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REVIEW

Surgical treatment of type 2 diabetes: the surgeon perspective

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Abstract Type 2 diabetes mellitus (T2DM) is a major health priority globally, having achieved pandemic status in the twenty-first century. Several gastrointestinal procedures that were primarily designed to treat morbid obesity result in dramatic remission of diabetes. Studies in experimental rodent models and humans have shown that the glycemic benefits of surgery are at least in part weight-independent and extend to non-morbidly obese subjects with T2DM. Bariatric procedures differ in their ability to ameliorate type 2 diabetes, with intestinal bypass procedures being more effective than purely restrictive procedures. Several studies have demonstrated that the benefits of bariatric surgery extend beyond amelioration of hyperglycemia and include improvement in other cardiovascular risk factors such as dyslipidemia and hypertension. The safety and cost-effectiveness of bariatric surgery are also well established by several studies. In this paper, the authors present the surgeon perspective on the management of type 2 diabetes focusing on the efficacy, safety and cost-effectiveness of metabolic surgery. The available evidence warrants the inclusion of metabolic surgery in the treatment algorithm of type 2 diabetes.

Keywords Type 2 diabetes mellitus (T2DM) · Metabolic surgery · Efficacy · Safety · Cost-effectiveness

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Introduction

Type 2 diabetes mellitus (T2DM) is a major health priority globally, having achieved pandemic status in the twenty-first century. Insulin resistance in muscle and liver and β-cell failure represent the core pathophysiologic defects in type 2 diabetes [1]. It is recognized that aggressive glucose lowering with medical therapy prevents microvascular complications although the impact on macrovascular end-points is modest [2, 3]. The natural history of type 2 DM suggests that insulin secretory capacity declines inexorably over time despite a combination of several pharmacological agents. The resulting worsening of glycemic control and other metabolic factors leads to debilitating consequences: retinopathy, neuropathy, nephropathy, end-stage renal disease and coronary artery disease.

Several gastrointestinal procedures that were primarily designed to treat morbid obesity result in dramatic remission of diabetes [4]. Studies in experimental rodent models [5, 6] and humans [7–9] have shown that the glycemic benefits of surgery are at least in part weight-independent and extend to non-morbidly obese subjects with T2DM. This has opened a new chapter in the pathophysiology and management of T2DM. The rapid accrual of data from both clinical and basic research in the last decade has expanded our understanding of the role of gut factors in the pathophysiology of T2DM and also provided a viable alternative for patients failing medical therapy.

Overview of bariatric procedures to treat type 2 DM

Conventional "Bariatric" procedures: A number of bariatric surgical procedures are currently in use. The simplest procedure is adjustable gastric banding (AGB, Fig. 1), where

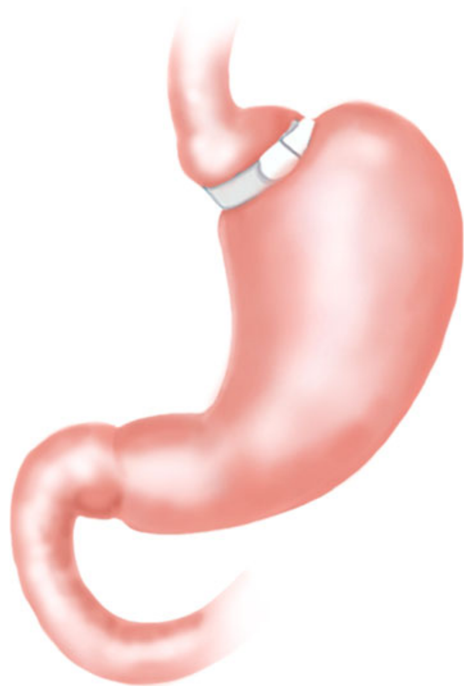

Fig. 1 Adjustable gastric banding

the size of the stomach is reduced with the laparoscopic placement of a band around it, restricting it to produce early satiety during meals. The size of the stomach can be decreased by injecting saline into the band. Sleeve gastrectomy (Fig. 2) consists in the removal of approximately 75% of the stomach along a line roughly parallel to the greater curvature, resulting in a thin, crescent-shaped stomach lacking the majority of its fundus. Biliopancreatic diversion (Fig. 3) is a malabsorptive procedure involving a gastric resection (usually leaving behind a 200–500-ml-sized stomach) in addition to a long intestinal bypass. Bile and nutrients mix in a short 50 cm "common limb" proximal to the ileocaecal valve. The gastric resection can be horizontal as in the Scopinaro procedure [10] or vertical—'sleeve gastrectomy' in its variant named BPD—Duodenal Switch. Roux-en-Y gastric bypass (RYGB, Fig. 4) is the most commonly performed bariatric procedure. A surgical stapler is used to create a small gastric pouch usually less than 30 cc in size, and a gastrojejunostomy is created between the small pouch and the jejunum; ingested food bypasses ~95% of the stomach, the entire duodenum and a portion of the jejunum. Bile and nutrients mix in the distal jejunum and can be absorbed through the remaining portion of the small bowel.

