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**Gastric Bypass Surgery as an Alternative Treatment to Pharmacologic Therapy for Lowering HbA1c in Obese Type 2 Diabetic Patients**

By

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## **Introduction**

Diabetes Mellitus is a chronic metabolic disease characterized by elevated blood glucose levels. This progressive disorder can lead to severe end organ damage, including heart disease, stroke, blindness, diabetic retinopathy, cataracts, glaucoma, kidney disease, as well as blood vessel and nerve damages leading to amputation. It is important to prevent or control diabetes with effective treatment due to the extent of the complications associated with uncontrolled diabetes. According to the World Health Organization, 422 million adults in the world have diabetes with 1.5 million deaths attributable to this disease annually. There are two types of diabetes mellitus— type 1 diabetes mellitus (T1DM), in which insulin is no longer adequately produced by the pancreas, and type 2 diabetes mellitus (T2DM), in which the body is unable to effectively utilize the diminishing insulin supply produced by the pancreas. The Centers for Disease Control and Prevention (CDC) states that T2DM accounts for up to 95% of all diagnosed cases of diabetes.<sup>2</sup>

Focusing on therapy, many options are available for treating T2DM; however, of the numerous treatment choices, determining the most effective disease control is paramount. T2DM therapeutic measures includes lifestyle modifications, such as eating healthfully, exercising regularly, and losing excess weight. In addition, medicines are also prescribed to lower blood sugar to help prevent and delay complications. While the use of prescription medications to treat T2DM is a widely accepted and effective intervention, recent studies have shown that Roux-en-Y gastric bypass procedure can be an alternate and potentially more effective treatment. Although it is primarily used for bariatric therapy, Roux-en-Y gastric bypass surgery is currently being studied as an option to aid in glycemic control in adults with T2DM.

This research paper explores the effectiveness of Roux-en-Y gastric bypass surgery compared to pharmacologic therapy for improving the plasma glucose and glycosylated hemoglobin (HbA1c) levels in obese T2DM patients.

### **Discussion**

Twelve articles were analyzed to determine if the Roux-en-Y gastric bypass procedure or traditional management with medication is most effective to control T2DM. These studies compared the effectiveness of Roux-en-Y gastric bypass surgery to pharmacologic therapy in reducing HbA1c and controlling T2DM in obese patients. Additionally, they examined the effectiveness of Roux-en-Y gastric bypass surgery compared to other bariatric surgeries in reducing HbA1c.

In a study conducted by Zhang et al in 2016, the effectiveness and safety of laparoscopic Roux-en-Y gastric bypass for the treatment of T2DM were investigated. The goal was to measure the effects on diabetes remission and metabolic syndrome in individuals with T2DM after undergoing gastric bypass surgery. Patient demographics, including body mass index (BMI), diabetes disease duration, and blood lipid levels were prospectively collected and analyzed. Of the 85 patients studied, the pre-operative BMI for each patient was above 28 kg/m<sup>2</sup>, indicating obesity, and the mean HbA1c level was 8.32%, consistent with uncontrolled T2DM.<sup>3</sup> After the patients received Roux-en-Y gastric bypass surgery, their blood lipid levels were checked at 6 months, 12 months and 18 months appointments post-operatively. The evidence showed significant changes in their preoperative blood lipid levels; blood cholesterol levels decreased at 12 and 18 months, triglyceride levels decreased at 6, 12, and 18 months, LDL levels decreased at 12 and 18 months. Moreover, HbA1c and plasma glucose were significantly reduced after this gastric bypass surgery. Thus, the evidence demonstrated that Roux-en-Y gastric bypass surgery was effective in

improving the HbA1c levels in obese T2DM patients. However, this study was limited by the lack of generalizability of the results to different populations, especially patients with BMIs of  $<28 \text{ kg/m}^2$ .

