EC ENDOCRINOLOGY AND METABOLIC RESEARCH
Review Article

Surgery is a Viable Longterm Option for the Treatment of Severe Obesity

Rajat Gusani*, Mohit Bhandari, MAL Fobi, Manoj Reddy, Prashant Salvi and Manoj Khurana

Department of Bariatric and Metabolic Surgery, Mohak Bariatric and Robotic Surgical Center, Shri Aurobindo Institute of Medical Sciences, Indore, Madhya Pradesh, India

***Corresponding Author**: Rajat Gusani, Research Fellow, Department of Bariatric and Metabolic Surgery, Mohak Bariatric and Robotic Surgical Center, Shri Aurobindo Institute of Medical Sciences, Indore, Madhya Pradesh, India.

Received: October 31, 2019; **Published:** January 31, 2020

Abstract

This Review focuses on obesity that is a world epidemic that is recalcitrant to non-surgical treatment and the only long-term option of management is surgical. Obesity is a chronic disease of excess fat storage due to a genetic predisposition and strong environmental contributions. Many treatment modalities have been proposed, however, bariatric metabolic surgery seems to be the only evidenced-based modality available that causes and maintains significant body weight loss over a long-term. Obesity has been implicated in multiple conditions such as cardiovascular diseases and diabetes amongst others. Though only 50 years old, bariatric metabolic surgery is under constant evolution. There are many procedures used for treatment of obesity. There is no one operation that is effective for all patients. We aim to illustrate surgery as a viable option in the treatment of the disease obesity.

Keywords: *Obesity; Metabolic; Surgery; Bariatric; Hypertension; Diabetes; Jejuno Ileal Bypass; Banding; Gastric Bypass; One Anastomosis Gastric Bypass; Mini Gastric Bypass; Surgical Procedures; Surgical Disease*

Introduction

The World Health Organization defines obesity as abnormal or excessive fat accumulation that presents a risk to health [1]. Grossly neglected, it remains one of recent times' most prominent public health problems. The health and lifestyle problems associated with obesity have been gradually gathering steam as the rate of obesity has multiplied dramatically in the past 15 years; approximately 2% to 10% in boys and 2% to 9% amongst girls based on recent studies [2]. If these growth trends are to be believed, approximately 38% of the world's population will be overweight and around 20% will be obese by 2030 [3]. Obesity is a serious health hazard with its social, psychological and economic implications. Though many treatment modalities and quick fixes have been at the forefront, bariatric and metabolic surgery seems to be the only modality available that causes and maintains significant body weight loss over a long-term.

Incidence of obesity

The first trends originating out of Europe and USA that obesity was reaching epidemic proportions was seen in early 2003 - 2004. Obesity gradually started being reported from the Asian countries as well. Today, overweight (25 - 30 kg/m^2) and obese (>30 kg/m^2) individuals account for twice the number of individuals whose BMI lies in the 18 - 25 kg/m^2 range in the USA [4]. In the late 1970s and 1980s, though the prevalence levels remained stable, there was a significant increase in childhood obesity. Studies done in 2003 - 2004 showed that prevalence had risen from 23% to 32%. The last decade has shown that the trend had leveled off at a prevalence of approximately

35%. In the USA, Hispanics and non-Hispanic African Americans had prevalence rates of 43% and 48% respectively, showing a skewed distribution [5].

In contrast, European studies showed a subtler trend. Participant countries in the EPIC (European Prospective Investigation into Cancer and Nutrition) study (Italy, UK, Netherlands, Germany, and Denmark) showed that obesity had increased from 13% to 17% [6].

India, at present, with its incredible over-burdened population is experiencing a rapid epidemiological transition. Poverty and under - nutrition, which were the problems of the past are being rapidly replaced by obesity; particularly in the densely populated urban areas. Prevalence rates have ranged from 7% to 32% and have been showing a gradual upward trend. India is ranked 3rd for the number of obese individuals in the world [7] (Figure 1).

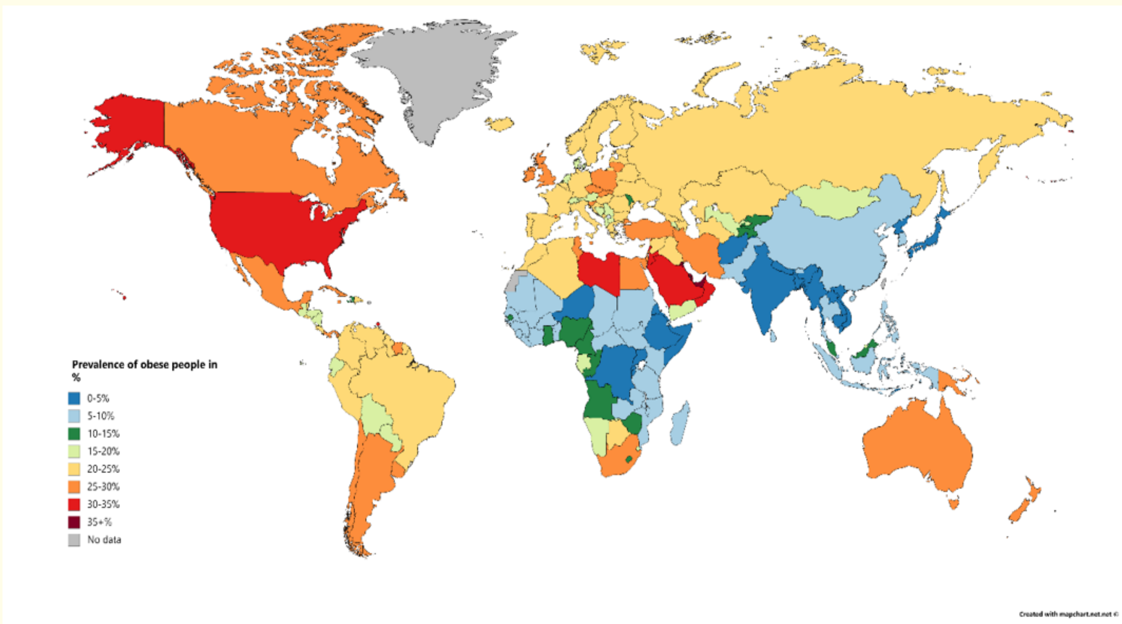

Figure 1

Methods to measure obesity

The most widely used method to measure obesity is the Body Mass Index (BMI). This is basically a weight - for - height ratio wherein the weight in kilograms is divided by the height in meters squared (Table 1). Its significant advantages lie in its quick and inexpensive nature of use. Factors such as age, sex and ethnicity are not considered. Additionally, its inability to measure fat directly is its major shortcoming, making it difficult to generalize its usage.

Another simple yet effective method of determining the severity of obesity is to measure waist circumference. This method is found to be a quick and acceptable predictor of obesity. It basically considers the fact that adipose deposition around the waist has a strong correlation with obesity related health problems. The technique involves measuring the circumference just above the iliac crests, making sure not to compress the skin too tight. According to values then obtained, patients can be classified as high or low risk (Table 2). The waist circumference may be combined with BMI to further classify risk ratio.

Classification	BMI (kilogram/m ²)
Underweight	< 18.5
Normal weight	18.5 - 24.9
Overweight	25 - 29.9
Obesity Class 1	30 - 34.9
Obesity Class II	35 - 39.9
Extreme Obesity Class III	40 - 49.9
Super Obese	50 - 59.9
Super Super Obese	> 60

Table 1

Gender	Low Risk	High Risk
Male	≤ 40 inches	> 40 inches
Female	≤ 35 inches	> 35 inches

Table 2

A Waist-to-hip ratio (WHR) Body shape may also be used to determine excess fat deposited. In addition to simply measuring weight circumference, the ratio has the additive effect of classifying patient according to their body shape: 'apple' or 'pear' shaped. The waist is measured just above the iliac crests and the hips at their widest point following which the values of the waist (inches) is divided by the hip (inches). The patient is then classified as Normal, Increased Risk or High Risk (Table 3).

Gender	Normal	Increased Risk	High Risk
Male	0.9 - 0.95	0.96 - 1	> 1
Female	0.7 - 0.8	0.81 - 0.85	> 0.85

Table 3

Skinfold thickness measurement is a simple and straight-forward measure of fat. The underlying principle being that subcutaneous fat deposition is directly proportional to the total body fat. The technique involves using specially designed calipers to measure fatty tissue in various sites of the body such as the lateral abdomen, biceps, triceps, chin and calf. Care must be taken to avoid ensnaring the underlying muscle. Multiple measurements are taken and an average value is obtained. An equation is then used to calculate the percentage body fat. The protocols set must be standardized and direct for every patient so as to prevent confounding values. Though simple, the method is strictly operator dependent and thus results may vary significantly. Presence of abdominal wall edema or Class III obesity may hamper the results.

Dual energy X-ray absorptiometry (DXA) is a method that is commonly used to determine bone mineral density for diagnosis of osteoporosis. Its application in the field of bariatrics was found to be highly advantageous in the measurement of fat content in the body. It provides one of the most accurate measurements. Two types of radioactive beams scan the body. One is absorbed more readily by fat than the other. After feeding the values through a processor, it is possible to differentiate the fat from other tissues and provide the percentage of body fat. DXA, though being considered gold standard, carries the burden of being expensive and unavailable at most centers.

Near-infrared interactance (NIR) is another method that uses a fiber optic probe and a digital analyzer to determine the total body fat composition. The patient's anthropometric measurements are fed into a computer following which a probe is placed at multiple sites on the patient's body. Light penetrates the tissue and reflects off of the bone back to the probe. Based on the amount of light reflected, the analyzer calculates a value of the percentage of body fat. The machine is inexpensive and easily available, though not being particularly reliable. Research is still required to establish the accuracy of this technique.

Underwater (hydrostatic) weighing is based on the fact that fat is less dense than other body tissues. Though providing accurate values, the equipment for such is available only in research institutes.

The air displacement plethysmography method of analyzing body composition utilizes a special enclosed chamber. Prior to entering the chamber, the person is weighed on a scale to determine the mass. The volume of air inside the chamber is then calculated. The patient then sits inside while sensors determine the volume of air displaced. This is used frequently in sports medicine. Though accurate, it is not suitable for patients with morbid obesity or those with claustrophobia.

Bioelectrical impedance analysis (BIA) is based on the principle that the more water the tissue contains, the faster electrical current is conducted through it. Thus, electrical current passes through body tissue and fluids (blood, urine, muscle) faster than air, bone or fat tissue. The equipment measures resistance and estimates body fat by combining measures with height, weight, gender, fitness level, and age. A low dose (500 to 800 micro-amp) electrical current passes through the electrodes and the body. The current is small so most people can't detect it.

Causes of obesity

In spite of the voluminous research into obesity, there still exists a void regarding the etiological factors of obesity. Obesity arises from an imbalance between the caloric intake and caloric expense, resulting in a positive balance of calories - stored in the body as adipose tissue.

Economic growth has been occurring in the developed countries. Developing countries have also shown a similar accelerated trend in obesity - a large surplus disposable income along with easy availability of low nutrition - 'fast' food. Previously, obesity had a direct correlation with the higher income groups, however, newer trends suggest that the contrary is true. Poverty, in fact, seems to have a direct link with obesity. Part of this is due to readily available, often nutrient - poor fast foods, along with their socio - cultural norms. There also seems to be an inverse relationship between education and obesity [8]. However, not all people living in the same obesogenic environment, exposed to the external factors described, have the same response. This goes to show that genetics also plays a significant role in the development of obesity. It can hence be concluded that there is a complex interplay between the genetic and external factors, each influencing the way the body uses its resources [9].

