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This is to acknowledge that Jaime Almandoz, MD has disclosed that he does not have any financial interests or other relationships with commercial concerns related directly or indirectly to this program. Dr. Almandoz will not be discussing off-label use in his presentation.

Jaime Almandoz, MD is an Assistant Professor in the Department of Internal Medicine and lead physician for the Division of Endocrinology's Weight Wellness Program. Dr. Almandoz is board certified in Obesity Medicine, Endocrinology and Internal Medicine. The mission of the Weight Wellness Program is to provide innovative and compassionate weight management and bariatric care in an integrated environment.

The goal of this Internal Medicine Grand Rounds is to provide internists and Internal Medicine subspecialists with an overview of common issues that arise in patients who have undergone bariatric surgery, including a simplified approach to nutritional screening and supplementation.

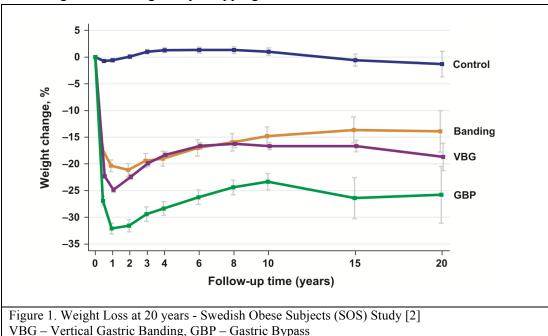
Educational Objectives:

- Describe the increasing trend in obesity and the role of bariatric surgery
- Discuss weight regain after bariatric surgery
- Review post-bariatric gastrointestinal symptoms and dumping syndromes
- Identify those at risk for nutritional deficiencies and formulate treatment plans

Obesity and the Role of Bariatric Surgery

Obesity is a multifactorial disease that results from chronic positive energy balance. It shortens lifespan, affects multiple organ systems and increases healthcare spending. Obesity continues to increase in the United States in spite of the billions of dollars spent on weight loss interventions every year. It is estimated that 40% of women and 35% of men are obese, and with this comes a plague of metabolic diseases, which include type 2 diabetes and other risk factors for atherosclerotic cardiovascular disease. [1]

The foundation of obesity management is to correct the positive energy balance through comprehensive lifestyle modification – typically a lower calorie intake and more physical activity. In our society, the availability of food and our attitudes towards it have dramatically changed in the last two generations. Our access to food is unprecedented with vending machines, restaurants and convenience stores that never close. Smart phone applications and online ordering allow us to have food delivered without expending significant amounts of energy or interacting with another human being. Energy-dense foods that are low in nutrients are cheap and out-compete healthier options due to marketing, palatability and price subsidization. In addition, Americans now spend more on dining out than on grocery shopping.

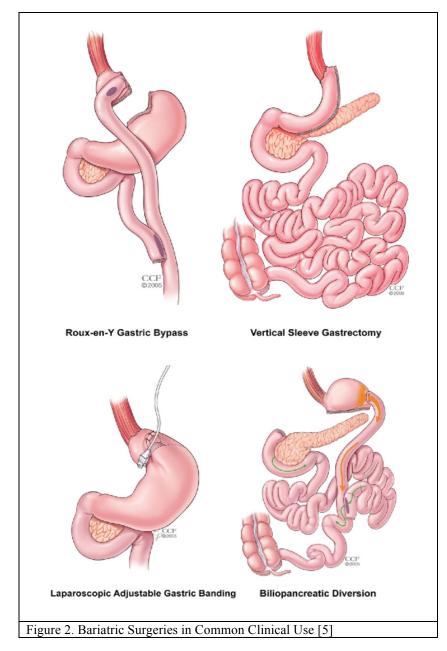


Bariatric surgery is currently the most effective and durable weight loss therapy available. It should be used in conjunction with lifestyle modification to optimize the weight loss effect. Post-operative weight loss decreases cardiovascular risk factors, resulting in less cardiovascular mortality and morbidity. There is also a reduction in microvascular complications associated with type 2 diabetes, *e.g.* retinopathy and nephropathy. [3]