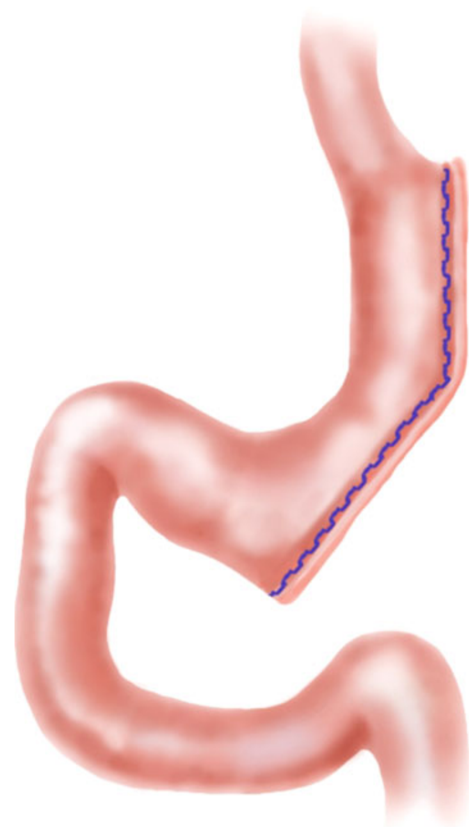

Fig. 2 Sleeve gastrectomy

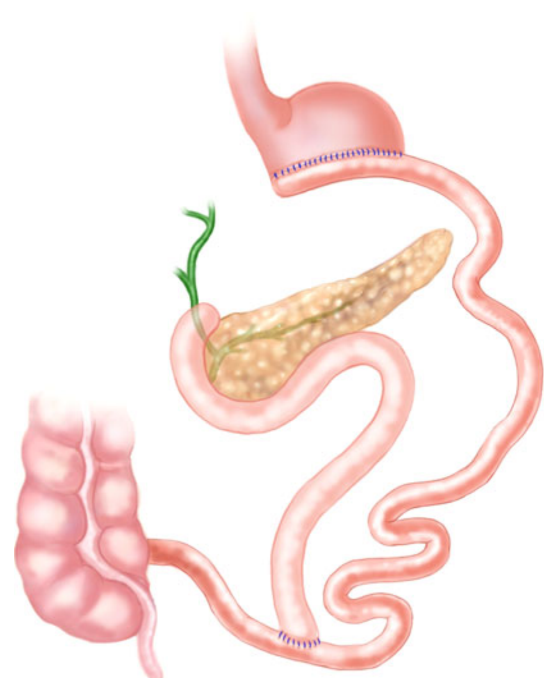

Fig. 3 Biliopancreatic diversion

Experimental procedures

Duodenal jejunal bypass (Fig. 5): It was originally described by Rubino [11] as an experimental procedure to investigate