The role genetics plays in obesity is being intensely studied. A total of 58 possible gene loci have been identified that possibly contribute to obesity. These explain the inheritable causes of obesity. By 2008, progress in the field led to the discovery of eight monogenic genes and four polygenic genes: Fat Mass and Obesity Associated Gene (*FTO),* Proprotein Convertase Subtilisin/Kexin Type 1 Gene (*PCSK1*), Melanocortin-4 receptor *(MC4R)*, Catenin beta-1 *(CTNNBL1*). Defects in these eight genes, have been shown to lead to human monogenic obesity with hyperphagia as a common feature [10]. Recent studies also point to a key role of the central nervous system in regulation of body weight [11]. Although these studies have pointed out a key role of genetics, there seems to be an unprecedented rise of obesity in developed countries. This may substantiate that environmental factors have an equal, if not greater role in the development of the global obesity epidemic.

Factors such as a sedentary lifestyle, smoking and gestational diabetes have been found to have a major effect. Lack of physical activity, stress factors have been demonstrated to have an independent effect on obesity [12]. All of these, when combined with an increased caloric intake have an additive effect on the patients' weight. Parental lifestyle continues to influence the rise of childhood obesity. Over the years, a lot of research has been done to study the effect of modifiable factors on obesity, such as diet. Increased caloric intake seems to be causing the most harm. This, in turn, has led to a vast majority of bariatric procedures being focused on restriction or malabsorption of the caloric intake. Vast public health programs along with stringent measures, such as banning sodas in schools, have been implemented to tackle childhood obesity.

Several viruses have been implicated to have a role in obesity. Ad - 36 is one of the most studied [13]. It has been shown to have increased adipose deposition in animals. Studies in the human population have shown that obese children and adults have a higher viral load [14] - though large-scale studies are required to validate this claim (Table 4).

Individual	• Energy intake in excess of energy needs • Calorie-dense, nutrient-poor food choices (e.g. sugar-sweetened beverages) • Low physical activity • Sedentariness • Little or excess sleep • Genetics • Pre- and perinatal exposures • Certain diseases (e.g. Cushing's disease) • Psychological conditions (e.g. depression, stress) • Specific drugs (e.g. steroids)
Socioeconomic	• Low education • Poverty
Environmental	• Lack of access to physical activity resources/low-walkability neighborhoods • Food deserts (i.e., geographic areas with little to no ready access to healthy food, such as fresh produce/grocery) • Viruses • Microbiota • 'Obesogens' (e.g. endocrine-disrupting chemicals) • Obese social ties

Table 4

Sequelae of obesity

There exists a strong overlap between diabetes and obesity. Approximately 50% diabetic patients are obese, however only 20% obese patients are diabetic [15]. Obesity is associated with increased free fatty acids (FFAs) in the bloodstream [16], which promote the production of reactive oxygen species which is thought to be the main cause of insulin resistance. A diet rich in fatty acids is associated with a reduction in the hepatic levels of the antioxidant glutathione (GSH) and diminished activity of antioxidant enzymes [17]. As the pancreas works extensively, ultimately blood glucose levels begin to rise because of insulin insufficiency. Long-term complications of T2DM include cardiovascular diseases, stroke, peripheral vascular diseases, retinopathy, nephropathy and neuropathy [18].

Sequelae	Hypertension
	Dyslipidemia
	Heart and Vascular Diseases
	Cancer (Esophageal/colon)
	Respiratory Conditions (OSA)
	Liver Diseases (NASH)
	Gall stones
	Infection
	Psychological Conditions (Depression)
	Physical Disability
	Higher medical costs
	Mortality

Table 5

Obesity also has a significant role in the development of hypertension. Multiple pathophysiologic mechanisms are present that interact with one another, including insulin resistance, inflammation, oxidative stress, the sympathetic nervous system and the renin-angiotensin aldosterone system [19]. The interplay between these factors causes an imbalance in the hemodynamics of the body thus causing increased blood pressure. Obesity is also linked to elevated C-reactive protein levels, erythrocyte sedimentation rate, and plasminogen-activator inhibitor 1 and inflammatory cytokines such as TNF-alpha and IL-6 [20].

In terms of the effects of hypertension on the renal system, the activation of the renin angiotensin aldosterone system causes an increased cardiac output and retention of water. These lead to increased glomerular perfusion. This result in glomerulomegaly, podocytopathy, focal glomerulosclerosis, and proteinuria. Obesity is associated with the development of renal disease in addition to worsening of existing kidney disease.

Hypertension in obesity is also associated with remodeling. There is presence of endothelial dysfunction which is caused by increased sympathetic activity, activation of the RAAS system, inflammatory cytokines and oxidative stress. This leads to left ventricular hypertrophy, ischemic heart disease, cardiac fibrosis, and cerebrovascular disease. These sequelae are heightened with obesity.

Obesity is also linked to cancer development. In depth studies have estimated that approximately 20% of all cancers are caused by obesity. The most common cancers in obese people include endometrial, esophageal adenocarcinoma, colorectal, postmenopausal breast, prostate, renal, malignant melanoma, thyroid cancers, and leukemia. The mechanisms that promote oncogenic activity are unclear, however, many theories have been proposed. A positive caloric balance appears to promote cancer cell proliferation and tumor progression [21]. Diets rich in calories, animal fats and alcohol show a positive correlation whereas there is a significant low - cancer risk associated with diets with increased fruits, vegetables and high fiber intake. These have an effect on the levels of insulin, insulin-like growth factor-I and other inflammatory markers. Recent studies have shown that a low carbohydrate diet, associated with ketosis may be associated with partial remission in patients with cancer [22].

Excessive body weight is directly related to insulin resistance leading to increased pancreatic insulin secretion. These have shown to promote quicker growth and increased aggressiveness of colorectal, pancreatic, liver, breast and endometrial tumors [23].

Increased adipose deposition is also directly correlated with increased circulation sex hormones which is well documented to increase cancer development. There are increased levels of dehydroepiandrosterone (DHEA), its sulfate (DHEAS), Δ4-androstenedione, testosterone, estrone, and total estradiol, and low levels of sex hormone binding globulin (SHBG). These promote tumor proliferation and mediate the oncogenic markers, particularly breast and endometrium [24,25]. Estrogens, particularly, appear to be mitogenic, induce free radical DNA damage and induce genetic mutation in cells [26].

There is also evidence that obesity promotes secretion of proinflammatory molecules such as interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), leptin, resistin, retinol binding protein-4, plasminogen activator inhibitor-1 (PAI-1) and hepatic growth factor (HGF) amongst others and decreases secretion of beneficial substrates such as adiponectin and visfatin [27].

Obesity has also been linked to the development and progression of OSA, the prevalence being twice that of normal-weight adults. Studies have shown that patients who gain 10% of their initial weight are 6-times more likely to develop progression of OSA [28]. There is fat deposition at particular sites, specifically surrounding the upper respiratory tract, resulting in compression of the trachea leading to apnea. In addition, fat deposits around the thorax and upper abdomen reduces chest compliance. However, a complex relation exists between OSA and obesity with recent studies suggesting OSA itself is an etiological factor for obesity [29].

Obesity-induced hepato-steatosis and nonalcoholic steatohepatitis (NASH) have been classified as nonalcoholic fatty liver disease (NAFLD). These, along with the development of HCC, are well demonstrated to be related to obesity [30].

The development of gall stones has been associated with obesity. Increased hepatic secretion of cholesterol is an important feature in obesity. Bile becomes saturated with excess cholesterol secreted by the liver [31]. The gall bladder also has impaired motility which predisposes to the micro-aggregation of cholesterol crystals and stone formation [32]. Furthermore, rapid weight loss induces risk of development of gall stones because of increased biliary cholesterol, decreased secretion of bile salts and bile acid pool, reduced biliary emptying and increased secretion of mucin and biliary calcium [33].

Recent evidence suggests that an increase in BMI is directly related to the risk of infection. Adipose tissue produces pro-inflammatory and anti-inflammatory agents including adipokines, leptin and adiponectin along with cytokines and chemokines [34]. Adiponectin has the most potent immunosuppressive activity [35], whereas leptin affects cytokine production. Leptin also has a proliferative effect on T-lymphocytes and seems to be a protective agent of the immune response. Genetic defects of leptin in humans is associated with increased morbidity and mortality due to an increased susceptibility to infections [36]. Increased susceptibility to infections in obese patients may be related to decreased availability of arginine and glutamine, resulting in decreased tumor necrosis factor (TNF)α production and increased nitric oxide release. Additive effects from microvascular inflammation and thrombosis contribute to the morbidity.

Though obesity has been extensively studied, one of the most understudied aspect of the disease are its psychological aspects. Early studies had very conflicting results. Some found a positive correlation whereas others found the opposite. The first weighted study found that BMI in women was related to depression, suicidal ideation or suicide attempts, however men were unaffected [37]. In contrast, underweight men were more at risk for depression and/or suicidal tendencies.

Obesity also appears to be associated with an increased risk for venous thromboembolism. Data have suggested the risk of VTE increases with a rising BMI among the individuals who are overweight or obese [38]. A similar pattern is also seen with pulmonary thromboembolism [39].

Obesity results in physical limitations, such as walking, climbing, crossing one's legs, tying one's shoes, and performing the daily acts of living. Social consequences include clothing limitations, sexual limitations, and limits to various accesses. Economic consequences of obesity include denial of employment, restriction of career advancement and higher educational opportunities, cost of futile weight-loss modalities, cost of special clothes, and un insurability or high insurance premiums.

For most patients with obesity, multiple attempts have been made to lose weight, however, most of them have been unsuccessful. With the advent of newer-age fad diets such as the Atkins or Ketogenic diet, some patients lose weight but to sustain it over a long period of time is a major challenge. Patients tend to regain the weight - sometimes in excess of weight at the start of the weight loss program. Pharmacological intervention and behavioral modification also have a similar effect. Bariatric and metabolic surgery seems to be the only modality available that causes and maintains significant body weight loss over a long-term.

Brief history of bariatric and metabolic surgery

Currently, metabolic bariatric surgery provides the only viable option for sustained weight loss and maintenance. This is practiced in individuals with a BMI > 35 kg/m^2 with comorbidities and definitely for those with BMI > 40 kg/m^2. Bariatric surgery as a discipline is fairly young, about 50 years. It is under constant evolution with changes being suggested by stalwarts at regular meets. Surgeons at the Department of Minnesota reported the first operation, the jejuno-ileal bypass operation (JIB). The surgeons had observed that patients with a shortened small bowel length lost weight in spite of increased caloric intake [40].

Similarly, in the late 1960s, surgeons made another observation. Patients undergoing gastrectomy surgery for ulcers or cancer, lost weight post the procedure and maintained it for a long period of time. Thus, a new operation, the gastric bypass was born. The bypass remained popular, replacing the jejuno-ileal bypass due to its decreased morbidity and a comparatively controlled malabsorption [41].

The 1980s witnessed the first biliopancreatic bypass (BPB), popularly called the biliopancreatic diversion (BPD) or the Scopinaro operation. This was largely advocated throughout Europe. It had an additional advantage of maintaining the benefits of the jejuno-ileal bypass without its harmful malabsorptive effects.

The 1980s also saw the advent of multiple restrictive procedures such as gastroplasty and banding operations. They promised similar weight loss without the dumping side effects of the bypass procedures and no malabsorptive syndromes. These procedures were comparatively easy to perform as well. Taking that into consideration, it comes as no surprise that these procedures took a quick liking to by the surgeons and patients alike. These promises were short lived however due to quick weight regain and worsening of reflux symptoms.

The 1990s saw the return of the gastric bypass surgeries, though with various modifications, such as increased restriction with the banded gastric bypass (BGBP), popularly called the Fobi Pouch Operation [42] or with an increased malabsorptive component with a shortened common limb, the distal Roux-en-Y gastric bypass (DRYGBP). The BPD with the duodenal switch also started gaining acceptance in the USA during the 1990s. Most bariatric operations are currently done via the laparoscopic approach by surgeons. Newer modifications to this approach include: Single Incision Laparoscopic Surgery, Robotic Approach and Endoscopy.

