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INVITED DEBATE

Bariatric Surgery for Obesity and Metabolic Syndrome

Ramen Goel[1] · Madhu Goel[1] · Amrit Nasta[1] · Hemraj B. Chandalia[2]

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(Pros) Bariatric Surgery: The Most Effective Treatment for Obesity and Metabolic Syndrome

Ramen Goel · Madhu Goel· Amrit Nasta

Non-communicable diseases have overtaken infectious diseases as the predominant cause of deaths worldwide. Obesity is the single most important contributor to the burden of chronic diseases. Obesity is associated with multiple comorbidities like type 2 diabetes, hypertension, dyslipidemia, polycystic ovarian syndrome, malignancies, coronary heart disease, cerebrovascular accidents, etc., and studies have also established that weight loss is associated with reduced metabolic and cardiovascular risks associated with obesity[1].

Though lifestyle modification remains the most important intervention for weight loss, most studies show up to 5% weight loss[2] and more than 50% are reported to regain weight within 1 year[3]. High recidivism rate or "yo–yo dieting" results in sarcopenic-type obesity (low muscle mass), apart from worsening of obesity-related comorbidities.

Bariatric surgery introduced over 60 years back for weight control in morbidly obese individuals has gained wide acceptance worldwide. Bariatric surgery has proven effective for moderate to severely obese people to lose weight, besides inducing significant long-term remission of type 2 diabetes and improvement in other metabolic disorders[4]. A meta-analysis of randomized trials[5] showed % excess weight loss (EWL) for the bariatric surgery versus non-surgical groups was 75.3% (57.2–94.6) versus 11.3% (5.7–29.8), respectively; overall diabetes remission rates were 63.5% (38.2–100) and 15.6% (0.0–46.7) ($p < 0.001$). In our own study[6], excess weight loss at 3 years post-sleeve gastrectomy was 71.8% and 85.8% after gastric bypass with 80% and 91% type 2 diabetes resolutions, respectively.

Bariatric procedures are of various types but principally work by reducing meal size and also altering gut physiology[7]. Patients become full after eating a very small meal and lose weight over a period of 1–2 years. The commonly performed procedures include laparoscopic sleeve gastrectomy, Roux-en-Y gastric bypass and adjustable gastric band. Contrary to popular perception, most of these do not result in malabsorption. However, some recent and/or uncommon procedures like one-anastomosis gastric bypass and duodenal switch work by creating malabsorption of food, leading to weight loss.

Patient selection for bariatric surgery is determined based on body mass index (BMI) and comorbidities. For Asians, the criteria are BMI > 37.5 kg/sq.m without comorbidities, BMI > 32.5 kg/sq.m with significant comorbidities and BMI > 27.5 kg/sq.m for uncontrolled diabetics. Comorbidities include type 2 diabetes, hypertension, obstructive sleep apnea (OSA), polycystic ovarian syndrome (PCOS), gastroesophageal reflux disease (GERD), obesity hypoventilation syndrome (OHS) and even impaired quality of life. Contraindications include uncontrolled psychiatric illness, alcohol or tobacco addiction, etc.

Bariatric and metabolic are interchangeably used terms as the beneficial effects of bariatric procedures are not merely

Dr. Ramen Goel is the Director, Centre for Metabolic Surgery at Wockhardt Hospitals, Mumbai. Dr. Madhu Goel is the Bariatric Physician at Wockhardt Hospitals, Mumbai. Dr. Amrit Nasta is the Clinical Associate, Bariatric Surgery at Wockhardt Hospitals, Mumbai. Hemraj B. Chandalia is Director, Endocrinology, Diabetes & Metabolism, Jaslok Hospital and Research Center, Mumbai.

