

MEDICAL MANAGEMENT OF THE POSTOPERATIVE BARIATRIC SURGERY PATIENT

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ABSTRACT

Bariatric surgery can result in substantial weight loss and significant metabolic improvements. Therefore, clinicians should be prepared to taper treatments for weight-related chronic metabolic diseases. For patients with type 2 diabetes, early and dramatic improvements in glucose homeostasis require anticipatory management. This includes insulin dose reductions, discontinuation of certain oral agents, and close monitoring. Antihypertensive medications should be adjusted to avoid hypotension. Even after postoperative improvements in dvslipidemia, some patients will continue to meet criteria for statin therapy. While many obesity-related diseases will improve, clinicians should also be prepared to manage postoperative medical and nutritional complications. Micronutrient deficiencies are common, and professional guidelines provide recommendations for preoperative screening, universal postoperative supplementation, micronutrient monitoring, and repletion strategies. Changes in gastrointestinal physiology may result in dumping syndrome, and patients may report early gastrointestinal and vasomotor symptoms after eating. In contrast, post-gastric bypass hypoglycemia is a rare complication of malabsorptive procedures, resulting in insulin-mediated hypoglycemia after

carbohydrate-containing meals. Rapid weight loss may increase risk of cholelithiasis, which can be by ursodiol. After mitigated malabsorptive procedures, enteric hyperoxaluria and other factors may result in nephrolithiasis, which can be addressed with hydration, dietary interventions, and calcium. All bariatric surgeries induce a high bone turnover state, with declining bone mineral density (BMD) and increased fracture risk. Appropriate strategies include adequate calcium and vitamin D supplementation and age-appropriate BMD screening. Long-term prevent weight strategies to regain include adherence to healthy lifestyle practices, identification and avoidance of medications that promote weight gain, and prescribing weight-loss medications. In summary, given dramatic physiologic changes with bariatric surgery, clinicians should be prepared to taper treatments for chronic metabolic diseases, to manage postoperative medical and nutritional complications, and to identify and manage risk for weight regain.

INTRODUCTION

Bariatric surgery is a highly effective treatment for obesity, inducing substantial and durable weight loss and improvement in obesity-related comorbidities (1). Moreover, it reduces mortality (2-4). The surgical treatment of obesity is discussed in another Endotext chapter, with sections devoted to the modern bariatric surgical procedures including the biliopancreatic diversion with duodenal switch (BPD/DS), Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG), and laparoscopic adjustable gastric band (LAGB) (5). This chapter also addresses the benefits of bariatric surgery on obesity-related conditions including type 2 diabetes (5). As the postoperative bariatric surgery patient population increases with time, it is crucial that endocrinologists and primary care providers have the training and tools required to meet the population's medical needs. In this chapter, we first review the postoperative approach to chronic co-morbid medical focusing 2 conditions. on type diabetes. hypertension, and dyslipidemia. We then discuss potential long-term complications of bariatric surgery (Table 1), including the pathophysiology, screening, and treatment of those potential complications.

Table 1. Potential Medical and Nutritional Complications of Bariatric Surgery om
Micronutrient deficiencies
Dumping syndrome
Post-gastric bypass hypoglycemia
Cholelithiasis
Nephrolithiasis
Bone loss and fracture

POSTOPERATIVE APPROACH TO CHRONIC METABOLIC CONDITIONS

In the perioperative and early postoperative periods (usually the first 30 to 90 days after surgery), a patient's surgeon will monitor closely for surgical complications such as anastomotic leak, deep vein thrombosis, and infection. An experienced dietitian generally assists with meal initiation and progression. Later, regular follow-up with the surgeon-including, eventually, annual follow-up for life-is important for the assessment of weight loss success and the reinforcement of necessary lifestyle modifications. Typically, provider the primary care or endocrinologist assumes responsibility for the early and later postoperative management of chronic medical conditions, including diabetes, hypertension, and dyslipidemia. This section summarizes the effects of bariatric surgery on those conditions and recommended approach to management.

