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BMH Med. J. 2017;4(1):6-16 **Review Article**

Role Of Bariatric Surgery In Type 2 Diabetes

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Abstract

The obesity pandemic resulted in an exponential rise in the incidence and prevalence of type 2 diabetes mellitus (T2 DM) globally. T2 DM as a consequence of obesity - the diabesity - is a difficult clinical problem faced by physicians with limited medical management options. Bariatric surgery or metabolic surgery has emerged as a promising treatment option in patients with diabesity that results in marked weight loss and remission of T2 DM in a majority of cases. Although invasive, costly and associated with complications in a minor proportion of patients, bariatric surgery is recommended as an important management option for severely obese individuals with or without diabesity by many professional bodies globally. This review discusses the important types, benefits, indications and complications of bariatric surgery in patients with diabesity with an up to date scientific evidence.

Keywords: Bariatric surgery, metabolic surgery, obesity, type 2 diabetes mellitus, and diabesity

Introduction

The obesity pandemic has resulted in an alarming increase in the incidence and prevalence of type 2 diabetes mellitus (T2DM) globally that affected 415 million people in the year 2015 [1]. A proportionate rise in other lifestyle related disorders such as hypertension and dyslipidemia in these individuals also resulted in an exponential increase in cardiovascular diseases worldwide. Obesity when associated with T2 DM, not only impairs glycemic control, but also increases the risk of various associated co-morbidities and cardiovascular morbidity and mortality. Management of obesity is challenging because even with lifestyle modification, exercise and pharmacological agents, the long term results are unsatisfactory. However, recent data from various surgical procedures, collectively called "Bariatric surgery or metabolic surgery", are promising that has now emerged as the standard treatment option for obese individuals with T2 DM. In this review we are discussing the role of metabolic surgery in the management of Type 2 diabetes.

The term "diabesity", coined by Ethan Sims, way back in 1973, is used to describe T2 DM when it

co-exists in patients with obesity, to show the pathophysiological interlink between the 2 conditions [2]. The clinical significance of diabesity is that weight loss may be associated with remission of T2 DM. Currently available medications for diabesity are associated with only marginal benefit in terms of weight loss. However, various bariatric procedures have shown to be associated with marked weight loss in obese subjects, and multiple clinical trials and meta-analyses have proven its role in the management of diabesity [3-6]. This has resulted in a major paradigm shift in the management diabesity in recent years [7]. Therefore, we outline the role of weight loss surgeries, collectively called 'bariatric surgery', 'metabolic surgery', 'diabetes surgery' or 'obesity surgery' to enable clinicians for optimal and appropriate management of diabesity.

Types of Bariatric / Metabolic Surgery

All bariatric surgical procedures aim to reduce the absorption of nutrients from the gastrointestinal tract (GIT) either by reducing the capacity to accommodate nutrients (restrictive), or by reducing the capacity of the effective absorptive area of GIT (mal- or dis- absorptive) or by both [7,8]. Choice of the procedure depends on multiple factors including patient characteristics, associated comorbidities, surgeons' expertise, cost, and sometimes patient preference. The commonly performed Bariatric surgical procedures include (**Figures 1 -4**):

1) Laparoscopic Adjustable Gastric Banding (LAGB)
2) Laparoscopic Sleeve Gastrectomy (LSG)
3) Roux-en-Y Gastric Bypass (RYGB)
4) Bilio-Pancreatic Diversion (BPD)

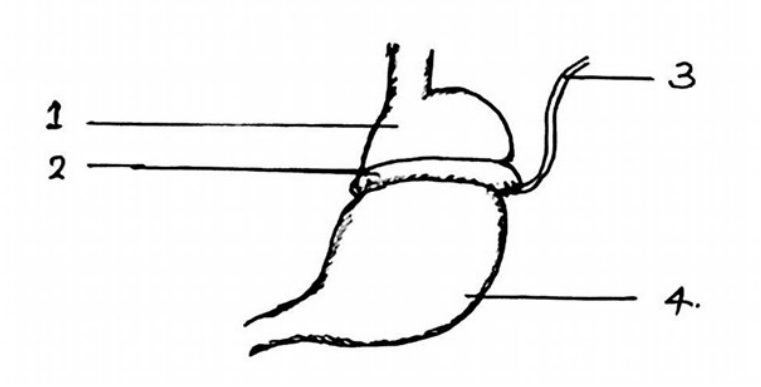

Figure 1: Laparoscopic Adjustable Gastric banding (LAGB). 1.Small upper stomach pouch 2. Adjustable gastric band 3. Tubing to inject water to adjust the gastric band size 4. Remainder of the body of stomach