✉ Ramen Goel
ramengoel@gmail.com

Madhu Goel
drgoelmadhu@gmail.com

Amrit Nasta
amritnasta@hotmail.com

Hemraj B. Chandalia
denmarc100@gmail.com

[1] Centre for Metabolic Surgery, C-10, Wockhardt Hospitals, Agripada, Mumbai 400008, India

[2] Jaslok Hospital and Research Center, Mumbai 400026, India

due to weight loss. The mechanisms which lead to this metabolic effect include alteration of gut hormones, microbiome, bile acids and nervous system[7]. Recent findings have suggested that gut microbiota could regulate the host's energy metabolism, and that an alteration in the intestinal flora contributes to the development of metabolic disorders[7]. Gut bacteria is believed to play an important role in the synthesis and metabolism of bile acids which are increasingly recognized as an important contributor to glucose homeostasis[8]. The "hindgut hypothesis" states that glycemic control results from the expedited delivery of nutrient chyme to the distal intestine, enhancing a physiologic signal (GLP-1) that improves glucose metabolism. GLP-1, an incretin hormone, is secreted by L cells of the distal bowel in response to intestinal nutrients and stimulates insulin secretion. It also exerts proliferative and anti-apoptotic effects on pancreatic beta cells[9]. An alternative hypothesis is that the effect of some bariatric operations on diabetes depends on the exclusion of the duodenum and proximal jejunum from the transit of nutrients, possibly preventing secretion of a putative signal that promotes insulin resistance and type 2 diabetes ("foregut hypothesis")[9].

Outcomes of weight loss and comorbidity resolution have been shown to be superior to medications and lifestyle modifications in morbidly obese individuals in randomized trials. In the STAMPEDE trial[10] after 5 years of follow-up, changes from baseline observed in the gastric bypass and sleeve gastrectomy groups were superior to the changes seen in the medical therapy group with respect to body weight, triglyceride level, HDL level, use of insulin and quality-of-life measures ($p < 0.05$ for all comparisons). A study by Adams et al.[11] showed long-term weight maintenance, remission and even prevention of type 2 diabetes, hypertension and dyslipidemia 12 years after Roux-en-Y gastric bypass versus medical therapy. A meta-analysis by Ashrafian et al.[12] showed bariatric surgery offers a significantly greater improvement in BMI and obstructive sleep apnea than non-surgical alternatives. Similarly, Roux-en-Y gastric bypass is considered a curative surgery for gastrointestinal reflux disease. Other illnesses known to benefit after bariatric surgery include fatty liver/non-alcoholic steatohepatitis, joint pathologies and hypertension to name a few.

Polycystic ovarian disease (PCOS) is the most common endocrine disease affecting reproductive age group women with a prevalence of approximately 8%[13] while current estimates suggest that obesity is present in at least 30% of women with PCOS[14]. Women with PCOS are at increased risk of impaired glucose tolerance, type 2 diabetes mellitus and cardiovascular diseases.

Significant clinical improvements in PCOS have been shown with only 5% weight loss[14]. Unfortunately, adequate weight loss can be difficult to achieve and maintain, especially for the morbidly obese. Bariatric surgery is found to improve most of the PCOS associated problems including abnormalities of glucose/lipid metabolism, hirsutism, hyperandrogenemia and menstrual irregularities.[13] A meta-analysis by Skubleny et al.[14] showed reduction in PCOS incidence, within 1 year of bariatric surgery, from 45.6 to 6.8% ($p < 0.001$) along with significant reduction in hirsutism and menstrual irregularity. Furthermore, improved fertility has been shown to be a key reason women seek bariatric surgery, as weight loss prior to assistive reproductive technologies has been shown to significantly increase live birth rates among women with PCOS.