Indications for Bariatric Surgery

Bariatric surgery is indicated for patients with a body mass index (BMI) \geq 40 kg/m² or for those with BMI \geq 35 kg/m² and one or more obesity related comorbidity: *e.g.* type 2

diabetes, hypertension, hyperlipidemia, obstructive sleep apnea, fatty liver disease, *etc*. Recently, bariatric surgery has been endorsed for the management of type 2 diabetes. The Diabetes Surgery Summit has proposed bariatric surgery for those with BMI ≥30 kg/m² and uncontrolled type 2 diabetes. [4]



Adjustable Gastric Banding

The adjustable gastric band (AGB) is placed around the upper part of the stomach using laparoscopy. The AGB's restriction is adjusted via a silicone reservoir, which is filled from a subcutaneous port. Patients must return regularly to have the band resistance adjusted for adequate restriction, according to weight loss and symptoms. The average weight loss observed at three years is 15%, which is the lowest of the bariatric procedures. However, the AGB has the lowest rates of post-operative complications.

Sleeve Gastrectomy

Sleeve gastrectomy (SG) is a restrictive surgery with no diversion of nutrient flow. Approximately 75% of the stomach is removed during sleeve gastrectomy (SG), which is performed as a minimally invasive procedure (Figure 2). SG was initially performed as the first stage of the

biliopancreatic diversion (BPD) surgery, but gained popularity when patients lost significant amounts of weight without undergoing the subsequent small bowel bypass. Mean weight loss at three years is around 21%, which is similar to the roux-en-Y gastric bypass (RYGB). However, metabolic improvements like remission of type 2 diabetes are not as profound with SG compared with RYGB.

Roux-en-Y Gastric Bypass

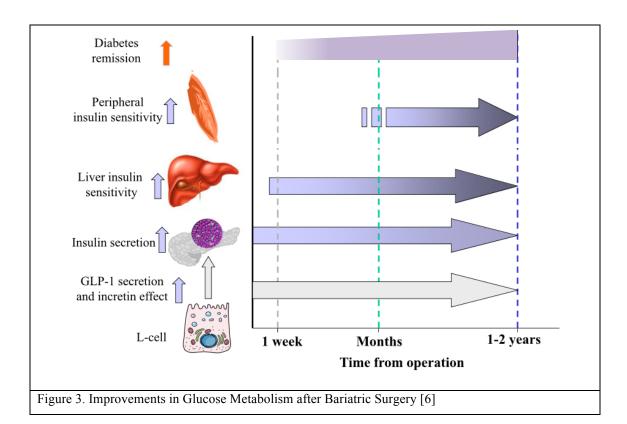
RYGB combines restriction from a small gastric pouch with diversion of nutrients, which bypass the duodenum and proximal jejunum (Figure 2). Average weight loss at three years is around 25% and is associated with significant improvements in metabolic health and cardiovascular risk factors.

Biliopancreatic Diversion with Duodenal Switch

After a SG is performed, the duodenum is divided distal to the pylorus and is attached to the small bowel, around 150 cm proximal to the ileocecal valve (Figure 2). This provides the restriction of a sleeve gastrectomy and bypass of a significant portion of the small bowel. BPD results in the most significant weight loss of the bariatric surgeries, ~34% at two years, and is associated with the highest rate of complications.

Mechanisms of Action of Bariatric Surgery

Bariatric surgery restricts calorie intake and decreases nutrient absorption. Although this appears to be the main mechanism for weight loss, there are metabolic improvements that occur within days of surgery and are independent of weight loss. Improvements in blood glucose control are attributed to increased levels of incretin hormones, *e.g.* glucagon-like peptide-1 (GLP-1), and improvements in insulin secretion (Figure 3). Other beneficial effects include changes in appetite, nutrient sensing, white and brown adipose tissue functions, and alterations in the gut microbiome.