Bariatric surgery, initially, was only appreciated for the weight loss effects. However, as the years have progressed and further studies being conducted, it has been established that these surgeries lead to a resolution of comorbidities such as type-2 diabetes, OSA, and hypertension to name a few. The results are varied with some reporting complete resolution and others reporting partial remission. What is for certain is that there is a decrease in the disease manifestation after the surgery. This resolution of comorbidities, along with the maintenance of a lower body weight, lead to a greatly increased quality of life. Over the years, there has been a steady increase in the number of bariatric surgeries being performed which makes it important for all healthcare professionals to be aware of the various options for obesity.

Mechanisms involved in weight loss and maintenance

Up until the early 90s, bariatric procedures were thought to be either restrictive or malabsorptive. Restrictive procedures are those in which the food intake is restricted by creating a small pouch at the proximal end of the stomach where the food enters from the esophagus. This leads to rapid satiety and therefore reduced intake. Malabsorptive bariatric procedures limit the amount of nutrients the body absorbs by bypassing portions of the small intestine. The degree of malabsorption varies according to the length of the small intestine bypassed. The more the bypassed small intestine, the more effective the weight loss. Today, we have come to appreciate that restriction and malabsorption are just part of myriad of mechanisms that are involved in weight reduction after surgery. Known mechanisms responsible for weight loss and maintenance include:

- **Restriction: Reduced food intake:** Due to the smaller size of the pouch created, patients tend to feel satiety faster than usual. This in turn leads to them consuming smaller frequent meals - which decreases the caloric effect and leads to weight loss. This effect is further increased with the use of a band which helps to increase weight loss and maintain the loss over a longer period of time. Eating behavior post bariatric surgery is a factor involved in weight loss. On follow up, patients report that they feel less hunger episodes and have a lower food intake to reach satiation.

  Patients who are non - compliant, compensate the restriction by consuming lower amounts of high - calorie foods.

- **Gastric emptying:** Quick passage from the stomach to the small bowel, fast gastric emptying, results in the ileal break thus reducing food intake and resultant weight.
- **Macronutrient malabsorption:** The length of the common channel after surgery determines the extent of malabsorption. Studies have shown that a minimum of 300cm of the common channel is required to prevent serious malabsorption. As most of the absorptive small bowel is bypassed, caloric absorption is limited.
- **Vagal signaling to the hypothalamus:** The Vagus nerve is a key conducting system between the gut and brain and plays a major role in regulation of food intake. Most of the gut hormones exert some part of their physiological effects through the vagus. The arcuate nucleus of the hypothalamus has 2 groups of neurons that have paradoxical effects. One of the group acts to decrease food intake and increase catabolism. The other has the opposite effect. The peptides secreted include neuropeptide Y, agouti-related protein (AgRP) and γ-aminobutyric acid. Food reward mechanism is one that has gained significant attention. Pre-surgery studies show that consuming calorie rich meals leads to activation of the orbito-frontal cortex and amygdala - which results in the patient feeling happier. Post bariatric surgery, there was a significant decrease in the threshold for this activation [43]. Though evidence regarding the interaction of these peptides is yet unclear, recent evidence suggests that it could have a significant role to play.
- **Plasma glucagon - like peptide-1 (GLP-1) and peptide YY (PYY) levels:** GLP-1 and PYY are distal gut peptides involved in regulation of hunger and appetite suppression. Both are produced by 'L-Cells' in the jejunum and ileum. Post metabolic surgery, there is rapid delivery of nutrients into the small bowel. This stimulates secretion of these hormones leading to satiety. Additionally, both of these gut peptides increase glucose absorption by the intestinal glucose metabolic pathway - leading to positive feedback to insulin and further GLP-1 secretion. Studies have been conducted showing a postsurgical rise in both these hormones further supporting the claim [44].
- **Plasma ghrelin levels:** Ghrelin is secreted from gastric and duodenal entero-endocrinal cells. Ghrelin acts by increasing hunger. It is one of the few hormones that show a decrease in its concentration post-surgery. There are doubts as to the extent of effect ghrelin levels have after metabolic surgery, however it can be concluded that, though limited, ghrelin levels do affect the outcome after surgery [45].
- **Cholecystokinin (CCK) levels:** Another primary peptide secreted from the duodenum is cholecystokinin. CCK acts by promoting gall bladder contraction, increasing gastric emptying time and increasing satiety. Because of rapid delivery into the small bowels after surgery, CCK levels have also shown an increase immediately after surgery. This, however, may have only a contributory effect [46].
- **Leptin levels:** Leptin is a hormone directly related to obesity and fat deposition. It is found in abundance in human adipose tissue and is also produced in small amounts from stomach, mammary epithelium, placenta and heart. Its receptors are highly abundant in the hypothalamus. In humans, leptin acts to reduce food intake and induce energy expenditure. Studies have demonstrated that after bariatric surgery, there is a rise in leptin levels [47].

- **Bile acid levels:** Changes in the levels of bile acids and salts in the gut and bloodstream have been implicated in the reduction of blood glucose levels and increased post prandial fullness after surgery, especially gastric bypass. They act through Takeda G Protein-Coupled Receptor 5 (TGR5) receptors, nuclear farnesoid X receptor (FXR) receptors and fibroblast growth factors which act on the hypothalamus to exert their effects. Detailed studies are yet to be published; thus, their exact role is yet to be determined [48].
- **Gut microflora:** The role of gut microflora in obesity has generated much interest. Obesity results in colonization of the gut by unfavorable organisms such as *Prevotellaceae, Archea* and *Firmicutes*. These organisms are more efficient at harvesting energy from food and converting them into fat. Multiple studies have shown that there is a decrease in these bacterial clusters after surgery and an increase in *Prevotella* ratio and γ-proteobacteria. These changes are largely due to changes in diet composition, pH and bile flow [49].
- **Energy expenditure:** Human and animal studies have shown that there is an increased thermogenesis and diet - induced energy expenditure after bariatric surgery. This can be corelated with an increase in bile acid after surgery, which themselves control energy expenditure. However exact mechanisms are yet to be determined [50].
- **Dumping syndrome causes food preferences:** Though bariatric and metabolic surgeries lead to an overall decrease in the caloric intake, certain patients have an increased predisposition to specifically avoid certain foods rich in sugars or carbohydrates. This is particularly true after gastric bypass - as this leads to 'dumping'. This phenomenon occurs when there is a rapid increase in calorie rich foods in the small bowel - leading to secretion of large quantities of juices into the small bowel causing hypercontractility of the bowel associated with tachycardia, sweating and feeling of unwellness. In extreme cases this is associated with release of insulin ultimately leading to hypoglycemia - causing severe symptoms of sweating and unwellness. Patient then self learns to avoid eating these foods - leading to further weight loss.

Metabolic and bariatric procedures

Jejuo-ileal bypass (JIB) (Figure 2)

The JIB was one of the first operations used for obesity. The principle of the JIB is reduced caloric absorption due to decreased exposure of ingested foods to the digestive juices in the bowel and the absorptive surface of the small bowel. The average small bowel length being about 550-cm long, the surgery leaves only about 40 cm of small bowel exposed to the ingested food. This shortened length results in a rapid transit time of food from the stomach to the colon. Because of the rapid transit time, frequent liquid stools are a common occurrence with the procedure. The combined decreased intake and malabsorption result in weight loss and maintenance. The JIB results in loss of about one-third of the initial weight or 60% excess weight loss in about 80% of the patients [51]. Complications from JIB are significant and have resulted in the procedure being completely abandoned. These include frequent loose stools or diarrhea with the associated electrolyte imbalance of potassium, magnesium, and calcium. The frequent stools result in anal excoriation, hemorrhoids and dehydration. Kidney stones and the associated nephropathy due to oxaluria are common. Cirrhosis is the most lethal complication from the JIB thus these patients must be monitored routinely with liver biopsy. The insipient liver problems are due to bacterial overgrowth in the bypassed segment of the small bowel, a syndrome called bypass enteritis. These bacteria produce toxins that are injurious to the liver, brain, skin and generalized myalgia. Complications such as hypoproteinemia, hypokalemia, hypocalcemia, hypomagnesaemia and hypovitaminosis are common. There was a moratorium on performing the JIB in 1977 and this operation is very rarely used.

Biliopancreatic diversion (BPD) (Figure 3)

The BPD is a modification of the JIB. This operation, first reported by Scopinaro [52] from Italy in 1979 as the biliopancreatic bypass, consists of a 200 - 250-cc horizontal gastric pouch, a distal gastrectomy and closure of the duodenal stump, a gastroenterostomy with a 250-cm Roux limb, and an anastomosis of the biliopancreatic limb to the Roux limb 50 cm proximal to the ileocecal junction. This operation has both limbs, with ingested food in the Roux limb, and bile and pancreatic juices in the biliopancreatic limb. This minimizes the bypass enteritis of the JIB and prevents the insipient hepatic failure due to the bypass enteritis. The incidence of nephropathy is markedly

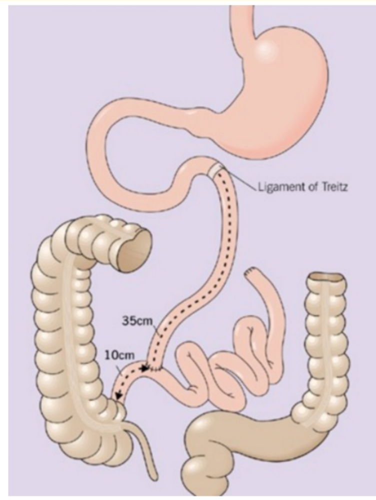

Figure 2

reduced in this operation, and the increased bowel length significantly reduces the incidence of diarrhea and its sequelae. Protein malnutrition, and calcium, iron, magnesium, and vitamin deficiencies have to be closely monitored in patients with this operation. Side effects such as passage of voluminous odorous stools have limited the use of this operation. %EBWL achieved after the procedure was between 74% - 77% at 10 years [53].

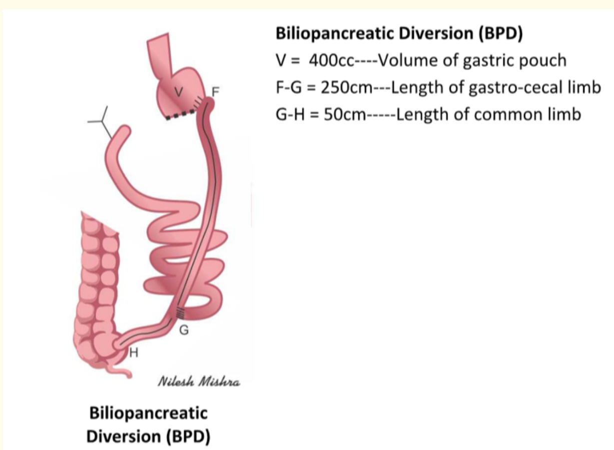

Figure 3

Biliopancreatic diversion with a duodenal switch (BPD-DS)-In short, the duodenal switch (DS) (Figure 4)

This was first described by Hess in 1988. The operation was a pylorus-preserving procedure that avoided the dumping syndrome, characteristic in other gastroenterostomy operations and decreased the occurrence of marginal ulcers. The BPD-DS has since been popularized by Marceau., *et al* [54]. The operation consists of a sleeve gastrectomy, preserving the pylorus, dividing the duodenum just beyond the pylorus, a duodeno-ileostomy with a 250-cm Roux limb and a long duodeno-biliopancreatic limb that is anastomosed to the Roux limb 100 cm from the ileocecal junction just as in the BPD. Gaining gradual acceptance throughout the world, it is commonly being performed all over. The incidence of dumping and marginal ulcers is greatly reduced. As with all malabsorptive procedures, monitoring is a must for calcium, iron, magnesium, vitamins, and protein deficiencies. However, this operation is characterized by the same frequent voluminous and malodorous stools, flatus, and body odor and bloating syndrome. It does result in about 70% long-term excess weight loss in more than 90% of the patients. It also achieves > 90% Type II Diabetes resolution [55].

