

Is Bariatric Surgery an Appropriate Treatment for Type 2 Diabetes?

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Overweight and obesity are a worldwide epidemic with detrimental consequences for health and wellness. More than 1.5 billion people worldwide are classified as either overweight or obese.¹ Rates of overweight and obesity have increased dramatically in the United States, having doubled in the past two decades. This leaves Americans with the highest reported BMI of developed countries and rates of obesity and overweight of 30–34 and 60–68%, respectively.²

Obesity is defined as an excess of adipose tissue, including both subcutaneous and visceral adiposity.² Obesity and overweight are most commonly defined via BMI calculations. Overweight is classified as a BMI ≥ 25.0 kg/m², whereas obesity is defined as a BMI ≥ 30.0 kg/m², and morbid obesity is defined as a BMI ≥ 40.0 kg/m².

Even in the absence of overt obesity, increased visceral adiposity is correlated with hyperinsulinemia and insulin resistance leading to glucose intolerance and metabolic syndrome.¹ Abnormal levels of the adipokines secreted by visceral adipose tissue may contribute to insulin resistance.² These metabolic abnormalities associated with obesity are strongly correlated with development of type 2 diabetes.

Type 2 diabetes is a chronic disorder defined by impairment of peripheral insulin sensitivity, hepatic glucose regulation, and insulin secretion by pancreatic β -cells,

resulting in end-organ damage and complications such as retinopathy, neuropathy, and nephropathy.¹ Both genetic and environmental factors cause insulin resistance and loss of β -cell function in type 2 diabetes. Obesity is the most important environmental causative factor of insulin resistance.²

Type 2 diabetes affects > 220 million people worldwide, and this statistic is projected to reach 366 million by 2030.³ More than 17 million cases of type 2 diabetes have been diagnosed in the United States, with another 5.7 million remaining undiagnosed.⁴

The correlation between elevated BMI and type 2 diabetes is well

IN BRIEF

Given the well-documented relationship between obesity and type 2 diabetes, it is a logical hypothesis that reduction in body weight from bariatric surgery would improve glycemic control in patients with type 2 diabetes. The evidence is even more compelling with the Roux-en-Y gastric bypass procedure, which often results in improved glycemic control even before significant weight loss has occurred. Many hypotheses have been proposed regarding the mechanisms of this phenomenon. This article reviews those hypotheses, as well as the risks and benefits of bariatric surgery for adults with type 2 diabetes.

documented, with overweight individuals having a considerably higher lifetime risk of diabetes. Research has shown that weight loss of a modest 5–10% of total body weight results in significant reductions in blood glucose levels, lipids, and blood pressure, but a total weight loss of ~ 20% is necessary to eliminate most comorbidities.³ Thus, long-term sustainable weight loss remains a mainstay in the medical management of type 2 diabetes. However, most patients with type 2 diabetes are unsuccessful in sustaining significant weight loss even with strong social support, and dietary modifications often produce limited results.³

Other standard treatments of type 2 diabetes, in addition to lifestyle measures aimed at weight loss, include oral medications and insulin. Many oral antihyperglycemic agents cause weight gain, which results in a secondary increase in insulin resistance necessitating a higher dose of the medication,³ thus creating a vicious circle. Overall, it is much more difficult for patients with diabetes than for those without diabetes to lose weight.⁵ Although the treatment of type 2 diabetes has improved over time, there remains a significant need for better treatment options and an eventual cure.