Complications of Bariatric Surgery

The complications of bariatric surgery vary by procedure and increase with the degree of weight loss and metabolic improvements (Figure 4). This patient population carries a higher perioperative risk because of obesity and related comorbidities, which increase the risk of cardiovascular events, venous thromboembolism, respiratory complications and wound infection.

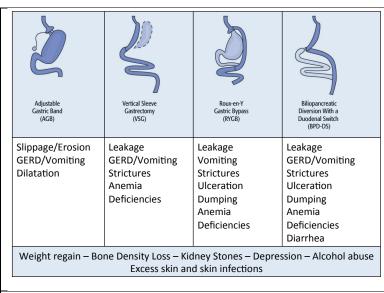


Figure 4. Complications of Bariatric Surgery

AGB and SG are more often associated with obstructive complications, including gastroesophageal reflux disease (GERD) and vomiting due to restrictions in the passage of food through the upper GI tract. RYGB and BPD have higher rates of complications related to malabsorption.

These include diarrhea, nutritional deficiencies, greater loss of bone density and increased risk for kidney stones.

Weight Regain

Weight loss after bariatric surgery is highly variable and occurs in a wide distribution curve. Inadequate post-bariatric weight loss is defined in the surgical literature as an excess weight loss (EWL) of <50%, where EWL is the loss of body weight that is above ideal body weight. There is not a standard definition for post-bariatric weight regain, but studies have used the following: increase in body weight >10 kg from weight loss nadir, increase in BMI >5 kg/m², achieving BMI >35 kg/m² or greater than 25% regain of EWL. [7]

Patients with weight regain are often ashamed to seek medical attention due to weight bias and stigma from healthcare providers. We should strive to address this common issue in a compassionate and patient-centered approach, which should minimize patient discomfort, facilitate adherence to recommendations and improve follow up rates. [8]

When weight regain occurs after bariatric surgery, surgery-specific causes should be excluded as they may require surgical intervention, e.g. gastro-gastric fistula after RYGB. Healthcare providers should evaluate for patient-related causes of weight regain in a systematic but sympathetic way (Figure 5).

Surgery Specific

ADJUSTABLE BAND

No Fill Follow Up Pouch Distension Band Slippage

R-en-Y GASTRIC BYPASS

Pouch Dilatation Wide G-J Anastomosis Gastro-Gastric Fistula

SLEEVE GASTRECTOMY

Sleeve Dilatation

Weight Regain



Patient Related

DIETARY INDISCRETION

Portion Sizes
Calorie Density
Dietitian Follow Up

PHYSICAL INACTIVITY

Loss of Lean Mass/REE Less expenditure

HORMONAL/METABOLIC

High Ghrelin, Low PYY Insulin, DM Meds Reactive hypoglycemia

MENTAL HEALTH

Eating Disorders – BED "Emotional Eating" Attention Deficit Disorder Psychiatric Medications

Figure 5. Causes of Weight Recidivism Post-Bariatric Surgery [9] REE – Resting Energy Expenditure, BED – Binge Eating Disorder

Our bodies resist weight loss through several homeostatic mechanisms. As adipose tissue depots shrink, circulating leptin levels fall and hunger-inducing ghrelin levels increase. These hormones act in the hypothalamus to centrally mediate a positive energy balance and weight regain.

Metabolic adaptation occurs when weight loss leads to a lowering of metabolic rate, which is greater than expected from measured changes in body composition. This phenomenon was recently highlighted in a study that evaluated contestants from the Biggest Loser television program. The winner of season nine, Danny Cahill, started the program at 430 lbs. and lost down to 191 lbs. Six years later, he had regained to 295 lbs. and his resting energy expenditure was 800 kcal/day less than expected for a man of his size. On average, contestants from the show needed 500 kcal/day fewer than estimated. [10] Metabolic adaptation not only facilitates weight regain, but can also confound patients who try to calculate their calorie intake goals. A study that evaluated resting energy expenditure after RYBG or SG determined that there is a metabolic adaptation of 130-300 kcal/day two years after surgery, when body weight is stable. [11]

Patients frequently ask how many calories they should eat to lose weight and there are several approaches to determine this goal. Calorie requirements can be estimated with

formulas like the Harris Benedict or Mifflin St. Jeor equations. Specialized equipment, such as indirect calorimeters and bioelectrical impedance scales, can also provide estimates of resting energy expenditure (REE). Our providers typically recommend a 500-kcal/day deficit from the REE and do not allow additional calories for activity, which will allow for metabolic adaptation and miscalculations in calorie intake.