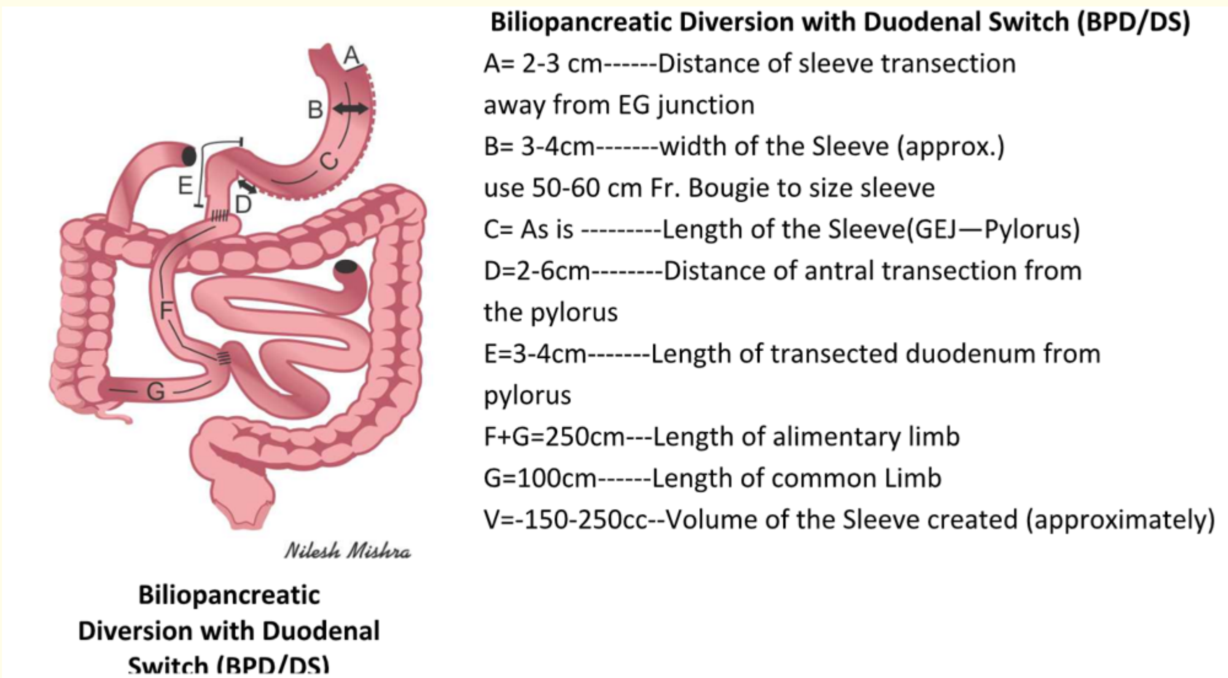

Figure 4

SADI-S (Figure 5)

The Single Anastomosis Duodenal/Sleeve Ileal Bypass is a modification of the biliopancreatic diversion with the duodenal switch. It is being performed throughout parts of Europe, though hasn't gained traction with US bariatric surgeons. It involves anastomosing the ileum approx. 300cm from the ileo-cecal junction to a transected proximal duodenum attached to a created sleeve [56]. Being a combined procedure, its major advantage lies in the fact that it negates the effect of dumping and decreases the incidence of marginal ulcers. As with all malabsorptive procedures, monitoring is a must for calcium, iron, magnesium, vitamins, and protein deficiencies. However, this operation is characterized by the same frequent voluminous and malodorous stools, flatus, and body odor; and bloating syndrome. It does result in about 70% long-term excess weight loss A fear with these surgeries is injury to the portal triad and duodenal stump leaks, which are very difficult to manage. The procedure is also technically demanding. Long-term results are pending however short-term results have provided good results [57].

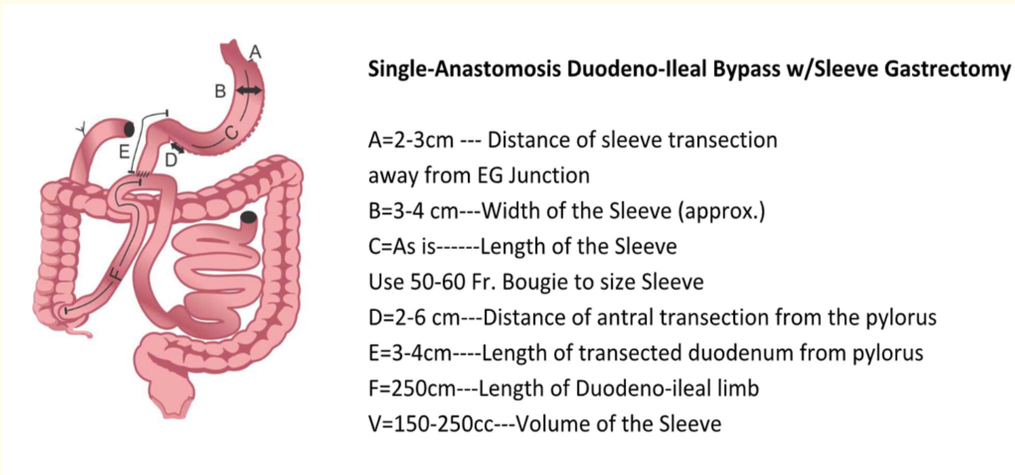

Figure 5

Gastroplasties (Figure 6)

There are two gastroplasty operations that were widely used in the 80s and early 90s for the treatment of obesity: vertical banded gastroplasty (VBG), introduced and popularized by Edward Mason [58]; and silastic ring vertical gastroplasty (SRVG), popularized by Henry Laws [59]. Both operations were preceded by various gastroplasties: horizontal gastroplasty, vertical stapling, gastric partitioning and horizontal gastroplasty with a Marlex band. Kroyer was the one who introduced the use of a nonabsorbable, reinforced stoma to prevent dilatation of the stoma in gastric-restrictive operations. Surgeons were quick to adapt these procedures because of their simplicity, less invasiveness, no rerouting of the gastrointestinal tract, few complications, no malabsorption and easy reversibility. Both gastroplasties were performed by stapling the stomach vertically to create a 30cc pouch. Initially the stomach was kept in continuity, however because of long term development of gastro-gastric fistulas, the staple lines were then transected. The small pouch restricts food intake and thus caloric intake. These procedures were introduced with the promise of providing results equal to the JIB and Roux -en-Y Gastric Bypass (RYGB), however in the long term there were multiple problems associated with them such as de novo GERD and weight regain in the long term. In view of these, the procedures are not currently in use. Both gastroplasties were performed by stapling the stomach vertically to create a 30cc pouch. Initially the stomach was kept in continuity, however because of long term development of gastro-gastric fistulas, the staple lines were then transected. The small pouch restricts food intake and thus caloric intake. A problem with gastroplasties is 'food-learning'. The patients learn what and how to eat - which results in them consuming high caloric fluids and semi solids for easier transition through the newly created pouch and stoma. This eventually results in weight regain.

Gastric banding (Figure 7)

The first band for weight reduction was placed by Wilkinson. However, Kolle, Molina and Kuzmak popularized the clinical use [60]. Gastric banding involved placing a ring around the upper stomach that created a small pouch which expedited the feeling of satiety. Its rapid acceptance in the scientific community was mainly due to the fact that it was comparatively a technically less demanding procedure with decreased operative risk, shorter hospital stays and an early recovery. However, complications such as band migration, erosion, pouch dilatation, GERD coupled with inadequate weight loss and weight regain in a significant number of patients led to fewer and fewer surgeons using the adjustable band.

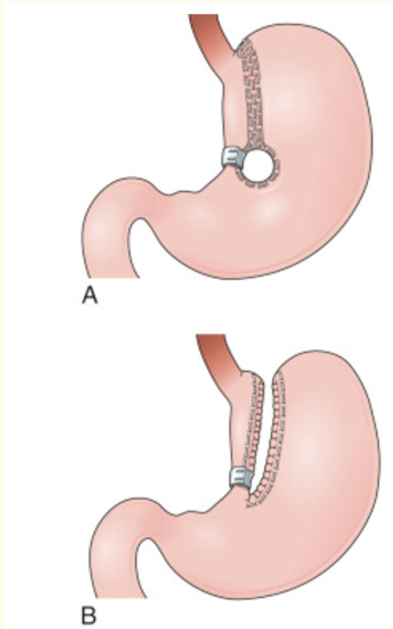

Figure 6

Figure 7

Gastric plication (Figure 8)

Greater curvature plication (LGCP) is a restrictive bariatric procedure that is used by some surgeons for the treatment of obesity. Gastric plication does not entail the use of either staples or any foreign body and so is one of the most cost-effective bariatric metabolic procedures. It is not a commonly performed procedure. It involves suturing the greater curvature of the stomach with 2 rows of 8 - 10 extra mucosal interrupted 2-0 polyester sutures starting approximately 3 - 5 cm from the pylorus and continuing proximally towards the angle of His. Polypropylene sutures have also been used. It is a purely restrictive procedure with the aim of decreasing the stomach capacity Complications have been reported which include nausea, vomiting, and micro leaks from the suture site. The long-term benefits of the procedure places it somewhere between the adjustable gastric band and the sleeve gastrectomy.

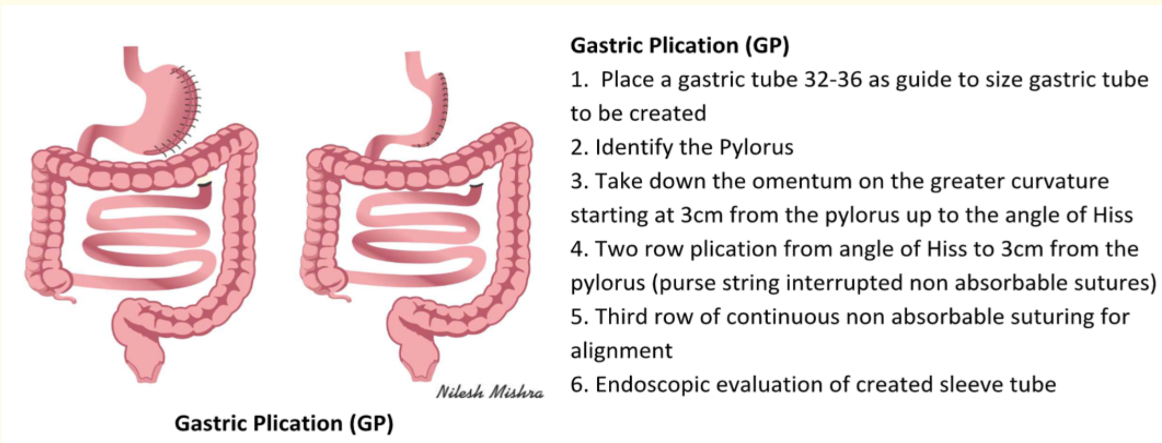

Figure 8

Sleeve gastrectomy (Figure 9)

Sleeve gastrectomy (SG) was initially conceived and first described in 1988 by Hess as the restrictive component of the BPD-DS and was later described as a 1st step surgery in patients with super obesity and high-risk patients to be followed by conversion to a gastric bypass or BPD-DS when the patient has lost some weight or when the risk of a complicated operation are markedly reduced. However, it was observed that many patients underwent significant loss of weight with acceptable resolution of their comorbidities after the 1st step and there was no need for the 2nd stage operation. This led to the use of the sleeve gastrectomy as a standalone procedure. The procedure involves separation of the greater omentum from the greater curvature from the left crus to approximately 2 - 5 cm from the pylorus. A stapling device is then used to create a sleeve over a 36F-40F bougie. Many surgeons have started placing a band over the sleeve to prevent weight regain and achieve greater weight loss. In addition to creating a restriction of food, it also induces anorexia through removal of the ghrelin producing cells located in the fundus. The restrictive component is a combination of the smaller capacity of the sleeve, low distensibility and increased intraluminal pressure within the sleeve. Recently observed phenomenon such as alliesthesia is based on the observation that repeated pleasant gustatory stimuli turn into unpleasantness in the process of satiation. Ghrelin levels are also markedly reduced in addition to increased PYY levels leading to greater appetite suppression. The advantages of the procedure lie in its technical simplicity, no major changes in anatomy, pyloric preservation, no malabsorption and easy convertibility to a gastric bypass. Staple line leaks and bleeding have been reported with the procedure but have been observed more in the early learning curve of the surgeon. In terms of a primary surgery, the sleeve gastrectomy has proven to be a safe procedure with good medium term and long-term efficacy. It is currently the most common bariatric procedure performed worldwide. Some surgeons place a non-adjustable ring around the proximal pouch of the sleeve to enhance its weight loss and maintenance effect [61] (Figure 10).