Bariatric Surgery and Diabetes

In the past two decades, bariatric surgery has become more prevalent, with multiple types of surgical pro-

cedures available. These procedures can be classified as either restrictive or malabsorptive based on their anatomical and physiological effects. Restrictive procedures are designed to reduce gastric volume and include procedures such as laparoscopic gastric banding and laparoscopic sleeve gastrectomy. Other procedures are both restrictive and malabsorptive in that they are designed to both reduce gastric volume and decrease the amount of nutrients absorbed by bypassing part of the gastrointestinal tract. These include procedures such as the Roux-en-Y gastric bypass (RYGB) and biliopancreatic diversion with duodenal switch (BPD-DS). These procedures with a malabsorptive component result in more rapid weight loss than purely restrictive procedures but carry a higher risk of long-term nutritional deficiencies.⁶

All of these surgical weight loss procedures have shown efficacy in improving glycemic control in patients with type 2 diabetes. A systematic review by Buchwald et al.⁷ showed a rate of complete resolution type 2 diabetes of 76.8% and a rate of resolution or improvement in 86.0% of patients after bariatric surgery. Gastric bypass procedures including RYGB demonstrated a type 2 diabetes resolution rate of 83.7% postoperatively. Only one other procedure—BPD-DS—has resulted in a higher resolution rate (98.9%). Other bariatric surgical procedures included in the review were gastroplasty and gastric banding, which resulted in rates of type 2 diabetes resolution of 71.6 and 47.9%, respectively.

RYGB is considered the gold standard for bariatric surgery. It has been performed for nearly 50 years and is the most commonly performed bariatric surgical procedure in the United States.^{4,8} Surgical techniques for RYGB have been modified over time, and the procedure may

be performed with either an open or laparoscopic approach. Advantages of laparoscopic RYGB compared to open RYGB include shorter hospital stays, decreased mortality, and reduced incidences of wound infections and incisional hernias.⁶ Given its efficacy and widespread use, RYGB will be the focus of discussion for the remainder of this article.

RYGB and Diabetes

RYGB is considered both a restrictive and malabsorptive surgical procedure. A small gastric pouch with a volume capacity of 20–30 ml is created with a proximal gastroenterostomy that bypasses the stomach and some of the small intestine with a Roux limb of 100–150 cm.⁸ The combination of dietary volume restriction and malabsorption results in significant weight loss, making the RYGB the most effective known treatment for obesity.

It is easy to understand how weight loss resulting from RYGB would result in improvement or even resolution of type 2 diabetes. However, studies have shown that serum insulin and glucose levels begin to normalize within days after surgery—before significant weight loss has occurred.³ RYGB restores the pancreatic β -cells' insulin response to serum glucose that is lost in type 2 diabetes.⁹ Because RYGB has been shown to restore β -cell function, it may be a good surgical option for obese patients with diabetes and poor β -cell function.¹⁰

This phenomenon suggests that mechanisms other than weight loss must be involved. Numerous hypotheses have been developed regarding this.

The hypothesis of the distal bowel, or the hindgut theory, holds that expedited delivery of ingested nutrients to the distal intestine stimulates L cells, resulting in increased secretion of incretin hormones.⁹

Incretin hormones increase levels of insulin secreted by pancreatic β -cells after eating but before blood glucose levels elevate.³ The incretins considered potential candidate mediators of this effect are glucagon-like peptide (GLP)-1, peptide YY (PYY), and other L-cell peptides.¹¹ These hormones result in a more appropriate insulin response to ingested food and subsequent improved glucose homeostasis.¹²

Stimulation of L cells also occurs by proximal nutrient-related signals transmitted from the duodenum to the distal bowel. The duodenum is bypassed in RYGB, which may theoretically lead to lower postprandial GLP-1 levels. However, secretion of GLP-1 and other L-cell peptides has been documented to increase postprandially after RYGB.⁹

The hypothesis of the proximal bowel, or the foregut theory, holds that exclusion of the proximal small intestine, including primarily the duodenum, from contact with nutrients results in decreased secretion of putative anti-incretins that reduce insulin secretion and/or promote insulin resistance.⁹ Reduction in these anti-incretins would result in improved insulin secretion and action resulting in improved glucose homeostasis. Furthermore, it is hypothesized that the marked underproduction of anti-incretins can result in an exaggerated incretin effect, which would cause severe postprandial hypoglycemia.⁹

Ghrelin is a hormone that stimulates hunger and is secreted by cells that line the fundus of the stomach and epsilon cells of the pancreas.³ Removal of the fundus of the stomach in RYGB and other bariatric surgical procedures results in elimination of the major site of ghrelin, thus decreasing appetite and perpetuating weight loss.