As noted, Roux-en-Y gastric bypass can help to alleviate the multiple factors causing metabolic syndrome, including hyperlipidemia, diabetes type 2, hypertension, and elevated visceral fat. To address the persistence of those changes, Cohen et al in 2017, examined whether Roux-en-Y gastric bypass improved metabolic outcomes in obese diabetic patients for at least five years. They found that Roux-en-Y gastric bypass performed in T2DM participants with a BMI of  $30\text{-}40 \text{ kg/m}^2$  increased the probability of achieving T2DM remission in a statistically significant way.<sup>12</sup> Both HbA1c levels and blood pressure decreased, and HDL levels increased. This bariatric surgery effectively controlled the three major endpoints of metabolic syndrome. Thus, this study confirmed that the Roux-en-Y gastric bypass procedure can effectively reduce plasma blood glucose and HbA1c levels in obese T2DM patients. It was limited by the maximum length of follow up of five years post-operative. Longer follow-up periods comparing Roux-en-Y gastric bypass surgery with medical management alone could identify their respective micro- and macrovascular outcomes in T2DM patients.

Other bariatric surgeries are available for patients with morbid obesity, hence the need to evaluate their effects on HbA1c levels and remission of T2DM. Courcoulas et al compared the remission of T2DM following different surgical and nonsurgical treatments. At 3 years, T2DM remission was achieved in 40% of patients after Roux-en-Y gastric bypass surgery, 29% after sleeve gastrectomy, and 0% with non-surgical management. The Roux-en-Y gastric bypass group had the greatest change in both HbA1c and fasting blood sugar levels from baseline.<sup>8</sup> It was superior to sleeve gastrectomy for both lowering HbA1c levels and inducing remission in type 2

diabetics. Non-surgical management compared to surgery was ineffective in inducing remission in type 2 diabetics. Furthermore, not only was Roux-en-Y gastric bypass surgery more effective for reducing HbA1c levels in obese T2DM patients than diabetes medications alone, it was also more effective than sleeve gastrectomy operations for inducing T2DM remissions. Greater than 40% of the sample were individuals with class I obesity (BMI of 30-<35), a strength in generalizability because the literature was largely lacking such data. However, the small sample size of 61, negatively affected the study's power, and thus, its ability to detect statistically significant differences. In another study from 2015, Musella et al compared the rates of remission achieved in morbidly obese T2DM patients after Roux-en-Y gastric bypass versus sleeve gastrectomy. Both surgical procedures were effective.<sup>9</sup> However, the Roux-en-Y gastric bypass procedure performed better than the sleeve gastrectomy at 1 year with diabetes remission rates of 85.4% versus 60.9%.

Roux-en-Y gastric bypass was also compared to bariatric procedures for its ability to reduce HbA1c and to induce diabetes remission. Purnell et al examined T2DM remission after Roux-en-Y gastric bypass versus laparoscopic gastric banding. Remission of diabetes at one year after Roux-en-Y gastric bypass was 71.0%, whereas remission after laparoscopic gastric banding was 29.9%.<sup>10</sup> This study was limited by its relatively short follow-up period of 12 months and a dropout rate of 15%. Nonetheless, Roux-en-Y gastric bypass surgery was more effective than gastric banding for inducing and maintaining remission in type 2 diabetics.

So far, the prevailing evidence in most studies shows that the Roux-en-Y gastric bypass procedure may not only cause significant reductions of HbA1c, but also complete remissions of T2DM. Supporting that evidence are results from Carranza et al in 2017. They examined the rate of T2DM remission 4 years following gastric bypass in a real-life clinic cohort in the U.S. Veterans

Health Care System. Eighty-eight percent of patients experienced improvement or remission of diabetes 4 years post the Roux-en-Y gastric bypass surgery. In fact, diabetes remission was achieved by 15% of patients at 6 months post-operation, a rate that increased to 49% at 4 years post-operation.<sup>7</sup> These findings confirm those found in the other studies; Roux-en-Y gastric bypass surgery as an intervention in obese T2DM can lead to reduction in HbA1c and even remission. However, the Carranza et al study was limited because it was a retrospective study and it was conducted in the US Veterans Health Care system, in which the majority of participants were war veterans with low-income; as such, these results may not be entirely generalizable to other populations.