Postoperative Diabetes Management

Bariatric surgery results in dramatic improvements in glucose homeostasis and type 2 diabetes (T2D). After RYGB in particular, these improvements are both weight loss-dependent and weight lossindependent, with weight loss-independent effects likely mediated by alterations in gut hormones, gastrointestinal tract nutrient sensing, bile acid metabolism, and the gut microbiome (6,7). Due to complex factors and the effects these of postoperative calorie restriction, improvement in glucose homeostasis is evident within days to weeks following RYGB (8,9). In an early systematic review and meta-analysis, diabetes remission was observed in 99% of those with T2D who underwent BPD/DS, 84% of those who underwent RYGB, and 48% of those who underwent LAGB (1). Of participants in the Longitudinal Assessment of Bariatric Surgery-2 (LABS-2) study with T2D, 59% of RYGB participants and 25% of LAGB participants were in diabetes remission 7 years after surgery (10). Even after controlling for differences in amount of weight lost, the diabetes remission rate after RYGB was almost double that after LAGB (11). The newer SG

procedure appears to be positioned between RYGB and LAGB in T2D effectiveness (12-14).

The endocrinologist or primary care provider caring for a bariatric surgery patient with T2D must quick and potentially anticipate а dramatic improvement in glycemic status. Typically, oral (sulfonylureas insulin secretagogues and meglitinides) are discontinued at the time of surgery in order to decrease hypoglycemia risk. Insulin doses should be decreased in the hospital and upon discharge home, with strict instructions provided to the patient for the self-monitoring of blood glucose levels and adjustments of insulin doses to avoid Metformin hypoglycemia. is often continued postoperatively, with appropriate caution exercised in patients with reduced kidney function, until blood glucose levels and hemoglobin A_{1c} in the subsequent months suggest that it can be discontinued. While incretin-based therapies (GLP-1 receptor agonists and DPP-4 inhibitors) theoretically could be continued safely, they are often discontinued postoperatively because of the clear effects of bariatric surgery on incretin physiology. Thiazolidinediones and SGLT2 inhibitors could also be theoretically continued but are often discontinued in part due to expected postoperative changes in sensitivity and volume status. insulin Alpha glucosidase inhibitors should be discontinued due to their gastrointestinal effects.

Regardless of the initial postoperative T2D medication regimen, close glucose monitoring is critical. For patients using insulin or an insulin secretagogue, this must include patient self-monitoring of blood glucose levels with a clear plan for adjustments. For others, self-monitoring may be reassuring and should be individualized. Hemoglobin A_{1c} monitoring should be routinely continued long-term (years). While glucose control improves to the point of full remission in most patients in the year after bariatric surgery (70% or more (10) depending on the procedure), certain patients are at higher risk

for not achieving remission or for having diabetes recur over time, including older patients, those with a longer-duration of diabetes, and those who were using insulin or required more than one non-insulin medication (11,15). Such patients are characterized by a greater impairment in insulin secretory capacity. Recently published long-term data elucidate the proportions of T2D patients who achieve and maintain full remission: In a cohort of RYGB patients, of those with T2D preoperatively, 75% had remitted 2 years postoperatively, 62% at 6 years, and 51% at 12 years (15). In the LABS-2 study, 7 years after surgery, 60% of RYGB participants and 20% of LAGB participants were in diabetes remission (10).

In patients not reaching glycemic targets or experiencing relapse, diabetes therapies can be resumed or added. A reasonable approach is first to add metformin, and then if needed to add one or more other weight-neutral or weight loss-promoting agents such as a GLP-1 receptor agonist, a DPP-4 inhibitor, or an SGLT2 inhibitor.

Postoperative Hypertension Management

Reductions in systolic and diastolic blood pressure have been demonstrated at just one week after RYGB (16), suggesting weight loss-dependent and weight loss-independent mechanisms (17). An early systematic review and meta-analysis of bariatric surgery outcomes demonstrated that, of patients with preoperative diagnosis of hypertension, hypertension resolved completely after surgery in 62% and resolved or improved in 79% (1). Frank remission was observed in 83% of those who underwent BPD/DS, 68% of those who underwent RYGB, and 43% of those who underwent LAGB. Subsequent studies have yielded less impressive but still very favorable results (17,18). For example, of participants in the LABS-2 study with hypertension, 38% of RYGB participants and 17% of LAGB participants had complete remission of hypertension 3 years after surgery (19), and 33% of RYGB participants and 17% of LAGB participants had complete remission after 7 years (10). The newer SG procedure also has a substantial effect on hypertension, with resolution or improvement in the majority of cases (20), although a recent meta-analysis concluded that the odds of resolution of hypertension was greater after RYGB than SG (21).