Increased levels of PYY have been noted postsurgically, as well.

PYY is co-secreted with GLP-1 from intestinal L cells when stimulated by ingested food. PYY is suspected to decrease insulin resistance and has been shown to decrease food intake in humans when injected.⁹

These hypotheses remain to be confirmed. Further research is needed to fully understand the physiological mechanisms by which RYGB improves glycemic control before significant weight loss occurs.

RYGB as a Diabetes Treatment

The American Diabetes Association's Standards of Medical Care in Diabetes¹³ recommends that bariatric surgery should only be considered for patients with type 2 diabetes and a BMI > 35 kg/m² if the diabetes or associated complications are difficult to control through lifestyle and pharmacological interventions. Bariatric surgery in patients with type 2 diabetes and a BMI < 35 kg/m² is not currently recommended for general use outside of a research protocol because of insufficient evidence of its efficacy.¹³ However, mean onset of type 2 diabetes occurs at a BMI of 31 kg/m².¹⁴

Serrot et al.¹⁴ investigated the efficacy of RYGB in adult patients with type 2 diabetes and a BMI < 35 kg/m² compared to nonsurgical therapy. Results of this study included a decrease in postsurgical BMI from an average 34.6 to 25.8 kg/m² and improvement in glycemic control as evidenced by decreases in A1C from an average of 8.2 to 6.1%. The nonsurgical group had no significant change in either BMI or A1C.

Although the beneficial effects of RYGB on type 2 diabetes are significant, the risks and cost-effectiveness of surgical intervention must also be considered. Buchwald et al.⁷ reported 30-day mortality rates of 0.5% for gastric bypass surgeries, including but not limited to

RYGB, with an average weight loss of 35% and a mean change in BMI of 16.7 kg/m². Acute complications of the procedure include nutritional deficiencies, sepsis, venous thromboembolism, hemorrhage, obstruction, anastomotic leaks, arrhythmias, and pulmonary embolism. Long-term complications include internal hernias, anastomotic stenosis, neuropathies, and emotional disorders.³ Use of antidepressants is higher in postsurgical patients, and the rate of death by accident or suicide after bariatric surgery is higher than in the nonsurgical patient population.¹⁵

Vomiting is very common in the first few months after RYGB, leading to potential dehydration, electrolyte imbalances, and nutrient deficiencies even more significant than those caused by the purposeful malabsorption of the surgery. Approximately half of patients experience dumping syndrome after RYGB, which also puts patients at further risk for fluid and electrolyte imbalances, as well as emotional distress related to frequent and abrupt occurrences of diarrhea.³

Nutritional deficiencies such as anemia related to insufficient vitamin B₁₂ and iron absorption are common and may require vitamin supplementation, special foods, or medications to meet the body's nutritional needs.⁶

These risks and potential complications associated with RYGB are important considerations when evaluating whether use of RYGB is an appropriate treatment for patients with type 2 diabetes.

The recurrence rate of type 2 diabetes after RYGB is another important point to consider. In a study by DiGiorgi et al.,¹⁶ all 42 patients in the study had total remission or improvement of type 2 diabetes shortly after RYGB at rates of 64 and 36%, respectively. After long-term follow-up of ≥ 3 years,

24% of patients experienced recurrence or worsening of type 2 diabetes as defined by an A1C > 6.0% plus a fasting glucose level > 124 mg/dl and/or medication requirement.

Variables that affected the likelihood of recurrence or worsening include lower preoperative BMI, weight regain, and higher postoperative glucose levels. Patients who required insulin before RYGB were also less likely to experience remission of type 2 diabetes.¹⁶ These variables may be pertinent factors in selection of potential candidates for RYGB.