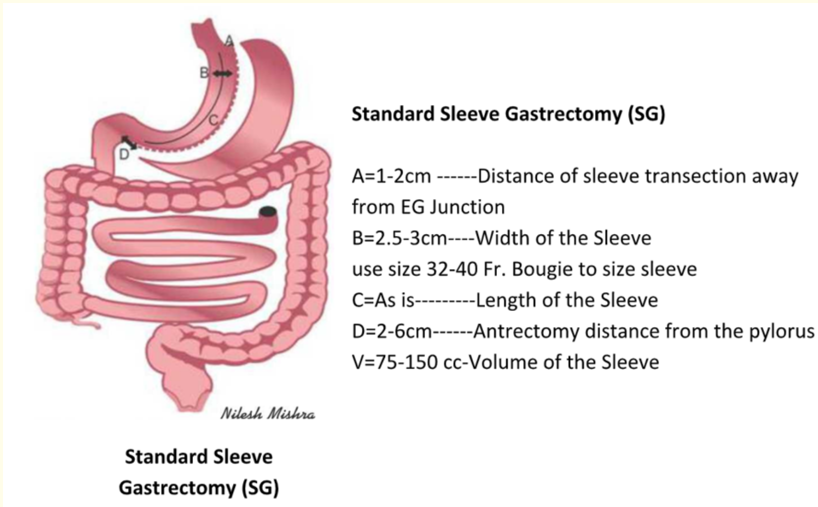

Figure 9

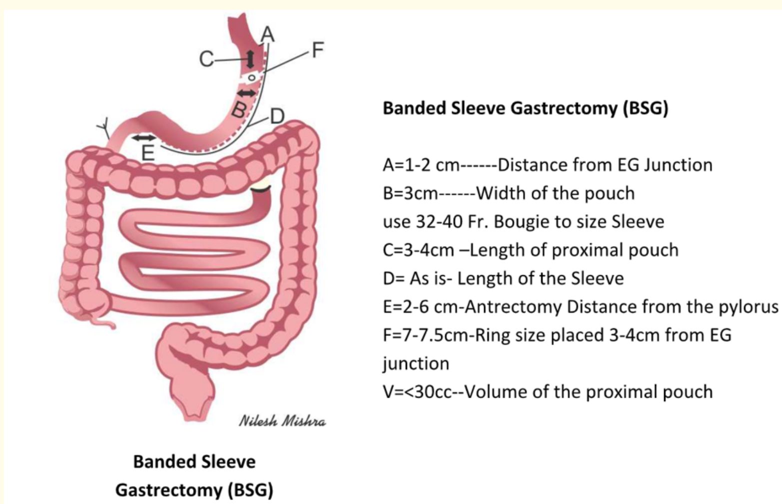

Figure 10

Gastro-Clip (Figure 11 and 12)

Though initially introduced in 1985 [62], the procedure never gained mainstream acceptance. Multiple modifications were made to the procedure. At present, a vertically placed clip is used. This clip is a silicone-covered clip with a titanium backbone that has an inferior hinged opening which separates a medial lumen from an excluded lateral gastric pouch. This inferior opening provides an outlet for the gastric juices from the fundus and the body of the stomach into the distal antrum with GI continuity. The mechanism is similar to a regular sleeve gastrectomy. The advantages of this procedure lie in the fact that it is completely reversible and the clip is easily removable.

The safety profile of it is also immense as it possesses no risk of anastomotic leak and negligible probability of bleeding. There is also no chance of kinking leading to obstruction. There are no long-term studies reported with the current gastro-clip.

Figure 11

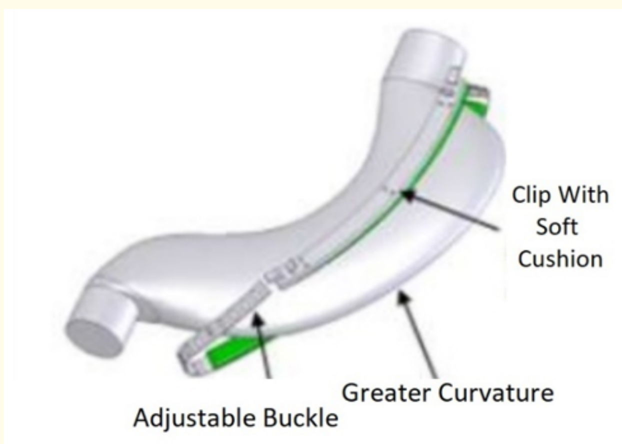

Figure 12

Gastric bypass (Figure 13)

Mason and Ito reported the first series of bypass operations that could be used for obesity [41]. They observed that patients who had undergone a partial gastrectomy for other causes, lost significant amount of weight. The surgery described by Mason involved transecting the stomach into a small proximal pouch that maintained continuity with the esophagus and a distal remnant stomach that had its continuity with the duodenum. The gut integrity was maintained by attaching a loop of the jejunum (approximately 2 feet from the

Duodeno-jejunal junction) to the proximal pouch. The gastric bypass has undergone several evolutions. The pouch is reduced to less than 30cc, made vertical on the lesser curvature and the bowel continuity is done with a roux limb. The operation is done laparoscopically. The weight loss is greater than 50% in more than 75% of the patients. The gastric bypass has been documented to maintain weight loss for as long as 20 years. There is good resolution of diabetes and hypertension after the gastric bypass. The Gastric bypass is the gold standard of bariatric operations. Untoward outcome after the gastric bypass include weight regain in a subset of patients, occasional vomiting, nausea, dumping syndrome, anorexia, weight loss failure, excessive weight loss, marginal ulcers, bile reflux gastritis of the pouch, gastritis of the bypassed stomach, afferent limb obstruction, acute gastric dilatation and blow out, pouch dilatation, stoma dilation, internal hernia, micro mineral and vitamin deficiencies.

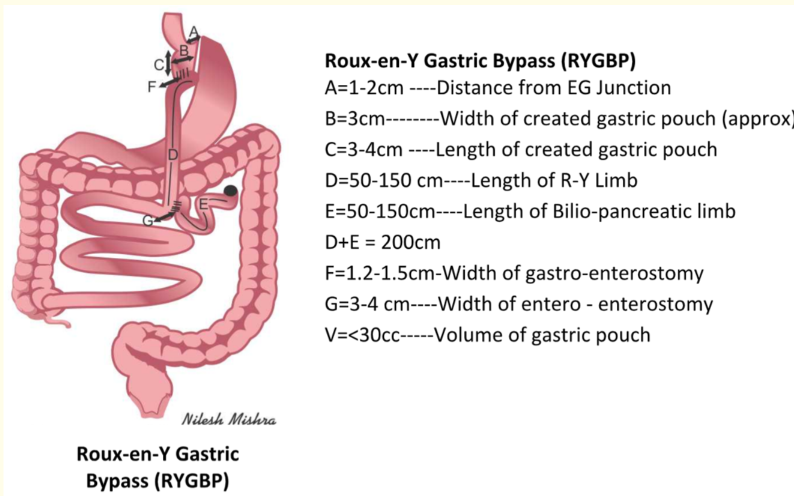

Figure 13

Banded gastric bypass (Figure 14)

The banded gastric bypass, popularized by Fobi [63], is a modification of the gastric bypass that has a band around the vertical pouch. This band addresses the problem of weight regain and pouch dilatation seen with non-banded procedures. The band used in the Fobi Pouch operation is typically made of silastic tubing with a length of approximately 6.5 to 7.5 cm. Many surgeons, though initially skeptical about using the band, have come to realize its potential in the long run, thus leading to gradual acceptance. Complications from the band include erosion, slippage amongst others. Band erosion is easily managed by doing an endoscopic removal or observation for self - extrusion. The weight loss with the banded gastric bypass is more than 70% in more than 90% of the patients.

Distal Roux-en-Y gastric bypass

Distal Roux-en-Y gastric bypass (DRYGP) is a gastric bypass with a 50 - 75 cm roux limb and a 250-cc alimentary limb. This operation was influenced by the work of Scopinaro with the BPD. Because of the comparatively shortened common channel, there was more than 80% excess weight loss, however, this also led to high incidence of protein calorie malnutrition and malabsorption of micronutrients. Though now not commonly favored as a primary procedure, it has gained popularity as a revision procedure [64]. Multiple modifications have been made to the procedure with different limb lengths to increase the weight loss accordingly. Complications from the DRYGBP include protein malnutrition, frequent watery and malodorous stools and flatus, peculiar body odor, anal excoriation, gas bloating syndrome, and increased incidence of micro nutrient deficiencies.

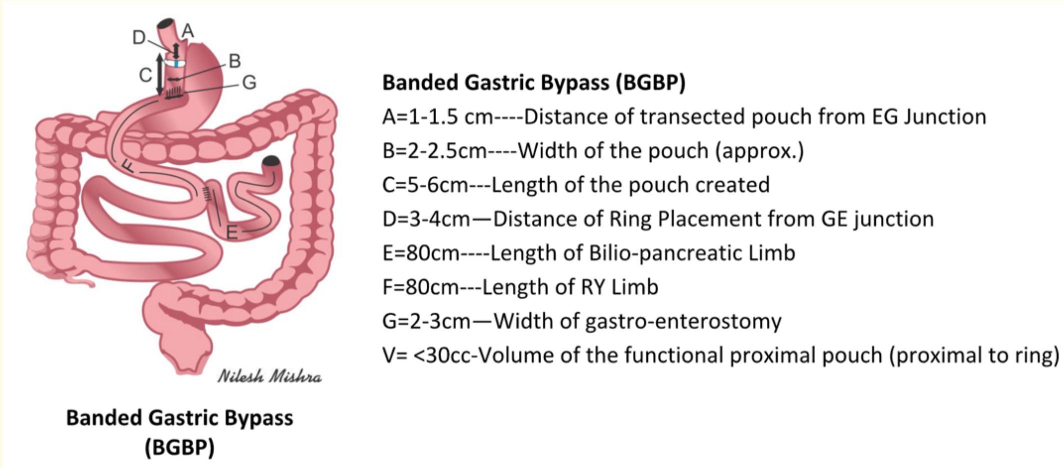

Figure 14

One anastomosis gastric bypass (Figure 15)

The OAGB/MGB is a bypass with an approximately 150 - 350 cm bilio-pancreatic limb (from the duodeno-jejunal junction) anastomosed to a 12 - 18 cm vertical lesser curvature tubular pouch. The longer vertical pouch was believed to help in decreasing symptomatic bile reflux. It was first described by Rutledge in 2001 [65]. The OAGB is safe, effects good weight loss, is easy to perform, has a short operative time, minimal blood loss, alleviates the need for ICU stay. It is also easy to reverse, has few adhesions, no internal hernias and has a low failure rate. Though initially bogged down by reports of bile reflux and marginal ulcers in the USA, it is now gaining thorough traction with majority of these. The procedure is still not accepted by many national societies. The Italian and British Societies have given it partial acceptance. This procedure continues to polarize the scientific bariatric community with a large number of bariatric surgeons considering it to be a modification of the outdated loop gastro jejunostomy with bile reflux, marginal ulcers and long-term risk of neo-carcinomatous conditions being the primary concerns. Its proponents claim the opposite with the advantages greatly outweighing the disadvantages and the lack of substantial evidence laying weight to the claims. It is also now widely acknowledged that the weight loss and resolution of type-2 diabetes mellitus is similar, if not better than with gastric bypass [66]. Some surgeons place a non-adjustable ring around the OAGB pouch which show similar advantages as in the banded gastric bypass. There are however concerns about the incidence of esophageal bile reflux, marginal ulcers and protein caloric malnutrition after OAGB, which still have to be resolved.