Most young women and family members are concerned about the impact of bariatric surgery on future pregnancies and fetal health. Obesity impacts maternal and fetal health adversely. A systematic review of 22 studies[15] showed gestational diabetes, preeclampsia, gestational hypertension, depression, instrumental and cesarean birth and surgical site infection to be more likely to occur in pregnant obese women compared with women with a healthy weight. Maternal obesity is also linked to greater risk of preterm birth, large-for-gestational-age babies, fetal defects, congenital anomalies and perinatal death. Even breastfeeding initiation rates are lower, and there is greater risk of early breastfeeding cessation in women with obesity compared with non-obese women. These adverse outcomes result in longer duration of hospital stay. It becomes crucial to reduce the burden of adverse maternal and fetal/child outcomes caused by maternal obesity. A meta-analysis[16] has shown a reduced risk of macrosomia, large-for-gestational-age (LGA) neonates and postterm birth but an increased risk of preterm birth and SGA neonates after bariatric surgery. Similarly, in another meta-analysis[17], women who had undergone bariatric surgery had significantly lower odds of gestational diabetes (OR 0.31; 95% CI 0.15–0.65), hypertensive disorders (OR 0.42; 95% CI 0.23–0.78) and macrosomia (OR 0.40; 95% CI 0.24–0.67). However, their odds of small-for-gestational-age newborns were increased (OR 2.16; 95% CI 1.28–3.66). No significant differences were recorded for cesarean, postpartum hemorrhage and preterm delivery.

Obesity is also associated with increased risk of breast and endometrial cancer. A prospective SOS study[18] showed bariatric surgery reduced the overall risk of female-specific cancers compared with the control group (hazard ratio = 0.68; 95% CI 0.52–0·88; $p = 0.004$). Separate analyses of different types of female-specific cancers showed that bariatric surgery was associated with reduced risk of endometrial cancer (hazard ratio = 0.56: 95% CI 0.35–0.89; $p = 0.014$).

As with any major surgery, bariatric surgery also has some potential but avoidable complications. Morbidly obese individuals are at a higher risk of anesthesia-related morbidities as well. With adequate preoperative preparation, optimization and procedure selection, complication

rates have reduced significantly. A meta-analysis by Chang et al.[19] showed mortality rate following anastomotic leak, myocardial infarction and pulmonary embolism was 0.12%, 0.37% and 0.18%, respectively. According to data from the IFSO-European Chapter Centre[20], postoperative complication rates for leak are 0.15–0.38%, stricture or intestinal obstruction are 0.07%. Mortality following bariatric surgery is usually within a range of 0.009–0.016% in typical obese patients. Long-term complications like protein malnutrition, GERD are seen in 0.02–0.03%. In our own study[6], we had no leaks, bleed, deep vein thrombosis or surgical mortality.

Bariatric surgery is the only means of providing long-term sustainable weight loss and significant resolution of comorbidities compared to non-surgical measures and lifestyle modifications. Apart from weight loss, surgery also significantly improves fertility, lowers pregnancy associated risks and improves overall quality of life. Thus, the burden of obesity on health can be managed by offering surgery not as the last, but as an early option to morbidly obese patients.

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(Cons) Bariatric Surgery—A Rarely Required Treatment of Obesity and Metabolic Syndrome

Hemraj B. Chandalia

Treatment of obesity has always been a very frustrating experience, both for the treating physician and patient. In this scenario, bariatric surgery emerged as the most effective therapy of obesity. The overall relapse rates in the management of obesity with conventional treatment were > 75% in the first one-year period after weight loss. The conventional treatment primarily involved a hypocaloric diet and increased physical activity with some help from anti-obesity drugs. Unfortunately, many anti-obesity drugs were withdrawn from the market soon after their introduction, some of them even after their use for a decade or more. This includes isomeride, sibutramine, rimonabant and many others. Most of them produce increased serotonin levels leading to the problem of pulmonary hypertension. Currently available drugs in India are only fluoxetine, orlistat (lipase inhibitor), topiramate (Off-label use in obesity) and GLP-1 receptor agonists (Liraglutide), thus limiting our ability to induce weight loss with drugs. Modification of lifestyle in Look AHEAD Study resulted in poor weight loss outcome, although certain cardiovascular benefits were reported (1).

In this debate, pros and cons of bariatric surgery as related to women's health are discussed.

Acute and Chronic Complications of Bariatric Surgery

The immediate complications of bariatric surgery occur in 0.2–1% of patients and include internal hemorrhage, infection and pulmonary embolism. These complications get less frequent with high-volume bariatric surgeons and with simpler operations like sleeve gastrectomy (SG) or adjustable gastric band (AGB). However, the more complex surgeries like Roux-En-Y gastric bypass (R-Y-GBP) and biliopancreatic diversion (BPD) which produce more weight loss and less relapses as compared to SG are accompanied by larger incidence of immediate postoperative complications (2,3).