Patients should be encouraged to track food intake prior to consumption to reinforce self-regulation principles. Aside from calorie restriction, we underscore the importance of intentional eating and meal planning. Many branded diets, *e.g.* Weight Watchers, simplify calorie restriction and utilize systems of accountability that may make them easier to follow. Studies have shown that weight loss tends to correlate with diet adherence and not with the macronutrient content of the diet. [12] However, diets that are higher in protein and lower in carbohydrates are thought to promote more satiety and better glucose control in patients after bariatric surgery. Also, a protein intake of >1g/kg/day has been associated with greater weight loss following bariatric surgery. [13]

Physical activity is important because it promotes weight loss and weight loss maintenance by calorie expenditure and preservation of lean body mass. Unfortunately, many patients with obesity may have negative beliefs and cognitions about exercise. They may also have physical limitations and variable levels of deconditioning to overcome. These patients may benefit from seeing a physical therapist, physical medicine specialist or orthopedic surgeon. Activity trackers can be used to capture daily activities like walking, but patients should be encouraged not to "buy" dietary calories with the reported calorie expenditure. The American College of Sports Medicine recommends 150-300 minutes per week of moderate physical activity in addition to strength training 2-3 times per week. [14]

Behavioral Interventions

Bariatric surgery may not change psychological factors that influenced preoperative eating behaviors and lifestyle. Studies estimate that depression and binge eating disorder are present in up to 20% of bariatric surgery patients, and that these conditions contribute to weight regain. [15] Mental health influences on bariatric weight regain should be evaluated and managed by trained behavioral health specialists. A recent meta-analysis and systematic review have identified greater weight loss in those who receive post-operative behavioral management, but no consensus exists on how these interventions should be delivered. Types of therapeutic interventions include cognitive behavioral therapy (CBT) and acceptance and commitment therapy (ACT). [16]

Weight Loss Medications

There are several FDA-approved weight loss medications that may be appropriate for patients after bariatric surgery that experience weight regain or sub-optimal weight loss. However, there are no randomized controlled trials that evaluate weight loss medications in this population. Orlistat, a lipase inhibitor, is not recommended after bariatric surgery as it can exacerbate nutrient malabsorption and gastrointestinal symptoms. Lorcaserin, a 5-HT_{2c}-receptor agonist, was shown to stop weight regain and promote weight loss in a case-series of veterans after bariatric surgery. [17] Treatment with phentermine, a

sympathetic agonist, was associated with a 5.7% weight loss in post-surgical patients who were 14 months out from surgery. [18] Topiramate therapy was associated with a 6.8% weight loss in patients with binge eating disorder who had previously undergone AGB. [19] Liraglutide, a GLP-1 receptor agonist, was associated with a 7.4% weight loss in patients after surgery in a case series of 15 patients. [20] There are currently no published data on post-bariatric weight loss with combined phentermine/topiramate or bupropion/naltrexone, which are available as sustained-release weight loss medications.

Gastrointestinal Symptoms and Dumping Syndromes

The gastrointestinal manipulation of bariatric surgery can lead to a constellation of symptoms and syndromes. The onset of symptoms can occur within hours of surgery or many years later.

