



## The Effect of Bariatric Surgery on Type 2 Diabetes Mellitus

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### ABSTRACT

**Background:** The prevalence of obesity has increased significantly in the last decades. Epidemiological studies confirmed the association of increasing obesity trends along with a high prevalence of type 2 diabetes mellitus (T2DM). Losing weight is a cardinal step to achieve better glycemic control when treating diabetic patients. Besides medical therapy, bariatric surgery has been considered as an option for obtaining the remission of T2DM. **Objective:** To review the published literature that discusses the effect of bariatric surgery on T2DM. **Method:** PubMed database was used for article selection, and the following keys were used in the mesh (["bariatric surgery" [Mesh]] and ["type 2 diabetes mellitus" [Mesh]]). The article selection was based on the relevance to the topic as their primary endpoint. **Conclusion:** The idea behind the positive effects of bariatric surgery in treating diabetes is not only because of weight loss alone. Changes in the responsiveness of beta cells, in incretins levels, and bile salts regulation also have effects on diabetes. A considerable number of randomized clinical trials have been evaluating the safety and the efficacy of the different bariatric procedures such as vertical sleeve gastrectomy (VSG), Roux-en-Y gastric bypass (RYGB), and biliopancreatic diversion/duodenal switch (BPD/DS) in treating T2DM. These procedures have shown to be associated with better outcomes regarding diabetes control and higher remission rates than medical therapy.

**Keywords:** Bariatric surgery, Type 2 Diabetes Mellitus

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### 1. INTRODUCTION

Recently, epidemic obesity has reached critical proportions worldwide (Mahassni, 2020). Consequently, there is a substantial increase in the global burden regarding obesity and obesity-related comorbidities especially T2DM (Tsilingiris *et al.*, 2019; Bogoriani *et al.*, 2019). Part of T2DM pathogenesis and insulin resistance in the body is the overall and/or visceral adiposity (Al Otaibi *et al.*, 2020). Moreover, epidemiological studies confirmed the association of increasing obesity trends along with the high prevalence of T2DM. During the last decades, obesity has reached epidemic proportions in both the developing and the developed world (Ng *et al.*, 2014; Field *et al.*, 2001; Verma and Hussain, 2017; American Diabetes Association, 2010; Al-waseif *et al.*, 2020). The prevalence of obesity has been increased significantly in the last decades. More than 1.9 billion adults have considered overweight in 2016 and 650 million of them were obese. Moreover, T2DM rates are increasing alongside obesity as the prevalence of

diabetes rose from 108 million in 1980 to 422 million in 2014 (Tham *et al.*, 2014).

In treating T2DM, losing weight is a cardinal step to achieve better glycemic control. Besides medical therapy, bariatric surgery has been considered as an option for obtaining the remission of T2DM for the long-term (Tsilingiris *et al.*, 2019). Therefore, we aim in this article to review the published literature that discussed the effect of bariatric surgery on T2DM.

### 2. METHODS:

PubMed database was used for article selection, and the following keys were used in the mesh (["bariatric surgery" [Mesh]] and ["type 2 diabetes mellitus" [Mesh]]). The article selection was based on the relevance to the topic as their primary endpoint.

Regarding the inclusion criteria, the articles were selected based on including one of the following topics: The Effect of Bariatric Surgery on Type 2 Diabetes Mellitus

Exclusion criteria were all other articles that do not have one of these topics as their primary endpoint.

### 3. DISCUSSION:

T2DM is a progressive complex metabolic disorder that results in a state of hyperglycemia due to insulin resistance and the failure of beta cells of the pancreas (DeFronzo, 2004; Kashyap and DeFronzo, 2007). One of the risk factors of T2DM is obesity as it induces insulin resistance and inflammation leading to impaired glucose regulation (Mokdad *et al.*, 2003; Unger, 2003). The inflammation pathways are mediated by the adipocyte-derived cytokines and increased free fatty acids circulation that resulted from the deposition of fat in the liver, abdomen, and muscles. It has been proven that diet and exercise reduce the incidence of T2DM as it improves the homeostasis of glucose. Therefore, the guidelines of T2DM management always recommend lifestyle modification to the patient as the first advice is losing weight (Kashyap *et al.*, 2010).

The traditional suggested surgical management of diabetes was mainly focused on pancreatic or islets cells transplantation. However, bariatric surgery recently became the mainstay surgical approach in diabetes. A considerable number of randomized clinical trials have been evaluating the safety and the efficacy of the different bariatric procedures such as vertical sleeve gastrectomy (VSG), Roux-en-Y gastric bypass (RYGB), and biliopancreatic diversion/duodenal switch (BPD/DS) in treating T2DM (Roslin and Cripps, 2016). These procedures are associated with better outcomes regarding diabetes control and higher remission rates than medical therapy (Yu *et al.*, 2015; Wang *et al.*, 2015; Brethauer *et al.*, 2013).