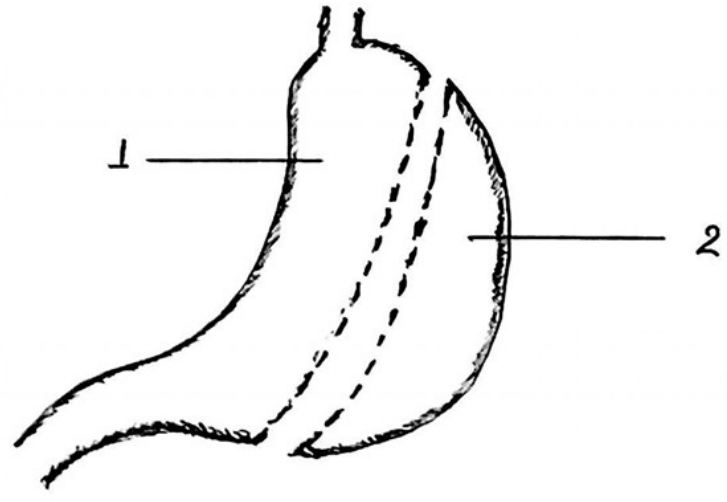

Figure 2: Laparoscopic Sleeve Gastrectomy (LSG). 1. Tube like reconstructed stomach 2. Portion of stomach removed

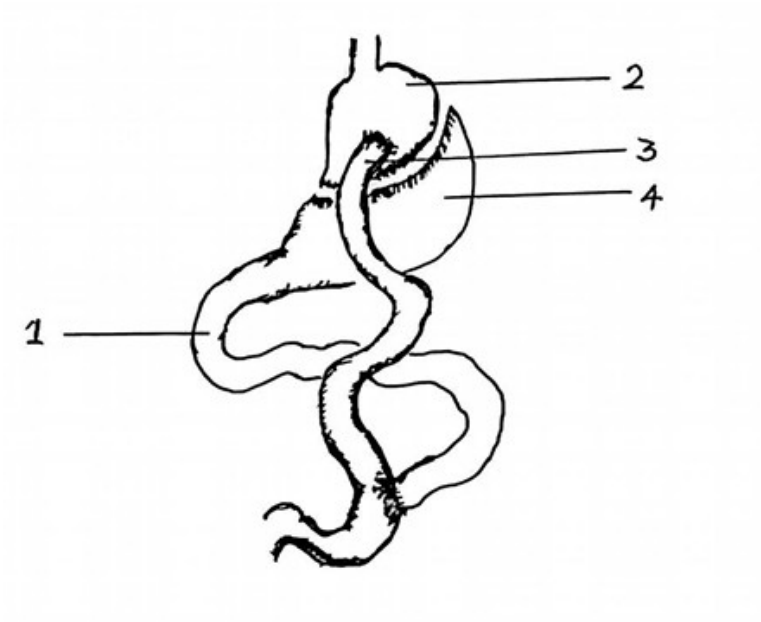

Figure 3: Roux-en-Y Gastric Bypass (RYGB). 1. Proximal portion of the small intestine 2. Upper stomach pouch 3. Distal portion of cut end of small intestine connected to the gastric pouch 4. Lower part of resected stomach.