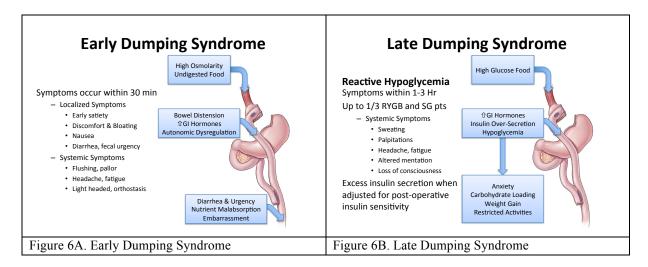
Dysphagia, Vomiting and Gastroesophageal Reflux Disease

Dysphagia occurs as the result of mechanical obstruction in the esophagus, most commonly when AGBs slip or esophageal strictures develop in the context of chronic gastroesophageal reflux disease (GERD). Vomiting is most often due to rapid ingestion of food that is inadequately chewed; but may be the result of band slippage, pouch dilatation, gastric stricture, anastomotic narrowing or other types of GI obstruction. In a non-acute presentation, dysphagia and vomiting can be investigated with upper GI barium or gastrograffin studies. Acute presentations, which include abdominal pain, warrant a more comprehensive evaluation with CT scanning or other cross-sectional imaging.

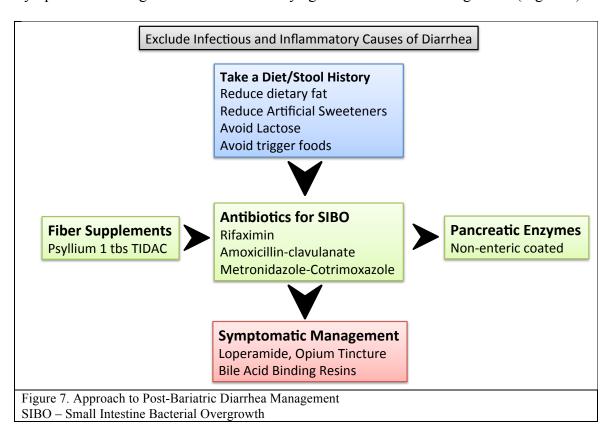
GERD may improve after bariatric surgery but gastric banding and sleeve gastrectomy are associated with the development of *de novo* GERD in up to 35% of cases. Consider evaluation with upper GI endoscopy for patients with GERD symptoms that do not respond to proton pump-inhibitor therapy. If the patient has a history of AGB, band removal should be considered if there is malposition or if symptoms do not respond to removal off all of the band's fluid. RYGB is considered to be an anti-reflux surgery as there is a reduction in gastric acid production and diversion of bile flow. Therefore, GERD does not usually worsen after RYGB unless there is a mechanical obstruction, typically at the gastro-jejunal anastomosis. SG or AGB can be revised to RYGB if there is severe GERD or dysplasia in the esophagus.

Diarrhea and Early Dumping Syndrome

Post-bariatric diarrhea is more common after RYGB and BPD. Post-surgical lactose intolerance and osmotic diarrhea from artificial sweeteners are common causes of diarrhea in the bariatric population. The diversion of bile flow and digestive enzymes can cause intestinal irritation and more frequent defecation. High-fat diets and fat malabsorption can cause steatorrhea and deficiencies in fat-soluble nutrients. Other causes of diarrhea include small intestine bacterial overgrowth (SIBO) and gastrointestinal infections.



Diarrhea within 1 hour of a high-osmolarity meal can be due to early-dumping syndrome (Figure 6A). Early dumping responds favorably to dietary modification and separating liquid ingestion from solid foods by at least 30 minutes. A focused dietary history may identify trigger foods or behaviors, which can guide therapies. If diarrhea is not responsive to fiber supplements, antibiotics or pancreatic enzyme therapy, consider symptomatic management with antimotility agents or bile acid binding resins (Figure 7).