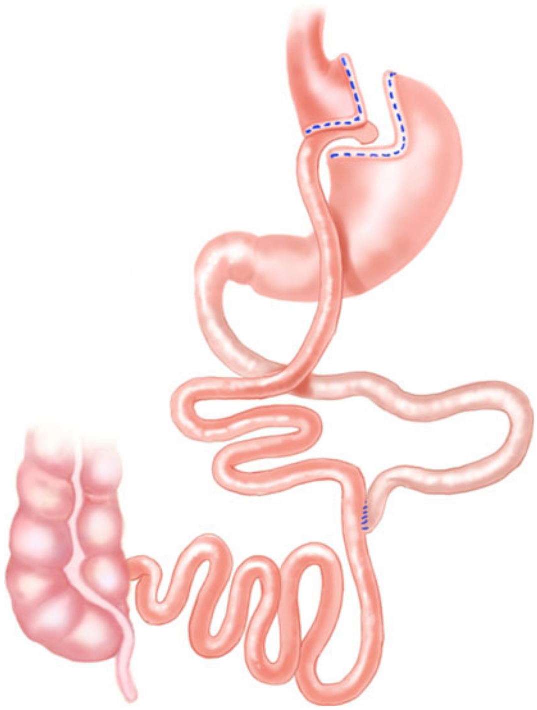

Fig. 4 Roux-en-Y gastric bypass

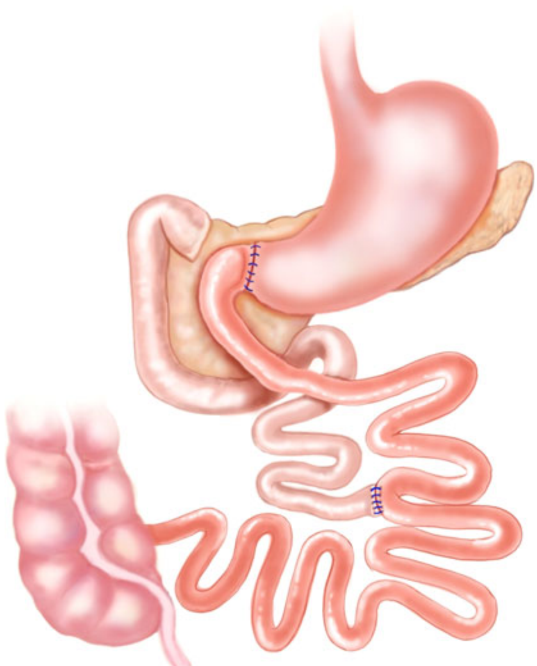

Fig. 5 Duodenal jejunal bypass

mechanisms of action of gastric bypass surgery. The operation consists of a stomach-sparing bypass of a short portion of proximal intestine, equivalent to the amount of intestine bypassed in a standard gastric bypass (RYGB). A variant of this procedure includes the association of proximal intestinal bypass with sleeve resection of the stomach (DJB-SG) to reduce potential for marginal ulcerations and increase clinical efficacy. This procedure, alone or in combination with sleeve gastrectomy, has been reported in humans first by Cohen et al. [12] and later by other teams in India, Japan, Korea and South America [13, 14].

Ileal Interposition (Fig. 6): The concept of ileal interposition (IT) was first described by Koopmans and Sclafani in rodent experiments as a weight loss procedure [15]. A small segment of ileum with its vascular and nervous supplies intact is surgically interposed into the proximal small intestine, accelerating its exposure to ingested nutrients. IT can be performed alone or in association with sleeve gastrectomy (IT-SG) or duodenal exclusion (IT-DSG). Human series of IT-SG and IT-DSG have been reported primarily by Dr. De Paula [16] from Brazil.

Efficacy of bariatric surgery in patients with type 2 DM and BMI >35 kg/m^2

Several studies have demonstrated dramatic improvements in T2DM among patients with morbid obesity following a variety of gastrointestinal surgical procedures. In a meta-analysis involving 136 studies and 22,094 patients with T2DM, Buchwald et al. [4] reported an overall 77% remission of T2DM after bariatric surgery, defined as persistent normoglycemia without diabetes medications. The mean procedure-specific remission of T2DM was 48% for laparoscopic adjustable gastric banding (LAGB), 68% for vertical banded gastroplasty, 84% for Roux-en-Y gastric bypass (RYGB) and 98% for biliopancreatic diversion (BPD). It must be noted, however, that most of these studies were retrospective with follow-up duration of 1–3 years only. Two large case-series studies by Pories et al. [17] (330 patients) and Schauer et al. [18] (191 patients) focused principally on diabetes outcomes after RYGB. Mean fasting blood glucose (FBG) decreased from clearly diabetic values to near normal levels (117 and 98 mg/dl in the two studies, respectively), and HbA1c fell to normal levels (6.6 and 5.6%) without diabetes medication in 89 and 82% of patients, respectively. The multicenter Swedish Obese Subjects (SOS) study [19] compared bariatric surgery (LAGB $n = 156$, VBG $n = 451$, RYGB $n = 34$) versus a control group of well-matched obese patients managed conservatively. At 2 years, 72% of diabetic subjects in the surgical group achieved remission of type 2 DM. At 10 years, the relative risk of incident T2DM was three times lower, and the rates of recovery from T2DM were three times greater, for patients who underwent surgery than for individuals in the control group. Although long-term data (>5 years) are not yet available for Laparoscopic sleeve gastrectomy (LSG), it has garnered considerable interest as a