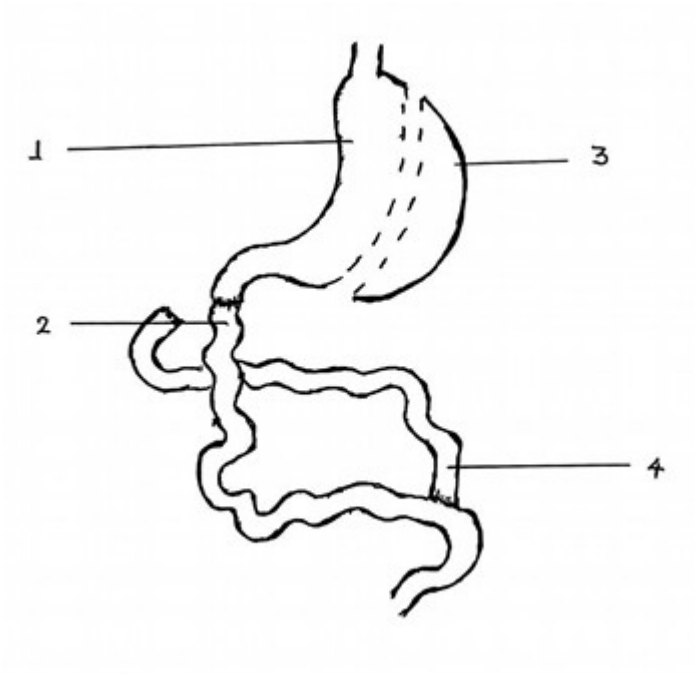

Figure 4: Bilio-Pancreatic diversion (BPD). 1.Tubular reconstructed stomach 2. Distal portion of small intestine 3. Removed portion of stomach 4. Proximal portion of small intestine connected to ileum.

Laparoscopic Adjustable Gastric Banding (LAGB)

In this restrictive procedure an inflatable band is placed around the upper part of the stomach that leads to reduction of the gastric capacity to accommodate food. The procedure is reversible, adjustable, not requiring resection of part of stomach, and having less hospital stay with lowest rate of post-operative complications. However, it is associated with slower and lesser weight loss compared to other bariatric procedures, and is associated with the highest rate of requirement of reoperation.

A previous meta-analysis involving 11 studies and 1004 obese patients (of these 616 underwent

LAGB, the remainder LSG) showed a mean percentage excess weight loss (EWL) of 33.9 % after 6 months in six studies, and 37.8 % after 12 months in four studies following LAGB [9]. Improvement of T2 DM was reported in 42 out of 68 (61.8 %) patients in 5 of these studies. A more recent meta-analysis revealed that the summary effect of body mass index (BMI) loss of 11.6 kg/m^2 (95% confidence interval; CI: 9.8-13.4) in nine studies that persisted even after 12 months in significant proportion of cases [10]. Data on immediate and long-term complications was available from 534 of patients from 13 of these studies. 10.8% of cases experienced some band-related complications on long-term follow up. Significant improvements in comorbidities such as hypertension, dyslipidemia, insulin resistance, obstructive sleep apnea, asthma, musculoskeletal complaints, menstrual problems and gastro-esophageal reflux along with improvement of T2 DM were reported in some of these studies (having follow up data on these parameters) in treated patients [10].

Laparoscopic Sleeve Gastrectomy (LSG)

In this predominantly restrictive procedure, a major portion (about 80%) of the stomach is removed and the remainder is converted into a tubular pouch, resembling a banana, thereby reducing the storage capacity of the stomach. It also leads to favorable changes in the gut hormones leading to reduced appetite and improved satiety. Even though it induces rapid and significant weight loss and requires short hospital stay, it is an irreversible procedure that is associated with higher rate of early post-operative complications compared to LAGB.

Better weight loss and improvement of diabesity parameters were obvious in patients undergoing LSG compared to LABG as shown in multiple observational studies and meta-analyses [9-14]. Although, the immediate complications were higher than that in LAGB, the long-term complications were less [10]. LSG was found to be a promising bariatric procedure in Indian patients [15]. The major drawback of the procedure is the irreversibility if patient develops any post-procedure complication unlike in other bariatric procedures.

Roux-en-Y Gastric Bypass (RYGB)

In this combined procedure, the upper part of the stomach is converted into a small stomach pouch, which is then connected to the divided distal end of the first part of small intestine, thereby reducing the capacity of stomach and also reducing the length of small intestine (*alimentary limb*) leading to effective reduction of the nutrient absorptive area. The proximal end of the divided first part of small intestine, which carries gastric acid and various digestive enzymes (*secretory limb*), but not the food, is connected to the lower part of small intestine so that the upper gastrointestinal secretions finally mix with the food consumed. This procedure also causes favorable changes in gut hormones that adds on to the significant long term weight loss [7,16]. It is considered as gold standard weight loss surgery, even though it is technically more complex and associated with higher risk of long term complications (like vitamins/mineral deficiency).

Multiple clinical trials [3,4,17], observational studies [11,12,18], and meta-analyses [13,14,19,20] showed the remarkable benefits of RYGB in terms of diabesity outcomes and other health related parameters. The benefits are mainly related to the marked weight loss resulting from RYGB (compared to LAGB and LSG) and may expect to translate into better long-term cardiovascular morbidity and mortality benefits as shown by previous systematic reviews and meta-analyses [21,22]. Reversibility of the procedure in unusual circumstances of intolerability or extreme adverse consequences makes RYGB a slightly better choice compared to LSG to some surgeons.