The idea behind the positive effects of bariatric surgery in treating diabetes is not only because of weight loss alone. Changes in the responsiveness of beta cells, in incretins levels, and bile salts regulation also have effects on diabetes (Rubino *et al.*, 2016). The other changes also contribute to improving glycemic level regulation even though weight loss is the main factor as there is a significant relationship between high rates of T2DM remissions and losing weight. The significant anatomical alterations after bariatric surgery significantly affect the physiological function of the metabolism in which the resulted mechanisms of metabolism positively affect insulin sensitivity and also insulin release. Eventually, these metabolic improvements will lead to better correction of hyperglycemia and even obtaining a euglycemic state (Tsilingiris *et al.*, 2019). Clinical trials have shown the efficacy of weight loss on increasing the probability of T2DM remissions in which individuals losing less than 5 kg and more than 15 kg of body weight have significantly different rates of remission after implementing strict lifestyle modifications like healthy dietary management and regular exercise. The rate of remission ranges from 3.6% to 86.1% at the end of the first year and 5.2% to 70% at the end of the second year, for individuals losing <5 kg and >15 kg of body weight, respectively (Lean *et al.*, 2018). The condition of stable negative energy balance that results after bariatric surgery is the major factor that leads to the long-term peripheral insulin sensitivity restoration. After surgery, the reduction of hunger and early induction of satiety is the reason behind the significant decrease in energy intake. It has been thought that this decrease is related to two reasons. First, the reduced upper gastrointestinal pouch capacity activates the satiety signals so early via the afferent pathways

of the vagus nerve. The second explanation is about the changes in energy intake regulation in subcortical brain areas because of the surgery-induced modulations of hunger and satiety signaling networks. An example of these changes in the early secretion of the gut peptides that induce satiety such as glucagon-like peptide 1, and peptide YY (Miras and Le Roux, 2013). These secretions are thought to help preserve beta cells' anatomy and physiology by preventing the apoptosis of beta cells (Ramracheya *et al.*, 2016). This can be associated also with decreased secretion of orexigenic hormones, which are responsible for stimulating the appetite, for example, ghrelin (Miras and Le Roux, 2013).

The proof that suggests there are positive effects of bariatric surgery on T2DM rather than weight loss is the glycemic control improvement seen a few days after the operation before any observed weight loss. Moreover, the sudden and significant decrease in calorie intake also contributes to several positive outcomes such as plasma glucose levels normalization, beta-cell function improvement, and increasing the sensitivity of hepatic insulin (Jackness *et al.*, 2013).

#### **Preoperative Predictors of the Remission of T2DM:**

Several studies have evaluated the predicted effect of bariatric surgery on T2DM using many preoperative predictive factors and several scores have been developed for this purpose (Yu *et al.*, 2015).

ABCD score (age, BMI (body mass index), C-peptide, duration of the disease) have shown to be superior over other scores because it can predict accurately the success of the bariatric surgery on the remission of T2DM. It is also a simple grading system that contains multiple important factors. It contains the patient's age which indicates relatively the general leverage of the body function, obesity level (BMI), C-peptide level which measures the islet cell mass, and the duration of T2DM diagnosis which assesses the competence of beta-cell function (Kassem *et al.*, 2017; Itariu *et al.*, 2014).

However, age is considered as the least valued predictor but it still has its importance regarding the general physiological results as the benefits from bariatric surgery decrease with advanced age (Lee *et al.*, 2016). Moreover, low BMI diabetic patients (less than 27 kg/m<sup>2</sup>) are not advised to undergo bariatric surgery as its effect is reduced in such patients (Rubino *et al.*, 2016). The C-peptide level is important in predicting the outcomes of bariatric surgery on T2DM as it reflects the condition of insulin secretion and the functionality of beta cells (Lee *et al.*, 2016).

#### **Surgical Procedures:**

- **Laparoscopic Adjustable Gastric Banding (LAGB):**

LAGB was the first laparoscopic bariatric procedure. It is considered a restrictive procedure, which consists of a silicone device connected with a band and an inflatable balloon wrapped around the upper part of the stomach. The band's purpose is the compartmentalization of the upper portion of the stomach to make a small pouch tightening the fundus of the stomach. The band inflation is controlled by the subcutaneous device as it controls the passage of food through the band-induced outlet and subsequently reducing the food intake. After LAGB, diabetes remission can be obtained with time to the pace of losing weight (Silecchia *et al.*, 2009; Nandagopal *et al.*, 2010).