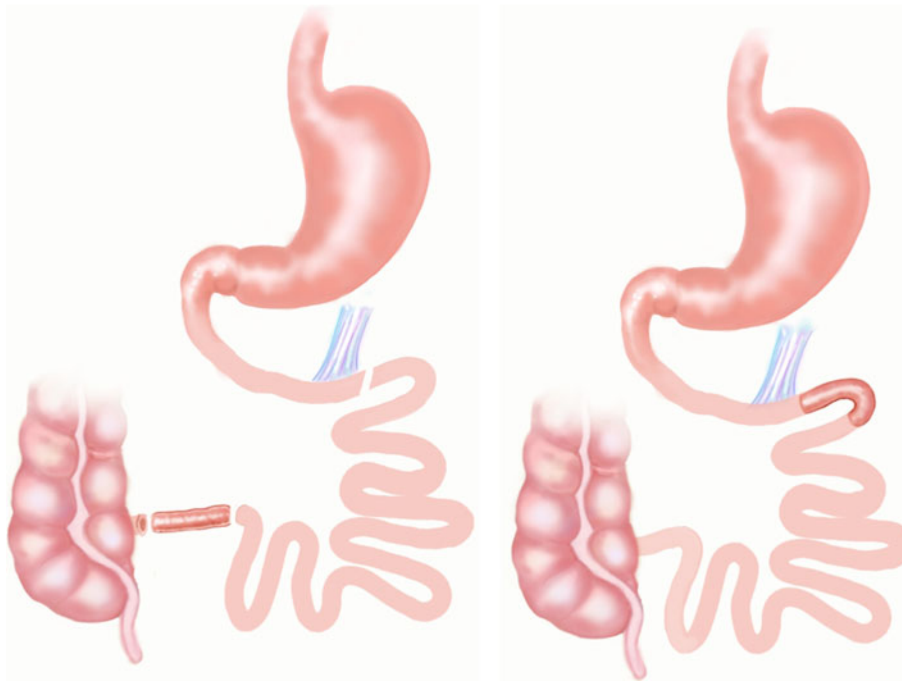

Fig. 6 Ileal interposition

low-morbidity bariatric surgical procedure that leads to effective weight loss and control of comorbid disease. A systematic review by Gill et al. [20] of 27 studies involving 673 patients (mean follow-up of 13.1 months) has reported a T2DM resolution rate of 66.2% in obese subjects and improved glycemic control in 26.9%. The mean decrease in blood glucose and hemoglobin A1c after sleeve gastrectomy was −88.2 mg/dl and −1.7%, respectively.

Efficacy of bariatric surgery in patients with type 2 DM and BMI <35 kg/m^2

While bariatric surgery is widely recognized for its positive effects on comorbidities in morbidly obese patients, there is also now mounting evidence for similar benefits of GI surgery on diabetes in patients with BMI <35 kg/m^2. Historically, sporadic but consistent observations of T2DM remission were reported as unexpected outcomes of gastric resections performed for other diseases in non-obese patients who had undergone GI operations with anatomical similarities to bariatric procedures, e.g., gastric resection with proximal intestinal reconstructions, performed for gastric ulcers or cancers [21, 22].

As concerns LAGB, two randomized trials assessed the effect of this procedure on diabetes and metabolic syndrome. Dixon et al. [23] assigned 60 patients with BMI 30–40 kg/m^2 to receive conventional medical/behavioral therapy or LAGB plus conventional therapy. Two years after surgery, 73% of post-LAGB patients achieved T2DM remission (defined as FBG <126 mg/dl and HbA1c <6.2% on no diabetes medications), in contrast to only 13% of the conventional therapy group experienced remission. In this study, the dominant predictive factor of T2DM remission in surgical patients was greater weight loss at 2 years (20.7% vs. 1.7%).

The results of Roux-en-Y gastric bypass in patients with BMI <35 kg/m^2 were studied by Cohen et al. [8], which showed significant reductions in FBG, cholesterol, LDL cholesterol and triglycerides, as well as a marked increase in HDL cholesterol in 37 diabetic patients. Excess weight loss at 20 months was 77% but, importantly, no patient experienced excessive weight loss. Lee et al. [9]. reported on the effect of loop gastric bypass, so-called “mini”—gastric bypass, for T2DM in a prospective study involving 44 patients with BMI <35 kg/m^2 (range 28.3–33.7 kg/m^2) versus 166 patients with BMI >35 kg/m^2 (4-year follow-up). This loop-type mini-gastric bypass normalized hyperglycemia in 90% of patients with BMI <35, with a mean HbA1c of 5.6% at 1 year postoperatively, and hyperglycemia normalized in 98% of patients with BMI >35 kg/m^2. In this study, 77% of patients with BMI <35 kg/m^2 and 92% of those with BMI >35 kg/m^2 achieved the American Diabetes Association target goals of HbA1c <7.0%, LDL <100 mg/dl and triglycerides <150 mg/dl. In the less obese group, mean BMI decreased from 31 to 23 kg/m^2.

