

## Students Section: Review Article

### Exploring Bariatric Surgery as a Cure for Type 2 Diabetes Mellitus

Kanika Kalra, Gurmeen Kaur

#### Abstract

India is facing an epidemic of type 2 diabetes mellitus. The increasing association of diabetes with obesity has led to the emergence of Bariatrics along with the conventional medical treatment of diabetes. Since weight reduction is difficult to attain and even harder to maintain, researchers all over the world are increasingly realizing the potential of bariatric surgery as an efficacious cure to morbid obesity and diabetes. Bariatric procedures mainly comprise of **malabsorptive procedures** where the length of intestine available for nutrient absorption is decreased and **restrictive procedures** where food intake is reduced. Roux-en-Y gastric bypass, a combination procedure, is considered the gold standard bariatric procedure for most patients. The proposed mechanisms responsible for cure of diabetes are weight loss, reduced caloric intake and alteration in pattern of secretion of gastrointestinal hormones. There is promising data proving the mettle of bariatric procedures in the remission of Diabetes Mellitus yet there are no studies comparing their efficacy against standard anti-diabetic medical treatment. Hence it would be still premature to conclude the superiority of Bariatric surgery as a long term treatment for Diabetes.

**Key Words:** Type 2 Diabetes, morbid obesity, Bariatric surgery

India is becoming the world capital of diabetes mellitus. The number of diabetics would reach up to 100 million by 2020 as predicted by WHO. The increase in the prevalence of type 2 diabetes is closely linked to the upsurge in obesity. About 90% [1] of type 2 diabetes is attributable to obesity which is further associated with worse outcomes like hypertension, coronary heart disease and dyslipidemia. This is where bariatrics comes into play in addition to the conventional medical treatment for diabetes. *Bari* means *weight* or *pressure* in ancient and modern Greek. However, in biblical Hebrew it denotes obese and in Modern Hebrew, *healthy* [2]. There is evidence from a number of studies that weight loss reduces mortality in diabetics. Weight loss is beneficial for long-term diabetes outcomes for overweight, obese and morbidly-obese participants [3]. Williamson et al found that overweight people with diabetes who reported intentional weight loss experienced 25% lower total mortality and a 28% reduction in cardiovascular disease and diabetes mortality. Intentional weight loss of 20-29 lbs. (9-14 kg) was associated with the largest reductions in mortality (approximately 33%) [4]. In a review of 11 long term studies, patients with the risk of developing diabetes due to either family history of diabetes or

impaired glucose tolerance, saw a reduction in this risk. Those with large weight losses achievable with surgical interventions reduced their risk by at least 63%. Metabolic handling of glucose improved in 80% of those already with type 2 diabetes who lost weight [5]. Even though the literature supports the effectiveness of weight loss in controlling diabetes, many physicians still find sustained weight loss difficult to achieve and maintain, even with intensive therapy using anti-obesity drugs especially in the current scenario of increasing morbid obesity (body mass index,  $BMI \geq 35 \text{ kg/m}^2$ ). Therefore, Bariatric surgery is being increasingly realized as a realistic treatment option for the morbidly obese population suffering from type 2 diabetes. The U.S. National Institutes of Health recommends bariatric surgery for obese people with a BMI of at least 40, and for people with  $BMI > 35$  and serious coexisting medical conditions such as diabetes. However, emerging research suggests bariatric surgery could be appropriate for those with a BMI of 35 to 40 with no co-morbidities or a BMI of 30 to 35 with significant co-morbidities [6].

Several Bariatric procedures are available to cure morbid obesity. **Predominantly malabsorptive procedures**, where the length of intestine available

Lady Hardinge Medical College, New Delhi

**Corresponding Author:** Kanika Kalra, AD-85A, Pitampura, Delhi-110088.  
E mail: kanikalra87@gmail.com

for nutrient absorption is decreased include 'Biliopancreatic diversion' (BPD) or 'Scopinaro Procedure' which has nowadays been replaced with 'Duodenal Switch' also known as BPD/DS; and 'Endoluminal Sleeve' which has only been performed in mice. **Predominantly restrictive procedures** which primarily reduce gastric size include 'Vertical Banded Gastroplasty' (Mason Procedure), 'Adjustable Gastric Band' (AGB), 'Laparoscopic Adjustable Gastric Band' (known as LABG/Lap Band), 'Sleeve Gastrectomy' and 'Intragastric balloon'. Roux-en-Y Gastric Bypass surgery, Sleeve Gastrectomy with Duodenal Switch and Implantable Gastric Stimulation are amongst the **mixed procedures** which employ both techniques simultaneously. Gastric Bypass and Sleeve Gastrectomy can also be performed laparoscopically [6]. The Roux-en-Y gastric bypass is currently considered the gold standard bariatric procedure for most patients. Most Bariatric procedures require life long compliance with multivitamins and supplements because of altered absorption of nutrients from the gastrointestinal tract [7]. Other adverse effects may be gastric dumping syndrome in about 20% (bloating and diarrhoea after eating, necessitating small meals or medication), leaks at the surgical site (12%), incisional hernia (7%), infections (6%) and pneumonia (4%), mortality (0.2%) [6]. Marginal ulcer and stomal stenosis are among the commoner complications of bariatric surgery, their incidence ranging from 5-15%. Clinical trials in South America and Europe in 2009 are testing a new surgery-free medical device called the 'EndoBarrier Gastrointestinal Liner'. It may offer effective surgery free weight loss. Lining part of the small intestines from the duodenum and into the first part of the jejunum, this mechanical bypass may alter hormonal responses in the body and result in metabolic changes that lead to weight loss and a potential solution for type 2 diabetes [6].