Bilio-Pancreatic Diversion (BPD)

In this combined procedure a tubular stomach of small capacity is created as in sleeve gastrectomy and connected to the distal divided portion of small intestine bypassing 3/4 of the small intestine, thereby reducing both the capacity to hold nutrients and effective absorptive area. The bypassed

small intestine, carrying biliary and pancreatic enzymes, is re-connected to the last portion of small intestine, so that it can finally mix with food. This procedure also causes favorable change in the gut hormones. Even though it is a complicated procedure, associated with longer hospital stay, higher potentials to cause Vitamin and mineral deficiency, it is the most effective weight loss surgery resulting in 60-70% of excess weight loss at 5 year follow up.

Compared to other bariatric procedures, BPD is associated with maximum weight loss and remission of obesity related comorbidities including diabetes remission. A recent large meta-analysis involving 94 studies and 94579 patients showed that BPD resulted in diabetes remission in 89% of cases (95% CI: 83-94) compared to 77% (95% CI: 72-82) in RYGB, 62% (95% CI: 46-79) in LAGB and 60% (95% CI: 51-70) in LSG procedures [23]. However, the immediate and long-term complications are much higher in patients undergoing BPD procedures that makes this a reserved surgery only for extreme cases of obesity.

Benefits of Bariatric surgery

The major benefit and attraction of bariatric surgery is not only the weight reduction and improvement in glycemic control, but it helps to achieve remission of diabetes and other diabesity parameters, in a significant proportion of patients with obesity. The benefits of Bariatric surgery are given in **Table 1**.

Table 1: Benefits of Bariatric surgery

- Improvement in glycemic control in T2 DM/ Remission of diabetes/ Gestational Diabetes
- Improvement in obstructive sleep apnea
- Cardiac protection
  - Regression of left ventricular hypertrophy
  - Improvement in Diastolic function,
  - Reduction of Left atrial size.
- Improvement of Hypertension.
- Improvement of Dyslipidemia
- Improvement of Gastro-Esophageal Reflux Disease (GERD)
- Improvement of Arthritis
- Improved quality of life

Nutritional management of patients after bariatric surgery

Nutritional deficiencies are not uncommon following bariatric surgery. In general, mal-absorptive procedures are associated with much higher chance of development of nutritional imbalance compared to the restrictive procedures. The diet related nutritional complications can be managed by adhering strictly to a nutritional program. The eating guidelines mainly stress on eating a balanced diet, small portions a time, chewing properly, taking water and food separately.

Patients commonly develop vitamin B12, folate, vitamin D and iron deficiencies, and at times other micronutrient deficiencies, although this is less often encountered in clinical practice. Therefore, a multi-vitamin supplement is routinely prescribed to patients after bariatric procedures. A daily record of the food portions and protein intake should be kept to help dieticians and physicians to get an overall idea about the diet taken by the patient and to advice changes in diet when necessary [24].

Perioperative complications

The reported perioperative mortality rate from large case series and RCTs for an average patient is low at <0.3% although this could vary greatly with rates ≥ 2.0% in some patient subgroups [25]. Most common causes of perioperative mortality are anastomotic leak with peritonitis and pulmonary embolism. Acute gastric distension secondary to edema of the enterostomy site is another complication of bypass surgery in the immediate postoperative period [26].

Patients should also be monitored for vitamin deficiencies and electrolyte imbalances. The patients should follow a gastroplasty diet i.e. eat undisturbed, chew meticulously, never drink with meals, and wait 2 hours before drinking after solid food is consumed or else they might develop nausea and vomiting. Anastomotic ulcers will also cause nausea and vomiting [27,28]. The common complications after bariatric surgical procedures are shown in the **Table 2**.

Table 2: Complications of Metabolic Surgery

Immediate Post-operative period
• Pulmonary complications like pulmonary embolism, aspiration & atelectasis. • Vomiting • Wound infection • Bleeding & anastomotic leak
Long term
• Iron deficiency anemia. • Risk of re-operation • Psychological issues (substance abuse/ alcoholism/ suicide). • Nutritional deficiency. ▪ Calcium ▪ Vitamin D ▪ Zinc ▪ Copper • Abnormal body contour after massive weight loss • Post-prandial hypoglycemia • ? Worsening of micro-vascular complications (e.g., diabetic retinopathy) • Internal hernia, incisional hernia and bowel obstruction • Stomal stenosis • Marginal ulcer
In pregnant women who already underwent metabolic surgery
• High risk of SFG (small for gestational age) infants • Still birth or neonatal death