The first prospective pilot study using BPD to intentionally treat T2DM in patients with BMI <35 kg/m^2 was performed at the Catholic University of Rome. In this study, five diabetic patients with BMI 27–33 kg/m^2 underwent BPD and were followed for 18 months [24]. As early as 1 month after surgery, patients experienced dramatic and significant reductions in hyperglycemia and improvements in insulin sensitivity. Diabetes remission (i.e., normalization of HbA1c and FBG levels without pharmacotherapy) was maintained throughout the study. More recently, Scopinaro et al. [25] have reported on the effects of BPD on T2DM in 30 patients (12 were on insulin) with BMI 25–35 kg/m^2. BMI progressively decreased, stabilizing around 25 since the fourth month postoperatively, without excessive weight loss. One year after BPD, mean HbA1c was 6.3 ± 0.8%, with 25 patients (83%) controlled (HbA1c ≤7%) on free diet, without antidiabetic drugs, and the remaining showing improved glycemic control. DJB has also been used to treat diabetes in low BMI patients with favorable short-term results [12–14, 26]. De Paula et al. [16] have reported remission of diabetes (HbA1c <6%) in 65.2% of patients with BMI 21–29 following laparoscopic ileal interposition associated with a duodenal bypass and sleeve gastrectomy. The long-term metabolic sequelae and safety of these novel procedures, however, remain to be evaluated, and therefore, they should be considered experimental in humans.

Comparative efficacy of different bariatric procedures

Bariatric procedures differ in their ability to ameliorate type 2 diabetes. Intestinal bypass procedures (i.e., RYGB, BPD) are generally associated with greater glycemic control and remission rates than purely restrictive procedures (i.e., LAGB). As indicated in the meta-analysis by Buchwald et al. [4], BPD appears to be the most efficacious closely followed by RYGB and then LAGB. There is a paucity of randomized studies that have directly compared the effects of various procedures. A systematic review by Tice et al. [27] of 14 comparative studies, albeit of low quality (mostly retrospective and unmatched), testified to the superior efficacy of RYGB over LAGB in treating type 2 diabetes. The highest-quality observational study by Cottam et al. [28] considered the outcomes of 181 patients matched for age, sex, BMI and date of surgery. The excess body weight loss at 1 year was 76% for Roux-en-Y gastric bypass versus 48% ($P < 0.001$) for laparoscopic adjustable gastric banding, and the results remained stable at 3 years ($P < 0.001$). Resolution of diabetes was observed in 78% of the patients treated with Roux-en-Y gastric bypass who had diabetes before surgery, compared with 50% resolution in previously diabetic patients who received laparoscopic adjustable gastric banding. In a recent 2 cohort pair matched study of 200 obese patients, diabetes resolution occurred in 76% of patients who underwent RYGB compared with 50% of those who had LAGB [29]. Lee et al. [30] have published the results of a RCT comparing gastric bypass versus sleeve gastrectomy in patients with BMI 25–35 kg/m^2; the remission rate for T2DM was 93% for patients who underwent RYGB compared with 47% for those who underwent sleeve gastrectomy.

Bariatric or metabolic surgery: evidence for weight-independent mechanisms of diabetes resolution

The term bariatric surgery implies that the principal goal of the intervention is weight loss, while the term metabolic surgery focuses on amelioration of metabolic dysfunction, in particular, diabetes. While this term is generally applied to the use of gastrointestinal surgical procedures to treat diabetes in non-morbidly obese patients, the increasing evidence that weight-loss-independent mechanisms are integral to the improved glucose homeostasis even in obese patients suggests that a change in terminology is warranted, regardless of patient's BMI or on the type of procedure utilized. Essentially, all gastrointestinal surgical procedures performed to treat diabetes and obesity, irrespective of the patient's BMI are "metabolic" surgical procedures.

Starvation-induced improvement in glucose homeostasis is well known. Postoperative food deprivation followed by major weight loss after bariatric surgery is an intuitive, if somewhat simplistic explanation for the glycemic improvements. The impact of weight loss on glucose control, whether due to medical or surgical intervention, is also well established. Insulin sensitivity indeed increases markedly after bariatric surgery, accompanied by elevated adiponectin levels, enhanced markers of insulin signaling in key target tissues, favorable changes in enzymes mediating glucose and fatty acid metabolism and decreases in intramuscular and intrahepatic lipids [31].