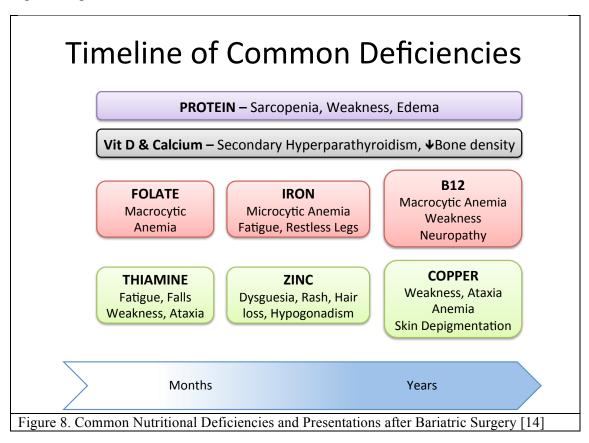
Reactive Hypoglycemia

Late dumping syndrome, also known as reactive hypoglycemia, is due to excessive secretion of insulin in response to oral glucose ingestion (Figure 6B). This can occur after bariatric surgery and other gastrointestinal surgeries. Pancreatic beta cells undergo hypertrophy in patients with obesity because of insulin resistance, which results in an

increased need for insulin production. Following weight loss surgery, there is less insulin resistance, rapid absorption of glucose, and a persistent exuberant insulin response to ingested glucose. This results in post-prandial hypoglycemia 1-3 hours after a meal, which can be severe enough to cause confusion or loss of consciousness. The primary management of this is patient education and dietary modification to a low-carbohydrate, low-glycemic index, high-fiber diet. Separating liquid ingestion from solid foods and avoidance of carbonated beverages is also helpful. In severe cases, medications like acarbose, diazoxide and octreotide have been used; or in extreme cases of neuroglycopenia, partial pancreatectomy has been performed – but this is not typically necessary.

Nutritional Deficiencies

Nutritional deficiencies are common after bariatric surgery (Figure 8). It was initially thought that AGB and SG would not cause deficiencies as there is no malabsorpitive component, but deficiencies are seen after all bariatric procedures, even when patients regain weight.



Patients are advised to take nutritional supplements for life and to have vitamin levels monitored regularly. After SG, RYGB and BPD, patients should take a complete multivitamin twice daily in addition to calcium and vitamin D (Figure 9). Even with this regimen, deficiencies in vitamin B12 and iron are common. Refractory iron and vitamin B12 deficiencies may require parenteral iron infusions and subcutaneous vitamin B12 injections.

Inadequate protein intake is common as many patients find it difficult to swallow sufficient quantities of solid animal protein. Protein malnutrition causes loss of lean body mass, which decreases metabolic rate and contributes to weight regain. Symptoms and signs of protein malnutrition include: fatigue, muscle wasting, anemia and edema.

Empiric Dietary Supplement Regimen

- · Multivitamin with minerals (chewable not gummies) 1 twice daily
- Vitamin D₃ 5,000 IU once daily
- Calcium citrate 600 mg twice daily
- ±Iron 65 mg once daily (menstruating women)
- ±Vitamin B₁₂ 500 mcg once daily



Figure 9. Recommended Empiric Dietary Supplement Regimen

Bone Metabolism and Kidney Stones

Several factors have detrimental effects on bone health after bariatric surgery. The amount of bone density loss appears to be related to the magnitude of surgically induced malabsorption and weight loss. Following RYGB, it is estimated that bone density in the hip decreases by 8-10% at 12 months. Malabsorption of calcium and vitamin D, due to nutrient and fat loss in the stool, leads to secondary hyperparathyroidism and bone loss. Mechanical unloading, changes in gastrointestinal peptide hormones and adipokines also play a role in bone loss. Studies have shown that calcium citrate is better absorbed after bariatric surgery. Guidelines recommend 1200-1500 mg of elemental calcium per day, taken in divided doses. Levels of 24-hour urinary calcium excretion can help to determine if the intake of dietary calcium and supplements is optimal.

Preoperative vitamin D deficiency is very common and vitamin D absorption after surgery is variable. Guidelines recommend 3,000 international units of vitamin D daily but patients may require significantly more to replete and maintain their levels within the optimal range of 30-80 ng/mL. Baseline bone density studies should be performed before surgery for those at risk for low bone density. It is recommended that patients have bone density studies every two years after bariatric surgery. In the management of post-bariatric osteoporosis, oral bisphosphonates should be avoided as they are poorly absorbed, and increase the risk of gastrointestinal irritation and ulceration. Healthcare providers should consider treating osteoporosis in these patients with a parenteral medication such as zoledronic acid or subcutaneous denosumab.