Indications for bariatric surgery in the management of diabesity

The common indications for bariatric surgery in the management of diabesity is shown in **Table 3**. The National Institute for Health and Care Excellence (NICE) of the United Kingdom revised its guidelines for bariatric surgery in November 2014 following the availability of data on its remarkable health benefits from multiple observational studies, RCTs and meta-analyses [29]. Similar guidelines and recommendations from other global professional bodies are being developed recently. There are still uncertainties about the BMI cut offs for metabolic surgery for different ethnic groups such as Afro-Caribbean races, Asians and primitive population groups of American and Australian continents.

Table 3: Indication for Bariatric surgery in Diabesity

If treatment target is not achieved or maintained with medical therapy/ intense lifestyle changes in patients with T2 DM having • BMI ≥ 35 kg/m² * • BMI is 30-34.9 kg/m², in presence of co-morbidities**- considered as an alternative treatment option

*In Asian, and some other ethnicities of increased risk, BMI action points may be reduced by 2.5 kg/m^2

**Co-morbidities: Hypertension, Hyperlipidemia, obstructive sleep apnea (OSA) obesity Hypoventilation syndrome (OHS), Non-alcoholic fatty liver disease or non-alcoholic steato-hepatitis, idiopathic intracranial hypertension, GERD, asthma, venous stasis disease, severe urinary incontinence, debilitating arthritis, impaired quality of life.

When considering the risk benefit ratio of bariatric surgery, the risk of death from diabetic complication is greater than the risk of death from bariatric surgery. The economic impact and the variety of health benefits along with the marked improvement in quality of life, makes metabolic surgery a unique and promising treatment option in patients with diabesity [30].

How bariatric surgery is beneficial in T2 DM

The glucose lowering effects of various bariatric surgical procedures are seen even before achieving significant weight loss. Typically, patients are allowed to consume a 400-800 Kcal diet in the immediate postoperative period that in itself improve the glucose control in many patients. Acute negative calorie balance and favorable changes in the entero-insular axis contribute to early benefit, and these along with weight reduction on long term basis help to achieve remission of T2 DM and improvement of diabesity (**Figure 5**)[7,31].