However, the following lines of evidence indicate that gastrointestinal rearrangement seems to confer additional antidiabetic effects independent of weight loss and caloric restriction:

1. The antidiabetic effects of gastric bypass are superior to lifestyle interventions in weight matched control studies [32] or after other procedures such as gastric banding [33–35]. Analogous experiments of gastric bypass in fatty diabetic zucker rats showed both glucose tolerance and insulin sensitivity are superior to the diabetic effects observed in sham-operated animals with equivalent dietary weight loss [36].
2. Improvement in glucose homeostasis occurs within days after RYGB and precedes significant weight loss. In contrast, purely gastric-restrictive operations, such as LAGB, ameliorate diabetes only after substantial weight loss is achieved [37].

3. Experimental evidence in favor of weight-independent mechanisms is derived from the animal investigations using the DJB model developed by Rubino in rodents [11]. This model was developed to study the effects of gastric bypass on glucose homeostasis. In lean diabetic GK rats, Rubino et al. found that DJB (a bypass of the proximal intestine by the same amount as RYGB but without gastric restriction) rapidly and durably improved fasting glucose and postprandial hyperglycemia. These effects were not observed in a sham-operated animals that had undergone equivalent weight loss by caloric restriction. Similar findings using DJB are replicated in other rat models [38] and in humans [12–14, 26]. To specifically investigate whether duodenal exclusion alone may have antidiabetic effects, Rubino et al. [14] developed an experimental model using an endoluminal sleeve (ELS) to prevent contact between nutrients and duodenal mucosa in rats. Rats undergoing ELS showed dramatic improvement in glucose tolerance compared to matched controls in which the ELS had been fenestrated to allow nutrients to come in contact with duodenal mucosa. Consistent results about the antidiabetic effects of endoluminal sleeve were also reported by Aguirre et al. [39] in a diet-induced rat model of insulin resistance and subsequently in human experimental studies [40, 41].
4. Ileal interposition has also been shown to improve glucose homeostasis out of proportion to weight loss in rat models of obesity and diabetes [42, 43]. Interposition of the ileum results in dramatically enhanced secretion of two important ileal produced hormones, glucagon-like peptide-1 (GLP-1) and peptide-YY (PYY). Enhanced GLP-1 secretion is an obvious candidate to explain at least some of the glycemic effects.
5. Further hints of weight-independent antidiabetic effects of RYGB come from rare though increasing reports of post-RYGB hyperinsulinemic hypoglycemia developing long after RYGB [44, 45]. This condition is characterized by pancreatic beta-cell hypertrophy, islet hyperplasia and increased beta-cell mass [45]. These observations constitute additional evidence favoring weight-independent glucose lowering effects of RYGB.

The precise mechanisms for the resolution of T2DM remain to be fully elucidated. It is known, however, that surgical manipulation of the gut results in significant alteration of the gut hormonal milieu. Changes in levels of GLP-1, GIP, PYY and Ghrelin have been described following metabolic surgery. Different surgical procedures differ in their respective ability to modulate gut hormones depending on whether they involve intestinal diversion or are purely restrictive. The postprandial GLP-1 response to an OGTT or mixed test meal is consistently augmented following gastric bypass surgery [32–34, 46–48] or biliopancreatic diversion [49], while no change is observed after gastric banding [33, 34]. Increased PYY levels have been reported following gastric bypass [50, 51] and ileal interposition [52]. Levels of ghrelin, an orexigenic hormone, do not show the expected physiological rise following weight loss due to gastric bypass [53, 54], although this is not consistently reported by all studies [55, 56]. Exclusion of proximal intestine (primarily the duodenum) from the nutrient flow has been proposed to exert its direct antidiabetic effects presumably by downregulating one or more unidentified anti-incretin factors [57]. Other hypothesized weight-independent antidiabetic mechanisms after GI surgery include the following: changes in intestinal nutrient-sensing mechanisms regulating insulin sensitivity; disruption of vagal afferent and efferent innervations; bile acid perturbations; taste alterations; and alterations in undiscovered gut factors.

Safety of bariatric surgery for treatment of obesity and diabetes

A large number of studies and systematic reviews have evaluated the safety of bariatric surgery for the treatment of obesity and diabetes. Contrary to popular perception, bariatric surgery confers low operative mortality. The Bariatric Outcomes Longitudinal Database (BOLD) [58] consisting of data from over 55,000 bariatric surgery patients reported an all-cause 30-day mortality rate in bariatric surgery patients of 0.09% (0.11% for 90-day all-cause mortality). This result is similar (albeit slightly lower) than other reviews, which have reported mortality rates of 0.28% within 30 days and 0.35% from 30 days to 2 years [59]. Similarly, the Longitudinal Assessment of Bariatric Surgery (LABS) Consortium, a 10-center prospective trial involving 4776 morbidly obese patients undergoing bariatric surgery, recently reported a 30-day postoperative mortality of 0.3% [60]. A systematic review of bariatric surgery to treat T2DM in patients with BMI <35 kg/m^2 showed a 0.29% mortality rate and a very low rate of complications (under 4%), thus confirming the safety of these procedures across a wide spectrum of patients [61]. In the aggregate, the mortality risk of bariatric procedures compares favorably with most general surgery operations, being equivalent to those after laparoscopic cholecystectomy [14].