Endoscopic procedures

In recent years, multiple newer endoscopic techniques have emerged that can be classified into space occupying devices (intragastric balloon, transpyloric shuttle), restrictive procedures (ESG), malabsorptive procedures (D-J bypass liner), regulation of gastric emptying time (Intragastric botulinum toxin, electric stimulation) and other such as aspiration therapy.

Endoscopic sleeve gastroplasty (ESG) (Figure 16 and 17)

Bariatric endoscopy has emerged as a forerunner for nonsurgical treatment of obesity, providing a treatment option for weight loss and associated comorbidities. Endoscopic Sleeve Gastroplasty is a restrictive procedure that involves gastric plication using polypropylene sutures that are applied using a double - channel flexible endoscope system such as the Apollo Overstitch device. This is guided through a flexible esophageal overtube with carbon dioxide gas insufflation. The chief aim of the procedure is to convert the J-shaped stomach

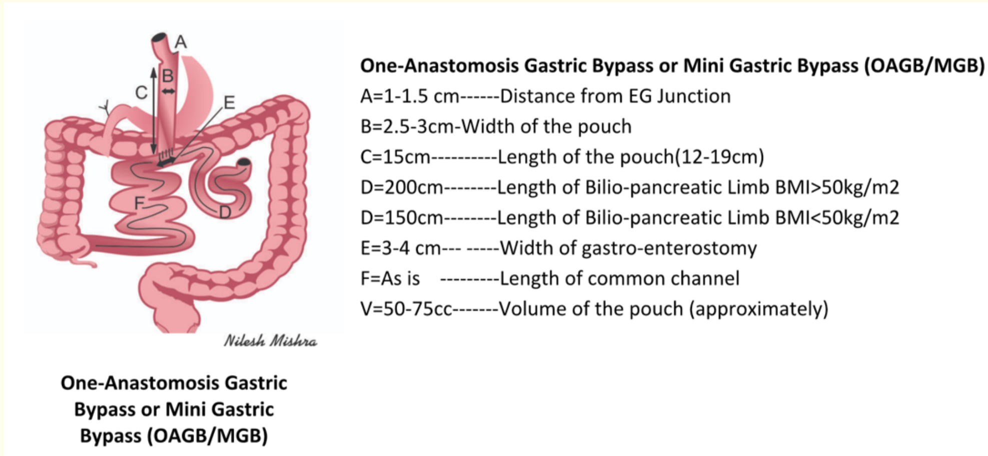

Figure 15

into a tubular configuration so as to reduce the gastric lumen. To perform this, interrupted sutures are applied from distal to proximal with multiple bites being taken along the way over the anterior wall greater curvature and posterior wall before being cinched. Different methods may be used for placating the greater curvature - single interrupted suture; w-shaped suture; u-shaped suture. It has significant advantages as to being effectively painless and being a day-care procedure. Patient may experience some discomfort in the form of nausea and blood-stained vomiting post procedure which is not of any significance. No long-term complications have been observed. Weight loss post endoscopic procedures is limited with patient selection being of primary importance. Resolution of co-morbidities after endoscopic procedures is yet to be determined. Overall, endoscopic procedures appear to be very promising, particularly for an intermediate group of patients who do not respond to medical therapy and may not qualify for an invasive bariatric procedure [67].

Figure 16

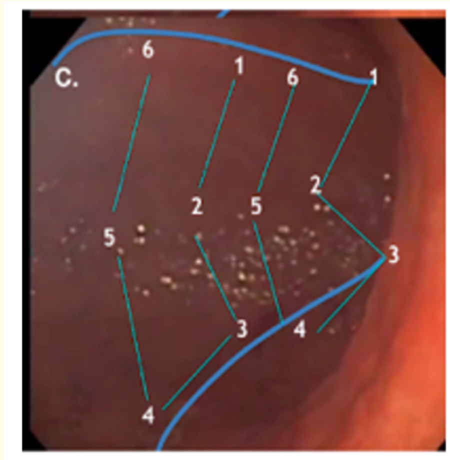

Figure 17

Intragastric balloon (Figure 18)

The primary reports of balloon insertion date back to 1985 [68]. These initially were filled with 220 ml of air and left in the stomach for 3 months following which they were removed. The procedure was discontinued due to complications observed during the time of insertion. The design of intragastric balloons has undergone major modifications over the years. The most commonly used balloon is the Orbera® Intragastric Balloon. Insertion involves insertion of the deflated balloon blindly within a sheath, following which it is inflated under vision with 600 ml of saline along with 5 ml of methylene blue solution. This increases the pickup rate of spontaneous deflation. They are kept for 6 months after which they are removed. Due to its space occupying nature, it decreases pre-prandial hunger and causes stimulation of the stretch receptors and reducing the residual volume within the lumen of the stomach. Its main advantages lie in the fact that it is technically easy to perform with the procedure being a day care procedure. Some patients have experienced severe abdominal pain, nausea, vomiting and discomfort. Spontaneous deflation has also been observed. The standing of the balloon at present is for patients that want a temporary non-surgical and non-pharmaceutical treatment for obesity which can easily be reversed or repeated.

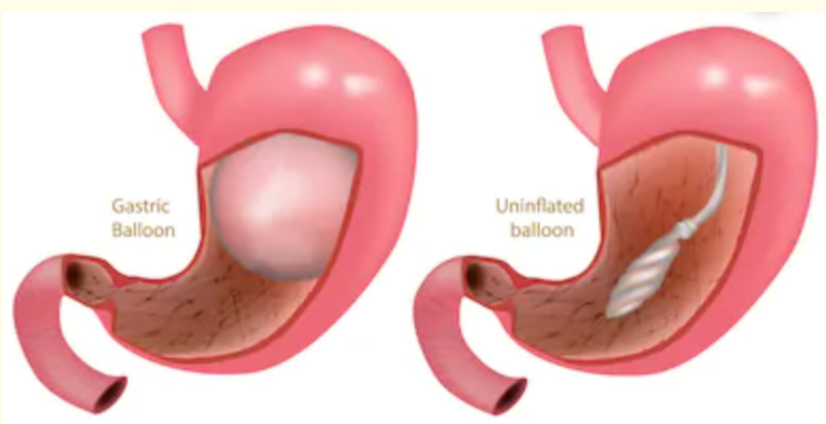

Figure 18

Endoliner (Figure 19)

It is a malabsorptive procedure first described by Milone in animal models in 2006 [69]. It basically involves placing an impermeable barrier between the food and the absorptive mucosa within the foregut. The device consists of a nitinol metal anchor that is attached to an impermeable fluoropolymer which extends approx. 60cm into the jejunum. The liner is open at both ends allowing the processed chyme from the stomach to enter the liner. The device has also been devised in a way that allows bile along with pancreatic secretions to flow on the outside of the liner. The food and secretions mix only when they come into contact after the end of the liner. The reversible nature along with decreased morbidity of the procedure has sparked serious interest. Though promising, there is an absolute lack of robust evidence. Long - term evidence of the use of the device is yet to be determined.

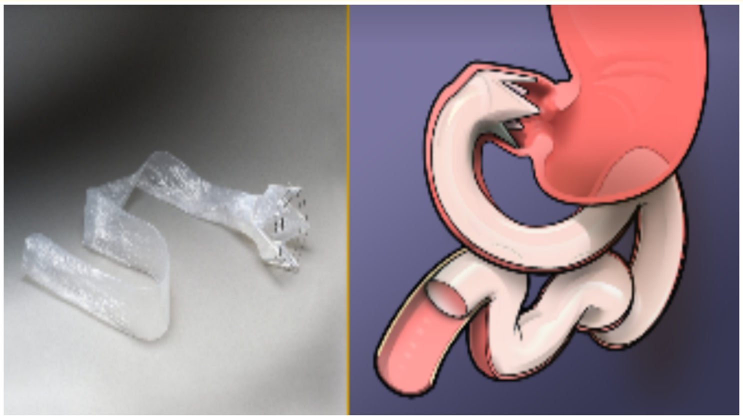

Figure 19

V - Bloc (Figure 20)

A device undergoing extensive research is the V - Bloc device. It is based on the principle that the gut-brain axis plays an important role in the pathogenesis of obesity [70]. Information of satiety from the gastrointestinal system is conveyed to the brain via hormones as well as the vagus nerve. The hypothalamus is considered to play a key role in regulating food intake. In addition to relaying signals, the vagus also controls gastric acid production and pancreatic secretion. This makes the vagus a target to control satiety. It consists of an in-

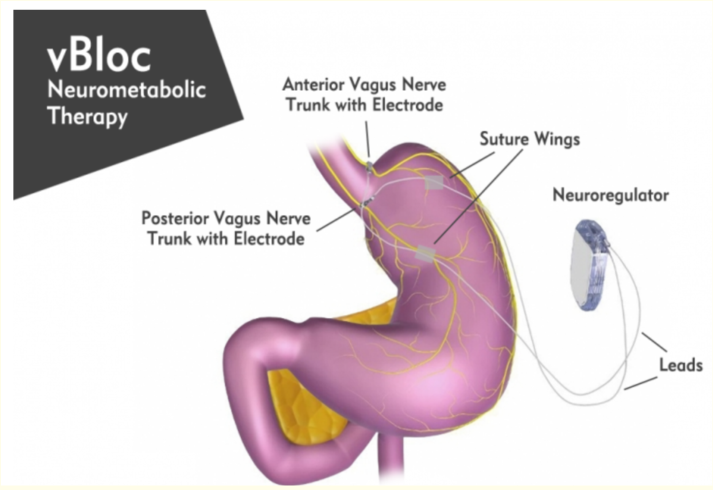

Figure 20

trabdominal device with leads placed around the vagus nerve. Cathodes are placed proximally and anodes are placed distally. The cathode induces depolarization leading to stimulation of the afferent fibers which lead to satiety. This results in weight loss. Though long-term results of the device are pending, it is in use in clinical trials around the world.