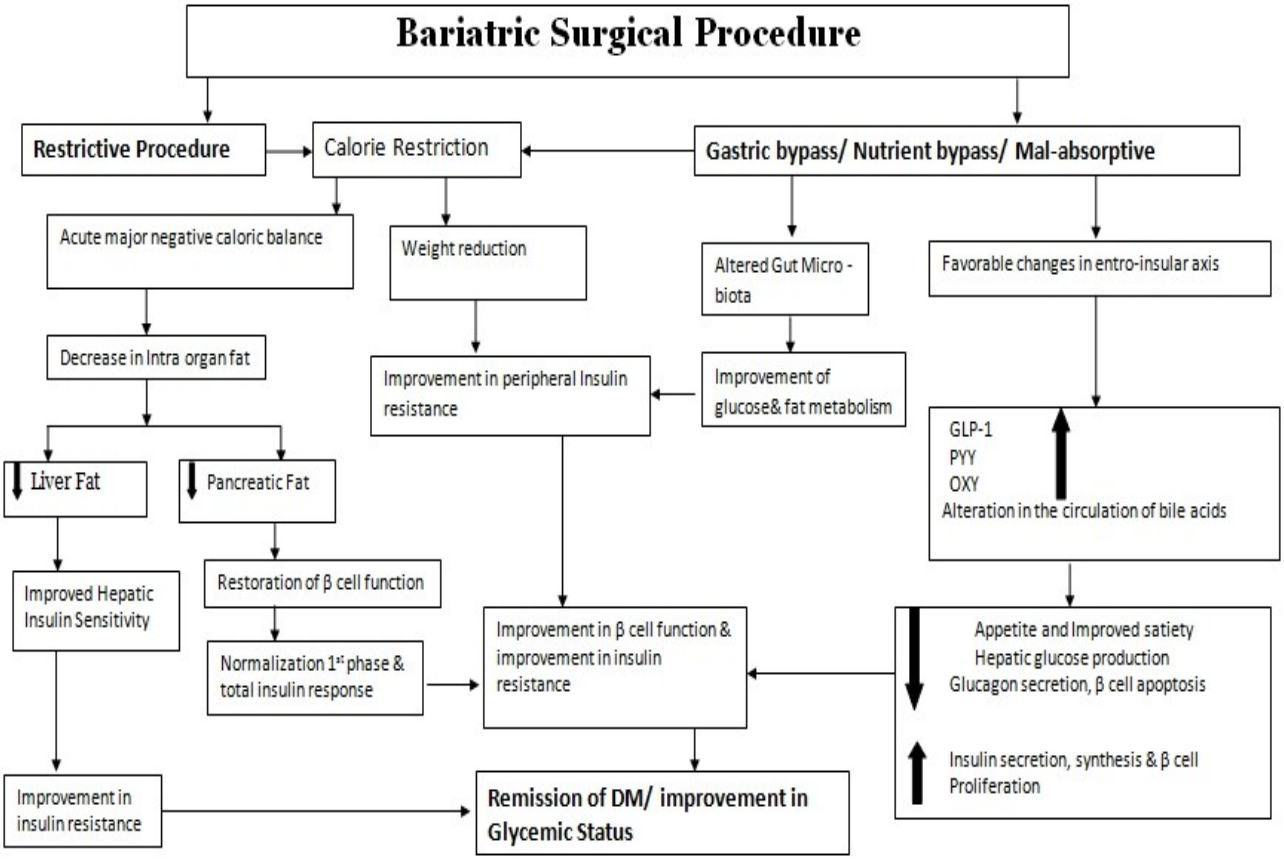

Figure 5: Role of bariatric surgery in T2 DM Remission

Effectiveness of bariatric surgery

Data from many observational studies as well as meta-analyses show that bariatric surgery is useful in marked improvement in diabesity parameters. The Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiently (STAMPEDE) trial investigators found that after the first year of randomization, gastric bypass and sleeve gastrectomy were superior to intensive medical therapy alone in achieving glycemic control and reducing cardiovascular risk factors [4]. The Stampede trial gives a 3-year follow up analysis of baratric surgery from a single centre. involving 150 obese patients in a 3-group randomized controlled design. The 3 arms of the Trial were: Intensive medical treatment group compared with sleeve gastrectomy or gastric bypass groups. The primary endpoint of HbA1c of less than 6% was attained by only 5% of patients in the intensive medical control arm while 38% of the patients in the surgery arm. Also the glucose lowering medication and insulin use was significantly reduced in the 2 groups of patients in the surgical arms. At 3 years, reductions in body weight, BMI, waist circumference, and waist-to-hip ratio were greater after gastric bypass and sleeve gastrectomy than after intensive medical therapy. There were also significant improvements in other diabesity parameters in patients of the surgical arms such as reduction of triglyceride levels and increase in high density lipoprotein levels. There was no excessive weight loss or hypoalbuminemia and no life-threatening complications or deaths in any of the groups.

Comparable results were reported in a more recent RCT with 5-year follow up data by Mingrone et al [3]. Remarkable improvements in the diabesity parameters and possible cardiovascular morbidity and mortality benefits make these clinical trials unique. The long-term follow up results of these major clinical trials should give us better insight into the morbidity and mortality benefits of metabolic surgery.

Even though obesity has been proposed to be cause for increased mortality due to various complications, it is still unclear with definitive evidence from RCTs whether weight reduction provides mortality benefit. Multiple retrospective cohort studies reported reduction in overall mortality in the surgery group compared to matched subjects in the control group [11,32-34]. Although it would be premature to conclude that metabolic surgery provides clear long-term mortality benefit without definitive evidence procured through multiple RCTs and meta-analyses, there are multiple studies showing the tendency towards beneficial effects [21,22,35].

Even though bariatric surgery in pregnant women was found to be associated with reduced risks of gestational diabetes and large-for-gestational-age infants as the beneficial effects, it was also associated with increased incidence of small-for-gestational-age babies, a shorter gestational length, and the probability of increased risks for stillbirth and neonatal death [36]. Therefore, increased surveillance during pregnancy and the neonatal period is necessary in women who underwent bariatric surgery.

Conclusions

Bariatric surgery or metabolic surgery has emerged as a very promising tool in our armamentarium in the battle against diabesity, an inevitable evil of the global obesity pandemic. Multiple observational studies, and recent RCTs, systematic reviews, and meta-analyses provide us amble evidence favoring diabetes surgery as the best option in patients diabesity. Limited availability, high costs and possibly immediate and long-term complications may restrict its use in day-to-day clinical practice. However, clinicians should always consider this excellent treatment option to their patients in the appropriate clinical context.

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