Because the effect of bariatric surgery on blood pressure is thought to be variable and potentially less durable than on glucose metabolism, the Clinical Practice Guidelines of the American Association of Clinical Endocrinologists (AACE), The Obesity Society (TOS), and American Society for Metabolic and Bariatric Surgery (ASMBS) recommend against the preemptive discontinuation of antihypertensive medications (22). Rather, endocrinologists and primary care providers should pay close attention to blood pressure at every postoperative clinic visit and adjust medications when indicated.

Postoperative Dyslipidemia Management

Bariatric surgery may improve dyslipidemia by altering diet, various endocrine and inflammatory factors, bile acid metabolism, and potentially even the intestinal microbiome (23). An early systematic review and meta-analysis of bariatric surgery outcomes demonstrated that among patients undergoing LAGB, RYGB, gastroplasty, or BPD/DS, hyperlipidemia improved in 79%. hypercholesterolemia in 71%, improved and hypertriglyceridemia improved in 82% (1). Of participants in the Longitudinal Assessment of Bariatric Surgery-2 (LABS-2) study, 62% of RYGB participants and 27% of LAGB participants had remission of dyslipidemia 3 years after surgery (19), and percentages were generally similar 7 years after surgery (10). Regarding SG, a systematic review confirmed its effectiveness for the treatment of dyslipidemia (24). In STAMPEDE, a randomized controlled trial (RCT) of RYGB, SG, or intensive medical therapy alone among overweight and obese patients with T2D, both RYGB and SG increased HDL and decreased TG levels compared to placebo (13). Changes in LDL levels were not different between groups, although the number of medications needed to treat hyperlipidemia was lower in the surgical groups than the medical therapy group.

Unlike insulin and antihypertensive medications, which must be decreased or discontinued when no longer needed in order to avoid the acute dangers of overtreatment, lipid-lowering medications may be continued during the metabolically dynamic early period. Moreover. postoperative even after postoperative improvement in dyslipidemia, many bariatric surgery patients will continue to meet criteria for statin use based on the current American College of Cardiology/American Heart Association guideline (25) and National Lipid Association recommendations especially those at very high risk for (26). cardiovascular events including secondary prevention. With this in mind, for many patients, endocrinologists and primary care providers should be cautious about creating expectations that statin therapy will be discontinued postoperatively. Instead, a patient's cardiovascular risk should be periodically evaluated and the potential of role of statins discussed in an individualized manner.

Medication Adjustments

Nonsteroidal anti-inflammatory drugs (NSAIDs) should be avoided after bariatric surgery because of risk of gastric and marginal ulcer development (27). In many bariatric centers, proton pump inhibitor therapy is prescribed postoperatively, as evidence from cohort studies suggests that it may decrease ulcer risk (28). Endocrinologists and primary care providers should be prepared to make adjustments to the dose of any medication that is dosed based on weight (*e.g.*, levothyroxine), and to consider potential effects of malabsorption on a patient's usual oral medications.

PREVENTION AND TREATMENT OF POSTOPERATIVE MEDICAL AND NUTRITIONAL COMPLICATIONS

While a patient's surgeon monitors closely for postoperative surgical complications, the primary care provider or endocrinologist often identifies and manages postoperative medical and nutritional complications. This section reviews these potential complications (Table 1), with attention to pathophysiology, screening, and therapeutic approach.

Micronutrient Deficiencies

Given the dietary changes, rerouting of nutrient flow, and gut anatomy/physiology alterations that occur after bariatric surgery, patients who undergo these procedures are at risk for micronutrient deficiencies. Some of these deficiencies can result in severe consequences, such as neuropathy, heart failure, and encephalopathy. Therefore, it is essential that patients comprehend the importance of compliance and the need for lifelong supplementation. Patients who have malabsorptive procedures, such as RYGB or BPD/DS, are at highest risk for micronutrient deficiencies and require а more extensive preoperative nutritional evaluation and postoperative monitoring and supplementation. But even with

restrictive procedures, decreased oral intake and poor tolerance to certain food groups may also increase the risk for micronutrient deficiencies.

Tables 2-5 represent recommendations that have been adapted and modified from the American Society for Metabolic and Bariatric Surgery (ASMBS) Integrated Health Nutrition Guidelines (29). Clinical Practice Guidelines from the combined American Association of Clinical Endocrinologists (AACE), The Obesity Society (TOS), and ASMBS (22), and The Endocrine Society Clinical Practice Guidelines (30). These recommendations for adults reflect general guidelines, and patients with specific diseases may require further evaluation and closer monitoring. For example. nutritional anemias resultina from malabsorptive bariatric surgical procedures in the setting of appropriate iron repletion might also involve other micronutrient deficiencies in vitamin B₁₂, folate, protein, copper, selenium and zinc, and these should be evaluated.