Studies conducted on the Greenville series of Roux-en-Y Gastric Bypass surgery established it as an effective and safe therapy for morbid obesity and its associated co-morbidities. Pories et al reported that 82.9% of diabetics maintained normal levels of plasma glucose, glycosylated hemoglobin, and insulin on 14 year follow-up. These antidiabetic effects were thought to be due primarily to a reduction in caloric intake, suggesting that insulin resistance is a secondary protective effect rather

than the initial lesion [8]. In another study conducted by them, 86 out of 88 diabetics became euglycemic within 4 months after surgery without any diabetic medication or special diets [9]. In 1998, Scopinaro et al reported normalization of glucose levels in 100% of their morbidly obese patients after BPD with no need for medication and on a totally free diet as early as 1 month after operation [10]. In the Swedish Obese Subjects study, weight reductions achieved in the surgical group reduced the 2-year incidence of diabetes 32 times as compared to the controls. After eight years there was still a 5-fold reduction in diabetes incidence [11]. Although weight loss has a role in the glycemic control achieved in the above studies by producing changes in release of adipocytokines which favorably impact insulin resistance, there maybe other mechanisms by which bariatric surgery controls diabetes. One of them is reduced caloric intake and early satiety which produces the profound long-term alterations in glucose metabolism and insulin action [12]. Supporting the above mechanism, there are cases in literature reporting resolution of diabetes after vertical banded gastroplasty [13], which reduces the stomach size thus limiting food intake, but there are no evidences of long term cure achieved by this procedure. Also not all procedures gave the same remission rates of diabetes thus underscoring the importance of other anti-diabetic mechanisms apart from reduced caloric intake. As one looks into the anatomical and physiological alterations caused by major bariatric surgeries (GBP and BPD), one finds that in both of them undigested or incompletely digested food is presented early to the ileum, and the duodenum and jejunum are excluded from the enteroinsular axis thus suggesting the possibility of a change in the pattern of secretion of gastrointestinal hormones [10]. Gut peptides, which mediate the enteroinsular axis, include the incretins glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide, as well as ghrelin and peptide YY (PYY). It has been hypothesized that bariatric procedures that expedite nutrient delivery to the distal ileum, such as BPD and RYGB, increase GLP-1 and PYY levels. In contrast, restrictive procedures do not increase levels of incretins or PYY. Augmented levels of GLP-1 probably account for the anti-diabetic effect of procedures that bypass the small bowel. In addition, altered secretion of anorexigenic peptides, such as GLP-1 and PYY, may mediate the reduction in

appetite and sustained weight loss that occurs more often after intestinal bypass procedures [14]. Biliopancreatic diversion reduced leptin levels before weight loss occurred and increased the enteroglucagon response to glucose test. Decreased plasma lipid levels have also been reported after biliopancreatic diversion [10]. Despite the above proposed mechanisms, there is no conclusive data on the anti-diabetic mechanisms of bariatric surgery. On analysis of the efficacy of different types of bariatric procedures, it has been found that resolution of diabetes after surgery occurs in 84% to 98% cases for bypass procedures and 48% to 68% cases for restrictive procedures [14]. A study conducted on Asian patients in Taiwan, revealed that Gastric Bypass surgery was better than Laparoscopic Vertical Banded Gastric partition (LVBG) and LAGB for curing diabetes because of better weight reduction that was achieved. Laparoscopic gastric bypass patients had a greater weight loss and a higher rate of glucose normalization (93.1%) than the LVBG patients (85.3%) and LAGB patients (73.9%) [15]. In another Italian study, AGB was found to be the least effective. The anti-diabetic effect was similarly precocious after GBP and SG compared with AGB [16]. In a study comparing the effects of Laparoscopic Sleeve Gastrectomy (LSG) and Laparoscopic Roux-en-Y Gastric Bypass (LRYGBP), both were found to result in a similar rate of type 2 diabetes resolution at 4-months after surgery [17]. Another study comparing the above procedures reported similar remission rates in Metabolic Syndrome along with type 2 diabetes mellitus [18]. A study was conducted to explore mechanisms other than weight reduction for the success of LSG and it was found that decreased gastric emptying half-time and small bowel transit time (measured by scintigraphic imaging) after LSG can possibly contribute to better glucose homeostasis in patients with type 2 diabetes mellitus [19]. Studies have also shown effectiveness of bariatric surgery in treatment of type 2 diabetes in patients with BMI < 35kg/m<sup>2</sup>. The treatment goal of type 2 diabetes mellitus (HbA1C < 7.0%, LDL < 150 mg/dL and triglycerides < 150 mg/dL) was met in 76.5% of BMI < 35 kg/m<sup>2</sup> and 92.4% of BMI > 35 kg/m<sup>2</sup> (p=0.059). Although a slightly lower response rate has been reported, they still had an acceptable diabetes resolution [20].

The effectiveness of Bariatric surgery in cure of Type

2 Diabetes Mellitus may seem impressive but to conclude that it should be offered to obese people with new or existing diabetes primarily to cure their diabetes is still premature. This is because all the above data is pertaining to diabetic patients who had undergone bariatric surgery primarily for other reasons. Therefore to establish surgery as a cure for diabetes, studies showing a more favourable long-term effect on diabetes than the other comparable treatments like standard medical treatment for diabetes, and intensive lifestyle modification including anti-obesity drugs to reduce weight, should be undertaken. Although probably bariatric surgery may prove to be superior to the above, it needs conclusive evidence to establish its role in the long term treatment of diabetes.

#### Key Points

- Diabetes Mellitus is being increasingly associated with obesity especially morbid obesity thus making weight reduction an essential component of the management of the disease.
- The potential of Bariatric surgery in achieving the above is being continuously explored with many studies yielding positive results.
- Comparisons with the conventional medical treatment are required to conclusively declare its superiority as a long term treatment option for Diabetes.

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