A study by Agency for Healthcare Research and Quality (AHRQ) reported that complication rates fell from 24 to 15% from 2002 to 2006, despite an increase in the percentage of older and sicker operative patients [62]. More recently, the multicenter LABS study reported a major complication rate of only 4.3% [60]. The most common complications of bariatric surgery include anastomotic leaks (3.1%), wound infections (2.3%), pulmonary events (2.2%) and hemorrhage (1.7%). Morbidity rates are lower after laparoscopic procedures, which constitute a steadily increasing proportion of bariatric operations [63]. Nutritional complications typically arise only after malabsorptive procedures. Protein malnutrition occurs more often following BPD or long-limb RYGB; it is rare after the standard proximal RYGB with an alimentary limb <150 cm [64]. Protein deficiency can be treated with diet modifications and, in rare extreme cases, total parenteral nutrition [65]. Intestinal bypass procedures that circumvent the duodenum and part of the jejunum can cause deficiencies in iron, calcium and vitamin D unless proper postoperative nutritional supplementation is taken. With RYGB, the incidence of iron deficiency is 6–33%, while calcium and vitamin D deficiencies range from 10 to 51% and can cause decreased bone mass and secondary hyperparathyroidism [14, 66, 67]. Vitamin B12 and folate deficiency can be as high as 66 and 38%, respectively [67]. Deficiencies in fat-soluble vitamins are more common after BPD. Up to 68% of patients undergoing BPD develop vitamin K deficiency [68], although clinical manifestations are uncommon. It is important to note that these higher estimates come from older studies and it is possible to prevent these nutritional complications with appropriate supplementation after surgery.

The impact of bariatric/metabolic surgery on CV risk and long-term survival

Several studies have demonstrated that the benefits of bariatric surgery extend beyond amelioration of hyperglycemia and include improvement in other cardiovascular risk factors such as dyslipidemia and hypertension. A meta-analysis involving 236 studies and 22,094 patients showed marked decrease in levels of total cholesterol, LDL cholesterol and triglycerides after bariatric procedures [4]. Approximately 70% of patients experienced an improvement in hyperlipidemia, whereas hypertension improved or resolved in 79% of patients. These beneficial effects of metabolic surgery have also been reported in patients with BMI <35 kg/m^2 [9]. In the SOS study, the 2- and 10-year recovery rates from diabetes, hypertriglyceridemia, low levels of high-density lipoprotein cholesterol, hypertension and hyperuricemia were more favorable in the surgery group than in the control group, whereas recovery from hypercholesterolemia did not differ between the groups [69].

Long-term survival in morbidly obese patients with and without T2DM is better in surgically treated patients than in matched control individuals who do not undergo surgery. A retrospective cohort study involving 7,925 severely obese patients treated surgically with RYGB and 7,925 similarly obese matched controls who did not undergo surgery examined long-term mortality from various causes [70]. After a mean follow-up of 8.4 years, surgery reduced overall mortality by 40%, cardiovascular mortality by 56%, cancer mortality by 60% and diabetes-related mortality by 92%. In the SOS study, patients in the surgical group (the majority had purely restrictive procedures—gastric banding or vertical gastroplasty) had a 24% non-adjusted decrease in overall mortality compared with matched controls. Another recent study by Busetto et al. [71] compared long-term mortality in 821 obese patients after laparoscopic adjustable gastric banding versus non-surgical age, gender and BMI matched controls. They reported a 60% lower risk of death at 5 years in surgically treated patients.

Cost-effectiveness of bariatric surgery for treatment of T2DM

In an era where health care is dictated by insurance companies in many countries and national health policy in others, it is imperative that any new intervention in medicine must establish not only efficacy and safety but also cost-effectiveness versus established modalities of treatment. Hoerger et al. [72] analyzed the cost-effectiveness of gastric banding and gastric bypass to treat type 2 diabetes in severely obese individuals in the United States, and they concluded that these procedures are cost-effective methods of reducing mortality and diabetes complications in severely obese adults with diabetes. Keating et al. [73] in an Australian study have also indicated that LAGB-induced weight loss is a dominant intervention (it both saves health care costs and generates health benefits) for managing recently diagnosed type 2 diabetes in class I/II obese patients in Australia. Ackroyd et al. [74] established a payer-perspective cost-effectiveness and budget impact model of LAGB and RYGB versus conventional treatment in patients with BMI $\geq$35 kg/m^2 and T2DM in Germany, UK and France. The authors concluded that, in patients with T2DM and BMI $\geq$35 kg/m^2, LAGB and RYGB are effective at 5-year follow-up in cost-saving in Germany and France and are cost effective in the United Kingdom. Anselmino et al. [75] replicated this model in Austria, Italy and Spain with similar results. While the cost-effectiveness of surgical treatment of T2DM in morbidly obese patients has been fairly well established, more studies are required to determine cost-effectiveness in less obese patients.

