually mild and can be treated with a low-carbohydrate diet. In a small sample of 12 patients with hyperinsulinaemic hypoglycaemia after RYGB, Kellogs et al. reported substantial improvement of symptoms in six patients and moderate improvement in 10 patients after treatment with a low-carbohydrate diet.[73] In refractory cases, acarbose, octreotide, diazoxide and calcium channel blocker are empirically used,[74] but data on the effectiveness of these treatments in patients with hypoglycaemia following gastric bypass are scarce. Other possible complications are gastroesophageal reflux,[75,76] bowel disturbances and cholelithiasis after rapid weight loss.[75]

Conclusion

Bariatric surgery has proven to be more effective in achieving sustained weight loss compared with lifestyle and medical interventions. In addition, there is a beneficial effect on co-morbidities as diabetes, hypertension, dyslipidaemia and sleep apnoea. Mortality and major morbidity rates are acceptable. In patients without diabetes, there is a clear consensus on the eligibility criteria for bariatric surgery.[15]

However, much needs to be carried out to clarify the place of metabolic surgery in diabetes treatment algorithms. There needs to be a clear consensus on the definition of diabetes remission. Studies are necessary to establish preoperative predictors of diabetes remission, to make it possible to select the patients who will benefit from bariatric surgery. Whether bariatric surgery should be a rescue treatment for those patients who fail to achieve metabolic targets with standard therapy, or whether it should be offered to patients in an earlier stadium of the disease to prevent long-term diabetes morbidity and mortality should be examined. Larger, multicentre randomised trials with long-lasting follow-ups are needed to answer the question of whether patients with a BMI < 35 kg/m² are eligible for metabolic surgery.

It also needs to be clarified which type of procedure should be chosen, taking into account results on weight loss, rates of diabetes remission and duration of diabetes remission, improvement of other metabolic factors and effects on cardiovascular morbidity and mortality in the long term.

The impact of long-term risks as nutrient deficiencies and postprandrial hyperinsulinaemic hypoglycaemia on morbidity and quality of life of patients must to be investigated. The cost-effectiveness of bariatric surgery compared to standard medical treatment must also be evaluated and, when solid evidence is available, a consensus statement that integrates bariatric surgery into diabetes treatment algorithms could be made. ■

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