Duodenal mucosal resurfacing (Figure 21)

Duodenal mucosal resurfacing (DMR) is a new, minimally invasive procedure. It involves ablation of the duodenal mucosa followed by mucosal healing. It is based on the principle that duodenal mucosa regulates the metabolic signaling post prandially. Once the duodenum

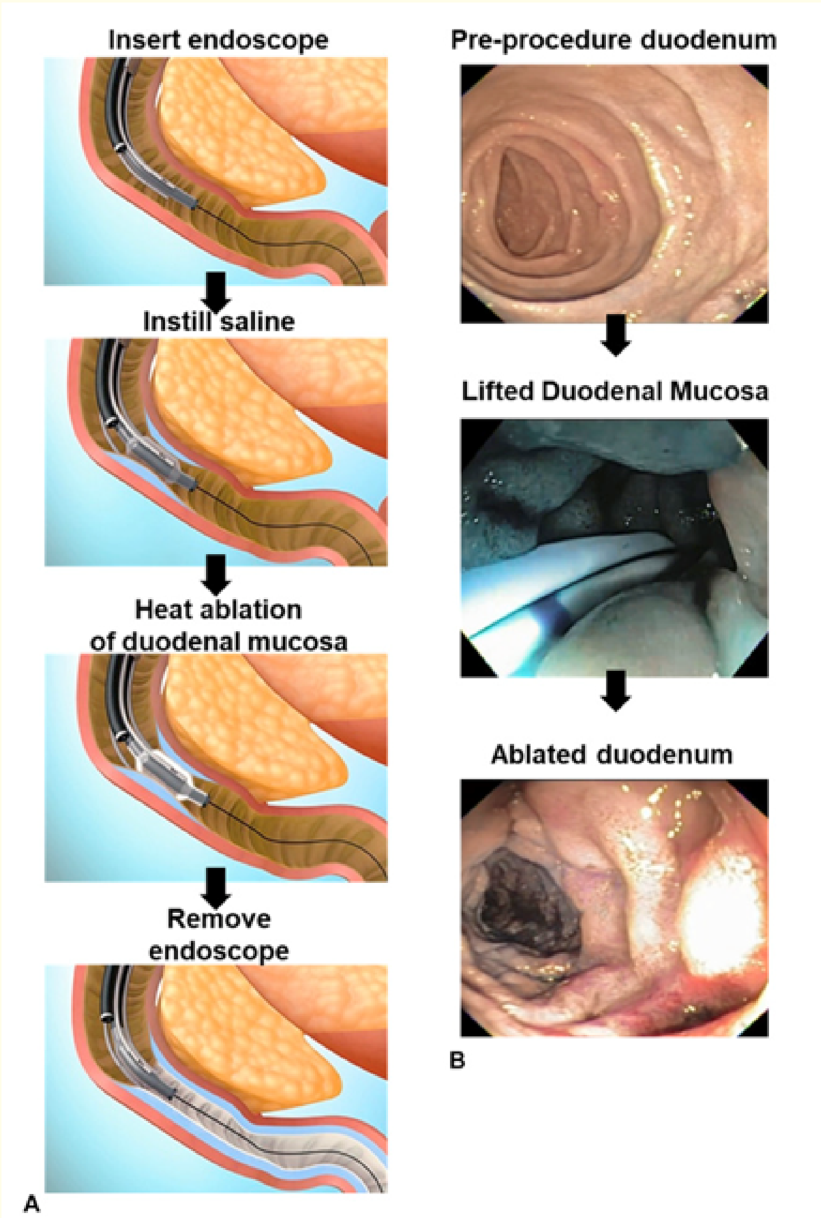

Figure 21

is calibrated, saline is injected into the submucosal plane followed by thermal ablation of the lifted mucosa. The process is then continued circumferentially along the length of the duodenum. Initial results after the procedure seem encouraging though long-term studies have not yet been done [71].

Aspiration therapy (Figure 22)

Aspiration therapy (AT) is an endoscopic weight loss therapy using a novel device, the AspireAssist®. The device is easily inserted using a simple endoscopic procedure. A prepared system is available in most countries. It involves a percutaneous gastrostomy tube and an external drainage bag for drainage of the contents. It relies on the positive abdominal pressure and gravity to facilitate drainage. A patient can empty the contents in private approximately 20 - 30 minutes after a meal. This can be done multiple times till the lavage is clear. It has provided excellent results in terms of weight loss however can appear daunting to some patients due to the crude nature of the procedure.

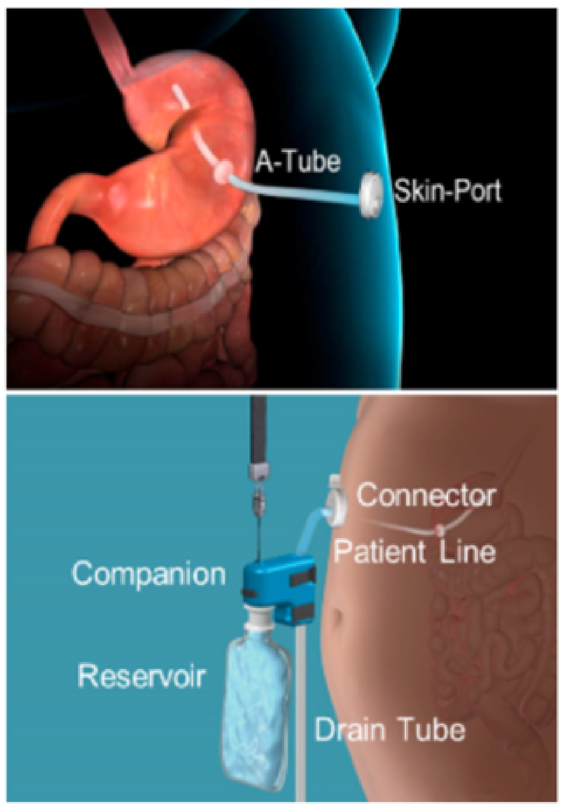

Figure 22

Indications for surgery

Bariatric surgery has proven to be effective in terms of resolution of multiple comorbidities such as cardiac disease, Type II Diabetes mellitus, OSA, OA, dyslipidemia, hypertension and infertility amongst others. Medical management of these comorbidities is at large expensive and inefficient. A consensus statement was issued in 1991 by the NIH stating the guidelines for metabolic and weight loss surgery.

- Patients should have a low likelihood of responding to traditional, nonsurgical therapy.
- Patients must be well informed and motivated and accept the operative risks.
- Patients should be able to participate in and comply with treatment and follow-up.
- Patients should have a BMI in excess of 40 kg/m^2 or body weight greater than 100 lbs. above ideal body weight.
- Patients are candidates if they have a BMI between 35 and 40 kg/m^2 along with more than one high-risk comorbid condition or body weight greater than 80 lbs. above ideal body weight with a comorbidity.
- Patients judged by experienced clinicians to have a low probability of success with non-surgical measures may be considered for surgical treatment.

The Society of American Gastrointestinal Endoscopic Surgeons (SAGES) also recommends that surgical therapy should be considered for individuals who have a body mass index (BMI) of greater than 40 kg/m^2 or have a BMI greater than 35 kg/m^2 with significant comorbidities and can show that dietary attempts at weight control have been ineffective. Guidelines in the past also recommended that patients should be over the age of 18 or under 60 years of age, however, currently there are no age limits.

Re-intervention after bariatric metabolic surgeries - Revision, reversals and conversions

Re-interventions after bariatric metabolic surgeries are not uncommon. Indications include complications, inadequate weight loss, excessive weight loss and most commonly weight regain. Complications that may need reintervention include leaks, bleeding, obstruction, intractable ulcers, intractable GERD, fistulas, hernias, protein caloric malnutrition and unexplained abdominal pain. In cases where obvious anatomic findings are determined to be needed for reintervention, correction of the anatomic derangement should be considered. This may entail endoscopic intervention or surgical intervention. Endoscopic intervention may involve pouch and/or stoma reduction or in the case of a fistula, endoscopic closure of the fistula. If surgical intervention is indicated because of anatomic derangement, revising the anatomy to that of the original operation or conversion to another operation may be the options. In cases with an intact anatomic configuration of the initial operation, surgical revision to another operation by enhancing one or more of the various mechanisms responsible for weight loss and/or maintenance are the options. The outcome of surgical reintervention, weight loss, weight loss maintenance and resolution of co morbid conditions depend on the initial operation and the choice of the revision operation. Generally speaking, surgical reintervention with revision to a particular operation results in suboptimal outcome than the primary operation and also has a higher complication rate. In rare cases conversion to open laparotomy is necessary for the re-intervention. Surgical reversal in all cases result in almost all weight regain and even more.

Evolution of the field of metabolic bariatric surgery

Over the course of many years, the field has undergone a radical change from its humble beginnings to where it stands today. Metabolic bariatric surgery has yet to evolve into a separate post graduate surgical program. However, multiple guidelines are in place to ensure that the surgeon performing the surgeries is adequately qualified. The surgeons post their surgical residency and a fellowship program require understanding of obesity as a disease and are required to have an in-depth understanding of diseases induced or aggravated by obesity. They should have the skills for patient education and selection along with follow-up. In terms of the field, it is imperative to understand the requirement of a multi-disciplined approach to metabolic bariatric surgery. This includes collaboration with anesthetists, diabetologists, cardiologists, pulmonologists, intensivists, physiotherapists and dieticians amongst others. In addition to the surgical skills required, a well-equipped center is also necessary. It should have adequate facilities and equipment along with a properly trained bariatric support staff. The operative room should have special operating tables and equipment that are able to accommodate over weight patients. Anesthesia for these patients should also be administered by a competent anesthetist with experience as these patients have higher predisposition to certain diseases and anatomical alterations for example: short neck leading to difficult intubation. Pre-operative radiological investigation may also warrant the need for specialized tables and equipment. Recovery rooms require special beds, chairs and other furniture. Toilet fixtures need to be specially adapted to their size to accommodate the patients. Nursing personnel should be adequately trained to administer respiratory care, assist mobilization among others. They should also be able to identify at the earliest signs of hemodynamic instability, hypoglycemia and other immediate post-operative problems.

Center of excellence guidelines

To identify world class surgeons and their centers performing bariatric surgeries, a Center of Excellence seal is awarded by bodies to recognize the institutes. There are certain requirements that have to be fulfilled before the certificate is awarded. The surgeon should perform at least 100 procedures per year and has more than 125 bariatric cases in his/her lifetime. This may not necessarily be at the same center. The primary procedures that are included are gastric bypass, gastric banding, duodenal switch, BPD, sleeve gastrectomy and one anastomosis gastric bypass. Revision cases, reversal cases and management of complications are also considered during calculations. The centers should also report mortality outcomes and compare it to a set benchmark as mentioned in the guidelines. A separate bariatric operating room is preferred with separate instruments and adequately trained staff.

Surgeons or centers applying for the excellence category should also have staff that provide information and guideline pre and post operatively to patients. It is the responsibility of the surgeon to ensure training and competency of the staff. Set guidelines should be in place for obtaining informed surgical consent after explaining in detail about the procedure that has to be performed. As with most feedback systems, quality assessment is a must to ensure proper working of the system and to make improvements if necessary. A Center of Excellence must participate in a data registry.

Conclusion

Despite the initial hesitation in its acceptance, bariatric metabolic surgery has gained rapid acceptance in society. All currently used metabolic bariatric procedures produce and sustain better weight loss than any nonsurgical management. No one surgical operation meets the needs of all patients. Today’s operations may someday in the future give way to other untried modalities. Hopefully, a drug or agent that induces satiety safely and effectively will emerge. Until then obesity is a surgical disease. Surgeons need to have many procedures in their armamentarium to adequately address the needs of the patient with obesity, particularly patients with severe obesity. The non-surgical community at this time, must embrace metabolic bariatric surgery as the only effective viable long-term option to treat obesity.

Conflict of Interest

The authors declare that they have no conflict of interest.

Bibliography

1. “WHO Obesity”. WHO. Online (2019).
2. MS Tremblay., *et al*. “Temporal trends in overweight and obesity in Canada, 1981-1996”. *International Journal of Obesity* 26.4 (2002): 538-543.
3. T Kelly., *et al*. “Global burden of obesity in 2005 and projections to 2030”. *International Journal of Obesity* 32.9 (2005): 1431-1437.
4. National Center for Health Statistics (US), Health, United States, 2017: With Special Feature on Mortality. Hyattsville (MD): National Center for Health Statistics (US) (2018).
5. CL Ogden., *et al*. “Prevalence of childhood and adult obesity in the United States, 2011-2012”. *Journal of the American Medical Association* 311.8 (2014): 806-814.

6. von Ruesten., *et al*. "Trend in obesity prevalence in European adult cohort populations during follow-up since 1996 and their predictions to 2015". *Plos One* 6.11 (2011): e27455.

7. M Ng., *et al*. "Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013". *Lancet* 384.9945 (2014): 766-781.

8. M Devaux and F Sassi. "Social inequalities in obesity and overweight in 11 OECD countries". *European Journal of Public Health* 23.3 (2013): 464-469.

9. B Sheikh., *et al*. "The Interplay of Genetics and Environmental Factors in the Development of Obesity". *Cureus* 9.7 (2017): e1435.