In a recent randomized, controlled trial by Mingrone et al.,¹⁷ 60 patients with a BMI ≥ 35 kg/m², a history of type 2 diabetes of at least 5 years, and an A1C ≥ 7.0% were randomly assigned to receive conventional medical therapy or surgery (either gastric bypass or BPD). At 2 years, none of the patients receiving medical therapy had experienced remission, but the surgical patients achieved remission at rates of 75 and 95%, respectively. The variables of age, sex, baseline BMI, duration of diabetes, and weight change were not significant predictors of remission.¹⁷

Although these data are quite promising, another recent study did not reveal such significant results when patients were followed over the long term. Arterburn et al.¹⁸ conducted a multisite study that included 4,434 patients with type 2 diabetes. These patients were followed for more than 10 years after gastric bypass surgery. Among the patients studied, 68.2% had achieved complete diabetes remission within 5 years, but about one-third of those patients (35.1%) experienced relapse within 5 years of initial remission.

Another important variable to consider is the cost-effectiveness of surgical versus nonsurgical treatment of type 2 diabetes. The question of cost-effectiveness is per-

tinant not only for patients, but also for health care providers and third-party payers. The economic impact of type 2 diabetes on the health care system is staggering, with an estimated total expenditure of \$376 billion in 2010.¹⁵ Patients with type 2 diabetes have more physician visits and longer lengths of hospital stay and incur medical costs that are two to three times higher than patients without type 2 diabetes.¹⁵

The initial investment in an RYGB bariatric surgery procedure is estimated to be \$23,583.¹⁵ Although the initial cost is high, an updated analysis by Cremieux et al.¹⁵ confirmed that, on average, cost savings begin to accrue for patients and third-party payers by 3 months after surgery, and surgery costs are fully recovered by 47 months post-operatively. Long-term cost savings may continue after RYGB as a result of discontinuation of diabetes medications, decreased occurrence of comorbid conditions requiring medical care, and, eventually, fewer physician visits.

The price of treating type 2 diabetes and its complications is high, as is the cost of bariatric surgery such as RYGB. However, the potential long-term savings may make surgical treatment a wise investment.

Implications for Primary Care Providers

Primary care providers play a pivotal role in the management of patients with type 2 diabetes, which may include bariatric surgery for select patients. Providers should screen all patients, including those with type 2 diabetes, to determine whether a bariatric surgical referral would be appropriate. All encounters should include weight, height, and BMI measurement to screen for overweight and obesity.

For patients with type 2 diabetes and a BMI > 35 kg/m², bariatric

surgery referral may be appropriate if dietary modifications and pharmacological therapy have failed to maintain optimal glycemic control. Providers should obtain a thorough history of their patients' experiences with weight gain and loss, glucose control, medication use, and lifestyle behaviors, including a food and exercise diary. Assessing patients' knowledge and perceptions of body size, food, eating patterns, and physical activity will help to determine whether lifestyle modifications have been properly implemented or whether the patient did not have an accurate understanding of what changes needed to be made.⁶

Patients should be informed of the long-term health risks of obesity and type 2 diabetes. All treatment options, including bariatric surgery if applicable, should be discussed, along with ongoing monitoring and support. Risks and benefits, as well as long-term management, should be discussed for any treatment option considered. Effective management of type 2 diabetes requires not only appropriate treatment selection, but also open communication and continuous education between patients and their health care providers.

Conclusion

There are sufficient data supporting the recommendation of bariatric surgery, including RYGB, as a treatment for type 2 diabetes in patients with a BMI > 35 kg/m². However, further research is needed to explore the efficacy of RYGB and other bariatric surgical procedures for patients with a BMI < 35 kg/m². Further investigation is also needed of long-term recurrence rates and determination of appropriate candidate selection criteria, including not only BMI, but also other potentially relevant factors such as medication usage. Furthermore, additional research is needed to conclusively determine the mechanisms

of diabetes remission after bariatric surgery, as well as potentially develop new treatment options based on this research.

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