An analysis of medical records of 538 morbidly obese subjects who underwent an R-Y-GBP showed an incidence of 9.6% early complications (2.6% internal bleeding, 1.1% intestinal obstruction, 3.2% peritoneal infection, 2.2% abdominal wall infection requiring hospitalization and 0.5% pulmonary thromboembolism). The mortality rate was 0.55%, mostly related to thromboembolism and advanced age over 65 years. Thus, bariatric surgery in postmenopausal women over 65 years of age has to be avoided or undertaken with extreme caution (4).

The chronic complications of bariatric surgery include nutritional deficiency of iron, B12, vitamin D3 and many others. The rapid weight loss experienced by patients of bariatric surgery creates a sense of well-being and exhilaration; thus, medical check-ups are often overlooked. Unfortunately, poor continuity of care characterizes Indian medical system. Specially, surgeons in India are trained to believe that their responsibility ends with a successful surgery, thus delaying diagnosis of chronic complications with disastrous consequences. A support system of nutritionist, endocrinologist and psychologist is not properly set up in bariatric surgery centers.

Bariatric surgery has to be undertaken cautiously in women of childbearing age (5) as metabolic changes emerging postoperatively are known to affect fetal development. Perinatal risk of complications like admission to neonatal intensive care unit (NICU), congenital malformations, small for gestational age (SGA), birth injury, low APGAR score (≤ 8) and neonatal mortality was compared in a cohort of 10,296 obese women between operated mothers and non-operated mothers. Infants from operated mothers had a higher risk of prematurity, NICU admission, SGA status and low APGAR scores. A comparison of mothers with operation-to-birth (OTB) interval of 2 years versus OTB interval of 4 years revealed higher risk of prematurity, NICU admission and SGA status in the group with shorter OTB interval.

Bariatric Surgery is Rarely Required

Insulin resistance is the basic pathophysiology of obesity and type 2 diabetes mellitus (T2DM). Bariatric surgery restores insulin sensitivity, but it can occur within the first day or two postoperatively, when weight loss has barely commenced (6). Medical starvation or a hypocaloric diet in the perioperative period is effective in reversing insulin resistance within a few days. Other health benefits like amelioration of hypertension, hyperlipidemia and metabolic control of T2DM set in and are sustained with a 6–10% body weight loss (7), an eminently feasible proposition.

In PCOS, 10% weight reduction resulted in restoring cyclicity of periods and normalizing FSH, LH and other hormonal parameters. Ovulation is improved with 13% weight loss. These beneficial effects of weight loss achieved by 6–10% weight loss are comparable to those achieved by bariatric surgery.

Pregnancy should be undertaken after 1–2 years of weight stabilization after bariatric surgery (8). Earlier pregnancies can result in low-birth-weight infants (5,9). Excessive maternal and fetal weight gain is reduced in post-bariatric surgery pregnant women. However, the same can be achieved by

restricting the total weight gain of mother by 8–10 kg at full term. This is possible by using a 1500 kcal diet, which is safe in pregnancy from a maternal and fetal standpoint.

In commercial weight loss clinics, some myths are being propagated, like the myth of "ideal body weight". This helps perpetuating dependency in such clinics and maintains the frustration level of the patient. Bariatric surgery creates the psychological picture of thin-fat women, who has set herself unrealistic weight loss goals and chases the same as an obsession. These women are also very cautious of their appearance and hence feel miserable after 30% body weight loss (the usual weight loss with bariatric surgery) as they have a haggard appearance now with sagging facial and abdomen apron of fat, thus necessitating multiple reconstructive surgeries.

Relapses Following Bariatric Surgery

The weight loss after bariatric surgery was seen to be very impressive but slowly reports of relapses started appearing (10). Most of the studies have reported relapses in about 50% of patients, the frequency being lower with R-Y-GBP and BPD as compared to SG. Fortunately, the weight gain did not reach the preoperative body weight but occasionally preoperative weights were achieved.