Predictors of remission of type 2 diabetes

From a surgical perspective, the choice of procedure is an important determinant of outcome. There is general consensus across several studies that RYGB leads to greater diabetes remission rates than LAGB [14]. Although some have suggested similar remission rates after SG and RYGB [76, 77], the only randomized trial by Lee et al. [30] confirms the superior efficacy of RYGB. Although BPD appears to have the most profound effect on diabetes remission in both obese and non-obese patients, it is not widely favored due to the greater surgical risk associated with it. Other factors that have been positively correlated with diabetes remission are percentage of excess weight loss (%EWL), younger age, lower preoperative HbA1c and shorter duration of diabetes (less than 5 years) [78, 79]. Severity of diabetes, as judged by preoperative treatment modality, has also been noted to be a significant factor. Schauer et al. [18] have reported in their series of 191 obese diabetic patients (the majority of whom were on oral agents or insulin) a diabetes remission rate of 97% in diet-controlled, 87% in oral agent-treated and 62% in insulin-treated subjects. Lee et al. [80] have identified C-peptide >3 ng/ml as an important predictor of diabetes resolution after LSG in non-morbidly obese diabetic subjects. It is likely that C-peptide and possibly GAD positivity will gain more utility in defining the best candidates for surgical treatment as the indications are expanded to include more non-morbidly obese patients. Current data support surgical intervention early in the course of T2DM for best outcome.

Metabolic surgery in the management algorithm for T2DM-a paradigm shift

Despite evidence that bariatric surgery in morbidly obese patients with T2DM results in remission or substantial improvement in diabetes in the vast majority of patients and also improves cardiovascular risk factors and reduces overall mortality, there is no mention of surgery as a treatment option in the current management algorithms of T2DM. The Diabetes Surgery Summit Consensus Conference in Rome 2007 was a timely attempt by leading scholars in the field of metabolic surgery and endocrinology to improve access to surgical options supported by sound evidence, while also preventing harm from inappropriate use of unproven procedures [81]. The DSS recognized the legitimacy of surgical approaches to treat diabetes in carefully selected patients. A significant step in this direction was also taken by the International Diabetes Federation (IDF), which issued its position statement at the recently concluded 2nd World Congress of Interventional Therapies to treat type 2 DM (New York City, March 28–30, 2011). The IDF statement reports that bariatric surgery should be an accepted option in people who have T2DM and BMI >35 and that surgery should be considered as an alternative treatment option in patients with a BMI between 39 and 35 when diabetes cannot be adequately controlled by optimal medical regimen, especially in the presence of other major cardiovascular risk factors. In Asians, and some other ethnicities of increased risk, BMI action points may be reduced by 25 kg/m^2 according to IDF [82].

The role of surgery in morbidly obese patients for the treatment of diabetes is clearly established. The typical patient with T2DM, however, is only mild or moderately obese. Clearly, our efforts must now be directed toward this vast population of afflicted individuals. Although it is challenging to obtain level 1 evidence to support surgical therapy, this must be the way forward. Fortunately, there are several ongoing RCTs addressing some key issues: the efficacy of metabolic surgery vs medical therapy, the comparative efficacy of different bariatric procedures and the impact of surgical treatment on diabetes-related complications—both microvascular and macrovascular [83, 84].

Conclusion

T2DM is a global pandemic sweeping across continents. There is a pressing need to devise strategies aimed both at prevention and treatment of this chronic disorder. While significant advances in medical therapy have been made with the introduction of GLP-1-based therapies, remission of diabetes remains an elusive target even with best combination of medical therapy. Metabolic surgery offers a unique opportunity for remission or control of T2DM in obese individuals, and it is now widely considered a standard of care option in patients with severe obesity and diabetes (BMI >35). It is envisaged that future studies will help identify the best surgical candidates among the vast population of less obese diabetic patients. Elucidating the mechanisms of action of GI metabolic surgery may help advance understanding of the disease and possibly shape the way we treat and think of diabetes in the twenty-first century.

Conflict of interest None.

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