10. S O'Rahilly and IS Farooqi. "Human obesity as a heritable disorder of the central control of energy balance". *International Journal of Obesity* 32.7 (2005): S55-61.

11. J Walley., *et al*. "The genetic contribution to non-syndromic human obesity". *Nature Reviews Genetics* 10.7 (2009): 431-442.

12. JE Donnelly., *et al*. "American College of Sports Medicine Position Stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults". *Medicine and Science in Sports and Exercise* 41.2 (2009): 459-471.

13. E Ponterio and L Gnessi. "Adenovirus 36 and Obesity: An Overview". *Viruses* 7.7 (2015): 3719-3740.

14. Parra-Rojas O., *et al*. "Adenovirus-36 seropositivity and its relation with obesity and metabolic profile in children". *International Journal of Endocrinology* (2013): 463194.

15. P Hossain., *et al*. "Obesity and diabetes in the developing world--a growing challenge". *The New England Journal of Medicine* 356.3 (2007): 213-215.

16. C Xiao., *et al*. "Oral taurine but not N-acetylcysteine ameliorates NEFA-induced impairment in insulin sensitivity and beta cell function in obese and overweight, non-diabetic men". *Diabetologia* 51.1 (2008): 139-146.

17. S Satapati., *et al*. "Elevated TCA cycle function in the pathology of diet-induced hepatic insulin resistance and fatty liver". *Journal of Lipid Research* 53.6 (2012): 1080-1092.

18. M Abdelaal CW le Roux and NG Docherty. "Morbidity and mortality associated with obesity". *Annals of Translational Medicine* 5.7 (2017).

19. A-C Huby., *et al*. "Adipocyte-Derived Hormone Leptin Is a Direct Regulator of Aldosterone Secretion, Which Promotes Endothelial Dysfunction and Cardiac Fibrosis". *Circulation* 132.22 (2015): 2134-2145.

20. J Cox NP West and AW Cripps. "Obesity, inflammation, and the gut microbiota". *The Lancet Diabetes and Endocrinology* 3.3 (2015): 207-215.

21. SR Spindler. "Rapid and reversible induction of the longevity, anticancer and genomic effects of caloric restriction". *Mechanisms of Ageing and Development* 126.9 (2005): 960-966.

22. EJ Fine., *et al*. "Targeting insulin inhibition as a metabolic therapy in advanced cancer: a pilot safety and feasibility dietary trial in 10 patients". *Nutrition Burbank* 28.10 (2012): 1028-1035.

23. S Tsugane and M Inoue. "Insulin resistance and cancer: epidemiological evidence". *Cancer Science* 101.5 (2010): 1073-1079.

24. R Kaaks., *et al*. "Serum sex steroids in premenopausal women and breast cancer risk within the European Prospective Investigation into Cancer and Nutrition (EPIC)". *Journal of the National Cancer Institute* 97.10 (2005): 755-765.

25. NE Allen., *et al*. "Endogenous sex hormones and endometrial cancer risk in women in the European Prospective Investigation into Cancer and Nutrition (EPIC)". *Endocrine-Related Cancer* 15.2 (2008): 485-497.

26. V Lee., *et al*. "Enhancement of insulin-like growth factor signaling in human breast cancer: estrogen regulation of insulin receptor substrate-1 expression *in vitro* and *in vivo*". *Molecular endocrinology (Baltimore, Md.)* 13.5 (1999): 787-796.

27. Y Matsuzawa. "Therapy Insight: adipocytokines in metabolic syndrome and related cardiovascular disease". *Nature Clinical Practice Cardiovascular Medicine* 3.1 (2006): 35-42.

28. PE Peppard., *et al*. "Longitudinal study of moderate weight change and sleep-disordered breathing". *The Journal of the American Medical Association* 284.23 (2000): 3015-3021.

29. BG Phillips., *et al*. "Increases in leptin levels, sympathetic drive, and weight gain in obstructive sleep apnea". *The American Journal of Physiology-Heart and Circulatory Physiology* 279.1 (2000): H234-237.

30. S Parekh and FA Anania. "Abnormal lipid and glucose metabolism in obesity: implications for nonalcoholic fatty liver disease". *Gastroenterology* 132.6 (2007): 2191-2207.

31. B Freeman., *et al*. "Analysis of gallbladder bile in morbid obesity". *The American Journal of Surgery* 129.2 (1975): 163-166.

32. P Portincasa., *et al*. "Effects of cholestyramine on gallbladder and gastric emptying in obese and lean subjects". *European Journal of Clinical Investigation* 25.10 (1995): 746-753.

33. P Portincasa and D Q-H Wang. "Intestinal absorption, hepatic synthesis, and biliary secretion of cholesterol: where are we for cholesterol gallstone formation?". *Hepatologists in Baltimore* 55.5 (2012): 1313-1316.

34. G Fantuzzi. "Adipose tissue, adipokines, and inflammation". *The Journal of Allergy and Clinical Immunology* 115.5 (2005): 911-920.

35. M Wolf., *et al*. "Adiponectin induces the anti-inflammatory cytokines IL-10 and IL-1RA in human leukocytes". *Biochemical and Biophysical Research Communications* 323.2 (2004): 630-635.

36. MOzata., *et al*. "Human leptin deficiency caused by a missense mutation: multiple endocrine defects, decreased sympathetic tone, and immune system dysfunction indicate new targets for leptin action, greater central than peripheral resistance to the effects of leptin, and spontaneous correction of leptin-mediated defects". *The Journal of Clinical Endocrinology and Metabolism* 84.10 (1999): 3686-3695.

37. Istvan K., *et al*. "Body weight and psychological distress in NHANES I". *International Journal of Obesity and Related Metabolic Disorders* 16.12 (1992): 999-1003.

38. EA Finkelstein., *et al*. "Obesity and severe obesity forecasts through 2030". *American Journal of Preventive Medicine* 42.6 (2012): 563-570.

39. PD Stein., *et al*. "Obesity and pulmonary embolism: the mounting evidence of risk and the mortality paradox". *Thrombosis Research* 128.6 (2011): 518-523.

40. J Kremen., *et al*. "An Experimental Evaluation of the Nutritional Importance of Proximal and Distal Small Intestine". *Annals of Surgery* 140.3 (1954): 439-447.

41. EE Mason and C Ito. "Gastric bypass in obesity". *Surgical Clinics of North America* 47.6 (1967): 1345-1351.

42. AL Fobi H Lee and AW Fleming. "The surgical technique of the banded Roux-en-Y gastric bypass". *Journal of Obesity and Weight-loss Medication* 8.2 (1989): 99-102.

43. S Scholtz., *et al*. "Obese patients after gastric bypass surgery have lower brain-hedonic responses to food than after gastric banding". *Gut* 63.6 (2014): 891-902.

44. De Silva and SR Bloom. "Gut Hormones and Appetite Control: A Focus on PYY and GLP-1 as Therapeutic Targets in Obesity". *Gut Liver* 6.1 (2012): 10-20.

45. Tschöp C., *et al*. "Circulating ghrelin levels are decreased in human obesity". *Diabetes* 50.4 (2001): 707-709, Apr.

46. Geary. "Endocrine controls of eating: CCK, leptin, and ghrelin". *Physiology and Behavior* 81.5 (2004): 719-733.

47. DE Cummings., *et al*. "Plasma ghrelin levels after diet-induced weight loss or gastric bypass surgery". *The New England Journal of Medicine* 346.21 (2002): 1623-1630.

48. H Ma and ME Patti. "Bile acids, obesity, and the metabolic syndrome". *Best Practice and Research Clinical Gastroenterology* 28.4 (2014): 573-583.

49. P Liou., *et al*. "Conserved shifts in the gut microbiota due to gastric bypass reduce host weight and adiposity". *Science Translational Medicine* 5.178 (2013): 178ra41.

50. SL Faria., *et al*. "Diet-induced thermogenesis and respiratory quotient after Roux-en-Y gastric bypass surgery: a prospective study". *Surgery for Obesity and Related Diseases* 10.1 (2014): 138-143.

51. LT DeWind and JH Payne. "Intestinal bypass surgery for morbid obesity: long-term results". *Journal of the American Medicine Association* 312.9 (2014): 966-966.

52. Scopinaro E., *et al*. "Bilio-pancreatic bypass for obesity: II. Initial experience in man". *British Journal of Surgery* 66.9 (1979): 618-620.

53. N Scopinaro., *et al*. "Biliopancreatic diversion". *World Journal of Surgery* 22.9 (1998): 936-946.

54. Marceau., *et al*. "Biliopancreatic diversion with duodenal switch". *World Journal of Surgery* 22.9 (1998): 947-954.

55. B Anderson., *et al*. "Biliopancreatic diversion: the effectiveness of duodenal switch and its limitations". *Gastroenterology Research and Practice* 2013 (2013): 974762.

56. JP. Gebelli., *et al*. "Sadi-S With Right Gastric Artery Ligation: Technical Systematization And Early Results". *Brazilian Archives of Digestive Surgery* 1.1 (2016): 85-90.

57. H Zaveri., *et al*. "Mid-term 4-Year Outcomes with Single Anastomosis Duodenal-Ileal Bypass with Sleeve Gastrectomy Surgery at a Single US Center". *Obesity Surgery* 28.10 (2018): 3062-3072.

58. EE. Mason. "Vertical banded gastroplasty for obesity". *Archives of Surgery* 1960 117.5 (1982): 701-706.

59. HL Laws. "Standardized gastroplasty orifice". *The American Journal of Surgery* 141.3 (1981): 393-394.

60. K Kolle O Bo and J Stadaas. "Gastric banding". In OMGI 7th Congress, Stockholm 145 (1982): 37.

61. JM Fink., *et al*. "Banding the Sleeve Improves Weight Loss in Midterm Follow-up". *Obesity Surgery* 27.4 (2017): 1098-1103.

62. SB Bashour and R W Hill. "The gastro-clip gastroplasty: an alternative surgical procedure for the treatment of morbid obesity". *Tex Med* 81.10 (1985): 36-38.

63. MA Fobi and H. Lee. "The surgical technique of the Fobi-Pouch operation for obesity (the transected silastic vertical gastric bypass)". *Obesity Surgery* 8.3 (1998): 283-288.

64. HJ Sugerman., *et al*. "Conversion of proximal to distal gastric bypass for failed gastric bypass for superobesity". *Journal of Gastrointestinal Surgery* 1.6 (1997): 517-524.

65. Rutledge. "The mini-gastric bypass: experience with the first 1,274 cases". *Obesity Surgery* 11.3 (2001): 276-280.

66. W-J Lee., *et al*. "Laparoscopic Roux-en-Y vs. mini-gastric bypass for the treatment of morbid obesity: a 10-year experience". *Obesity Surgery* 22.12 (2012): 1827-1834.

67. G Lopez-Nava., *et al*. "Endoscopic sleeve gastroplasty with 1-year follow-up: factors predictive of success". *Endoscopy International* 4.2 (2016): E222-227.

68. Gaur S., *et al*. "Balancing risk and reward: a critical review of the intragastric balloon for weight loss". *Gastrointestinal Endoscopy* 81.6 (2015): 1330-1336.

69. L Milone., *et al*. "Effect of a polyethylene endoluminal duodeno-jejunal tube (EDJT) on weight gain: a feasibility study in a porcine model". *Obesity Surgery* 16.5 (2006): 620-626.

70. H Sam., *et al*. "The role of the gut/brain axis in modulating food intake". *Neuropharmacology* 63.1 (2012): 46-56.

71. H Rajagopalan., *et al*. "Endoscopic Duodenal Mucosal Resurfacing for the Treatment of Type 2 Diabetes: 6-Month Interim Analysis from the First-in-Human Proof-of-Concept Study". *Diabetes Care* 39.12 (2016): 2254-2261.

Volume 5 Issue 2 February 2020