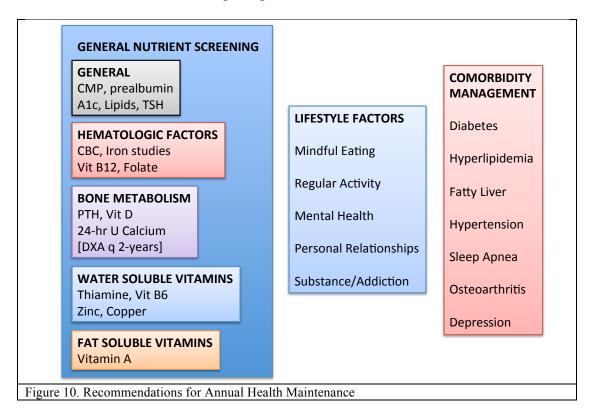
The incidence of kidney stones after RYGB is more than twice what is seen in obese controls (11% vs. 4.3%). Following AGB and SG, the incidence of kidney stones is lower than after RYGB, which is attributed to the higher prevalence of hyperoxaluria after RYGB. Ordinarily, calcium binds to oxalate in the intestinal lumen and is excreted in the feces. After RYGB, unabsorbed fatty acids complex with calcium in the intestinal lumen and permit greater absorption of dietary oxalate from the intestine. Patients should receive counseling about the risk of kidney stones and the importance adequate fluid intake after bariatric surgery. [21]

Fertility and Pregnancy

It is estimated that half of all bariatric procedures occur in women of reproductive age. Weight loss surgery may improve polycystic ovarian syndrome, leading to more ovulatory menstrual cycles and better fertility. The oral contraceptive pill may not be as effective after bariatric surgery and alternative methods, such as a levonorgestrel-releasing intrauterine device (IUD) may be more reliable. Many providers favor Levonorgestrel IUDs for contraception, as they tend to decrease menstrual blood loss and thereby reduce the risk of iron deficiency anemia. Preconception counseling and optimization of vitamin levels are advised for all bariatric patients who plan to become pregnant. Bariatric surgery appears to decrease the risk for gestational diabetes and fetal macrosomia, but increases the chances for shorter gestation and a small for gestational-age baby. It is not clear if bariatric surgery increases infant mortality. [22, 23] Pregnancies should be planned at least 18 months after surgery to facilitate maximal weight loss, weight stabilization and optimization of nutrition before conception.

Annual Health Maintenance

In addition to age and sex-specific screening recommendations, bariatric patients require specialized follow up. Many patients go years without systematic nutrient screening or dietary supplements, and these patients are at risk for deficiencies and complications. In addition to nutrient screening, patients should be encouraged to adopt and maintain healthy eating and physical activity habits (Figure 10). Patients should be screened for depression and substance abuse, as these may become issues after bariatric surgery. Obesity-related comorbidities, like type 2 diabetes and hypertension, may return after time or in association with weight regain.



Conclusion

Bariatric surgery is an effective tool for weight loss and results in significant improvements in obesity-related comorbidities; however, bariatric surgery does not address many of the causes for obesity and weight regain is common. Healthcare providers should approach post-bariatric weight regain in a coordinated and compassionate manner to facilitate lifestyle modifications. The judicious uses of weight loss medications or surgical revision may be necessary to address insufficient weight loss or weight regain. Bariatric surgeries that result in greater weight loss are associated with more complications, including gastrointestinal syndromes and nutritional deficiencies. Patients require lifelong screening for nutritional deficiencies and metabolic bone disease after bariatric surgery, even if they regain weight. Special populations, such as women planning pregnancy, may require more intensive follow up. Primary care providers should incorporate post-bariatric care into annual health maintenance visits, but more complicated patients may need to be followed in specialized multidisciplinary clinics.

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