The mechanism of weight loss following bariatric surgery is under intense studies. Besides restricted calorie intake, there are many hormonal changes, e.g., decreased ghrelin and peptide YY levels, which may facilitate weight loss or make weight loss maintenance possible. Research into these mechanisms most optimistically may open new avenues of research into medical management which may be more effective and safe.

A longitudinal prospective follow-up of 782 obese patients post-bariatric surgery revealed maximum weight loss at 18 months postoperatively. Weight loss was no longer significant after 24 months and significant weight regain leading to surgical failure occurred at 48 months postoperatively in 18.8%. This was especially seen in super-obese subjects (11). A review of weight gain following sleeve gastrectomy described rates of weight regain ranging from 5.7% at 2 years to 75.6% at 6 years. The causes of weight gain were identified as incorrect initial sleeve size, sleeve dilatation, increased ghrelin levels, inadequate follow-up strategy and maladaptive lifestyle behaviors (10).

Conservative treatment of obesity is usually disappointing, but programs incorporating sustained counseling and behavioral therapy can be quite successful. We ran a program of Education and Empowerment for obesity at our center employing such intensive methods. In 13 patients undergoing a 3-month education program, the average weight loss was 5.2 kg (initial average weight 87.7 kg, at 3 months 82.5 kg). Interestingly, these patients continued to lose weight so that at a 27-month follow-up, an additional average weight loss of 3.4 kg was achieved. Although relapses on medical management are common, prolonged follow-up up to 3 years can produce higher success rates, as relapses get infrequent (12) probably due to the development of an effective adaptive behavior.

A six-month study in morbidly obese subjects compared intensive lifestyle intervention ($n = 60$) and conventional medical management ($n = 46$) with a bariatric surgery group ($n = 37$). As expected, intensive lifestyle intervention produced significantly more weight loss than conventional medical management. Notably, at the end of 2 years, 44.4% of intensive lifestyle group were no longer morbidly obese (13), thus proving to be an effective treatment for morbid obesity.

To summarize, bariatric surgery is a highly successful tool for weight loss but three important lines of evidence discussed above militate strongly against its use in majority of obese subjects.

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About the Author

(Pros) Bariatric Surgery: The Most Effective Treatment for Obesityand Metabolic Syndrome

About the Author: Dr. Ramen Goel, MS, FICS, FIAGES, FALS, an ex Associate Professor of Surgery at Grant Medical College and JJ Group of Hospitals, Mumbai, started therapeutic laparoscopy and GI endoscopy in 1990. A pioneer bariatric surgeon, he is founder member of Obesity Surgery Society of India (OSSI). He was President of All India Association of Advancing Research in Obesity (AIAARO). He was Co-Chief Editor of Journal of Obesity and Metabolic Research and is currently member of editorial boards of Indian Journal of Surgery (IJS) and Journal of Minimal Access Surgery (JMAS). He has contributed chapters in many surgical books and has multiple publications in peer-reviewed international journals to his credit. Director of Center of Metabolic and Bariatric Surgery, Wockhardt Hospital, Mumbai, he is President Elect (2019–2020) of Indian Association of Gastrointestinal Endo Surgeons (IAGES).

About the Author

(Cons) Bariatric Surgery- a rarely required treatment of obesity and metabolic syndrome

About the Author: Hemraj B Chandalia, Current Designation and Affiliation: Director, Endocrinology, Diabetes, Metabolism, Jaslok Hospital and Research Centre. Director, Dr Chandalia's Diabetes, Endocrine Nutrition Management and Research Centre. He has been on the Faculty of University of Alabama, School of Medicine (4yrs) and Grant Medical College, Mumbai (30yrs). He has authored 80 scientific papers and 30 books or contributions to books. He is Patron of Research Society for Study of Diabetes in India (RSSDI) and was editor of its journal, International Journal of Diabetes in Developing countries for 21 years. He was editor-in-chief of RSSDI Text Book of Diabetes, 3rd edition, 2015. Qualifications/Credentials: M.D., F.A.C.P.