However, this technique may be associated with serious complications like infection, bleeding, leakage, and perforation, which may need urgent surgical intervention at rates of 2–8.9%. A slipped band is also a possibility in which a hernia may originate in the distal portion of the stomach leading to an obstruction (Schauer and Ikramuddin, 2001).

- **Vertical Banded Gastroplasty (VBG):**

VBG is also considered a restrictive procedure in which a small pouch is made in the proximal part of the stomach causing a reduction of food flow to the lower part. The pouch is stapled, cut, and bisected from the proximal part to limit the food flow. Then, a polypropylene mesh should be put to cover the stoma to prevent any expansion. Nevertheless, the stoma may dilate especially if the mesh material caused a foreign-body reaction to the patients leading to weight regain. Regarding complications, infection, leakage, bleeding, perforation, anastomotic stenosis, and internal hernia/small bowel obstruction can develop after VBG (Nandagopal et al., 2010; Schauer and Ikramuddin, 2001).

- **Roux-en-Y Gastric Bypass (RYGB):**

In the United States, RYGB is the gold standard procedure for bariatric surgery, as its components are considered restrictive as well as malabsorptive. It is now primarily approached laparoscopically and is done by creating a gastric pouch by separating the stomach from the distal portion at first which is considered the restrictive part of the technique. Then, an anastomosis is done between the gastric pouch and the jejunum. Another anastomosis is done between the alimentary limb and pancreaticobiliary limb after fashioning it to allow pancreatic and biliary secretions to pass until they emerge with the chyme that is coming from the gastric pouch. This delay in emerging and mixing the secretions with the chyme reduces the nutrient absorption, which is responsible for the malabsorptive part of the technique (Rubino, 2006). Therefore, many patients who have undergone RYGB face nutritional problems such as iron deficiency anemia, vitamin B12 deficiency, and folate deficiency (Brolin, 2001). Besides, leak and gastric perforation are reported complications at rates of less than 5% of cases (Schauer and Ikramuddin, 2001).

- **Biliopancreatic Diversion (BPD) and biliopancreatic diversion with duodenal switch (BPD/DS):**

The BPD and the BPD/DS procedures are also considered restrictive and malabsorptive as they consist of fashioning of the small intestines along with gastrectomy. First, a partial gastrectomy of 60% of the stomach is conducted creating a distally closed gastric pouch. The fashioning of the small intestines includes transection of small intestines 2.5 m from the ileocecal valve and anatomizing the distal end of the ileum to the gastric pouch to allow the chyme to pass. The remaining portion of the small intestines will be anastomosed to the bowel above the ileocecal valve. The purpose of this portion is to carry the biliopancreatic secretions only and thus delaying the mixing of the ingested food and the digestive biliopancreatic juices, which contributes to the malabsorptive component of this approach. The BPD/DS approach is different from BPD by preserving the pylorus. Preserving the pylorus helps in reducing the associated symptoms of dumping such as epigastric pain, nausea, dizziness, sweating, and palpitation.

The risks of this approach are like the risks of RYGB in types and rates (Nandagopal et al., 2010; Marceau et al., 1998; Marceau et al., 2001; Buchwald et al., 2004; Vidal et al., 2008).

- **Vertical Sleeve Gastrectomy (VSG):**

VSG is considered a new bariatric procedure relatively. It is considered as a simple surgical technique, which is mostly conducted as a first step for obtaining weight loss in morbidly obese patients and in patients who have a high risk of perioperative morbidity and mortality because of weight-related severe co-morbidities. It can be an initial step before performing the RYGB and duodenal switch (Vidal et al., 2008; Baltasar et al., 2005).

It is done by resecting the greater curvature of the stomach from the distal antrum to the fundus by a stapler and then removing the resected gastric part making the stomach smaller. This technique is associated with a low complication rate and limited nutritional deficiencies. Moreover, it is associated with a high remission rate of T2DM and reducing other comorbidities within 18 months after the operation (Lee et al., 2016; Silecchia et al., 2009). It has become the first choice for many surgeons instead of LABG because it has a lower complication rate and higher T2DM remission rate (Kassem et al., 2017).

#### 4. CONCLUSION:

The idea behind the positive effects of bariatric surgery in treating diabetes is not only because of weight loss alone. Changes in the responsiveness of beta cells, in incretins levels, and bile salts regulation also have effects on diabetes.

A considerable number of randomized clinical trials have been evaluating the safety and the efficacy of the different bariatric procedures such as vertical sleeve gastrectomy (VSG), Roux-en-Y Gastric Bypass (RYGB), and biliopancreatic diversion/duodenal switch (BPD/DS) in treating T2DM. These procedures have shown to be associated with better outcomes regarding diabetes control and higher remission rates than medical therapy.

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