A study by Kaska et al in 2014 characterized the dynamics of T2DM remission in patients with BMI <35 and >35 kg/m<sup>2</sup> after Roux-en-Y gastric bypass surgery. T2DM remission was determined by fasting plasma glucose and HbA1c levels. T2DM regression was observed in 80% of patients with a BMI <35 kg/m<sup>2</sup>, and 83% of patients with a BMI >35 kg/m<sup>2</sup> one year after the surgery. Two and three years after the surgery, the T2DM regression plateaued to 80% of the patients in both groups,<sup>4</sup> establishing that Roux-en-Y gastric bypass surgery reduces HbA1c levels and can lead to T2DM remission in patients with BMI <35 and >35 kg/m<sup>2</sup>.

The effectiveness of Roux-en-Y gastric bypass surgery to reduce HbA1c levels and induce remission may not be generalizable to obese type 2 diabetics of all ethnicities. Chong et al conducted a study that addressed this concern. They investigated the impact of Roux-en-Y gastric bypass and intensive medical management in an Asian population and a non-Asian American (United States) cohort; specifically, patients who were Taiwanese were compared with Americans. At 24 months, none of the participants in the intensive medical management groups achieved partial or complete diabetes remission. In contrast, the Roux-en-Y groups showed significant

partial or complete remission in 29% of Taiwanese cohort and 14% in the American cohort.<sup>11</sup> These findings confirm that T2DM remission or HbA1c reductions occurring with Roux-en-Y gastric bypass are generalizable to more than one ethnicity. In addition, the remission rates suggest that this surgery is more effective in the Taiwanese population. This study was limited by its small sample size, 120 participants.

In the aforementioned studies, many patients continued their diabetes medications after the Roux-en-Y gastric bypass procedure. Ammori et al in 2014 studied the effectiveness of stopping glucose-lowering treatment at the time of gastric bypass surgery in T2DM patients. After surgery patients still had significant weight losses with a mean reduction in BMIs by 16.4% and reductions in HbA1c of 23.6%.<sup>5</sup> HbA1c reductions were maintained up to 24 months post-operatively. Thus, patients were able to maintain their HbA1c reduced status post-operatively through weight reduction alone and did not need to restart hypoglycemic agents. Although this study was limited by its retrospective design, it provided evidence that Roux-en-Y gastric bypass surgery in obese T2DM patients is effective for controlling HbA1c levels, without the reinstitution of diabetes medications.

While it is clear that T2DM medications may not be necessary for HbA1c control after Roux-en-Y gastric bypass in certain patients, continuing lifestyle modifications and medications after surgery can provide effective control of diabetes. In 2018, Ikramuddin et al compared the durability of Roux-en-Y gastric bypass added to intensive lifestyle and medical management to lifestyle-medication management only for control of diabetes. Five years after the procedure, 55% of participants in the gastric bypass group versus 14% of participants in the lifestyle-medical management group achieved HbA1c of less than 7.0% (P=0.002).<sup>6</sup> The target goal of HbA1c less than 7.0% was maintained by 70% of patients at five years. Thus, if intensive lifestyle



modifications and medical management are not effective in controlling diabetes adequately, Roux-en-Y gastric bypass may help to bridge that gap. The generalizability of these findings is limited because the mean baseline HbA1c concentration in the participants was 9.5%, which indicated relatively poorly controlled hyperglycemia at baseline; thus, whether the results would be different with better controlled baseline hyperglycemia is unknown for this comparison.

### **Conclusion**

The currently available studies provide evidence that Roux-en-Y gastric bypass surgery effectively reduces the plasma glucose and HbA1c levels in obese patients with T2DM. Moreover, Roux-en-Y gastric bypass surgery can promote the regression of T2DM in obese patients. These findings support the practice of referring obese T2DM patients for Roux-en-Y gastric bypass surgery in order to control and possibly induce remission of their diabetes. In fact, this bariatric surgery may be more beneficial for obese diabetics than following the current practice of prescribing T2DM medications. Roux-en-Y gastric bypass surgery is, at a minimum, an effective alternative treatment for obese T2DM patients, and may become a preferred treatment option. Whether Roux-en-Y gastric bypass without glucose-lowering medications would provide more significant HbA1c reduction than traditional pharmacologic therapy needs confirmation with additional studies.

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