Preoperative micronutrient screening recommendations are listed in Table 2. Ideally, preexisting micronutrient deficiencies would be corrected prior to surgery in order to avoid clinically symptomatic or severe disease. Suboptimal levels of 25-hydroxyvitamin D are particularly common and may require supplementation prior to surgery.

Table 2. Preoperative Micronutrient Screening Recommendations				
Micronutrient	Surgical population	Screening laboratory test (optional tests)		
Thiamine	All	Thiamine		
Vitamin B ₁₂	All	Vitamin B ₁₂ (optional: MMA)		
(cobalamin)				
Folate	All	Folate (optional: RBC folate, homocysteine, MMA)		
(folic acid)				
Iron	All	Iron, TIBC, ferritin		
Vitamin D	All	25-hydroxyvitamin D		
Calcium	All	Calcium (optional: intact PTH, 24-hour urinary calcium)		
Vitamin A	RYGB, BPD/DS*	Vitamin A		
Zinc	RYGB, BPD/DS	Zinc		
Copper	RYGB, BPD/DS	Copper and ceruloplasmin		

Table modified from the ASMBS Integrated Health Nutritional Guidelines (29) *Recommendation from the Endocrine Society Clinical Practice Guideline (30)

Universal postoperative supplementation (Table 3) is an important component of postoperative care. For example, vitamin B_{12} deficiency is common after RYGB without adequate supplementation, and oral doses of 350 mcg/day have been shown to maintain normal plasma B₁₂ levels. Other suggested micronutrient doses are either based on expert opinion or are similar to the recommended dietary allowance (RDA).

Table 3. Recommended Postoperative Supplementation of Vitamins and Minerals				
Micronutrient	Supplementation			
Within a multivitamin with minerals product				
Thiamine	12 mg/day			
Vitamin B ₁₂ (cobalamin)	Oral or sublingual: 350-500 mcg/day			
	Intranasal: 1000 mcg/week*			
	Intramuscular: 1000 mcg/month			
Folate (folic acid)	400-800 mcg/day			
	Women of childbearing age: 800-1000 mcg/day			
Iron	18 mg/day elemental iron			
	RYGB, SG, BPD/DS or menstruating women: 45-60 mg/day			
	Take separately from calcium supplements			
Vitamin D	D ₃ 3000 IU/day			
Vitamin A	LAGB: vitamin A 5000 IU/day			
	RYGB or SG: vitamin A 5,000-10,000 IU/day			
	BPD/DS: vitamin A 10,000 IU/day			
Vitamin E	15 mg/day			
Vitamin K	LAGB, SG or RYGB: 90-120 mcg/day			
	BPD/DS: 300 mcg/day			
Zinc	SG or LAGB: 8-11 mg/day			
	RYGB: 8-22 mg/day			
	BPD/DS: 16-22 mg/day			
Copper	SG or LAGB: 1 mg/day			
	RYGB or BPD/DS: 2 mg/day			
As separate supplementat	ion			
Calcium	LAGB, SG, RYGB: calcium 1200-1500 mg/day (diet + supplements)			
	BPD/DS: calcium 1800-2400 mg/day (diet + supplements)			
	(as calcium citrate, in divided doses)			

Table modified from the ASMBS Integrated Health Nutritional Guidelines (29) *Recommendation from the Endocrine Society Clinical Practice Guideline (30)

Most micronutrients are provided in multivitamins, and chewable multivitamins are recommended

postoperatively. Multivitamins for the general population can be used, provided that attention is

paid to the product's micronutrient contents. The ASMBS recommends one general multivitamin tablet daily for patients who have had LAGB, or 2 general multivitamin tablets daily for those undergoing SG, RYGB or BPD/DS. As an alternative to general multivitamins, bariatric surgery-specific, high-potency multivitamins are available and often contain the recommended doses of micronutrients in one tablet daily.

Multivitamins do not contain the recommended doses of calcium, as calcium can impede the absorption of other micronutrients. Therefore, separate calcium supplementation is usually required. Calcium citrate is the preferred form of supplemental calcium, as it is better absorbed than calcium carbonate in the state of impaired gastric acid production. A patient's dietary calcium intake should be considered when determining the dose of a calcium supplement, as the recommended intakes are generally total daily intakes (diet plus supplements). Iron absorption may be enhanced by co-administration of vitamin C (500-1000 mg) to create an acidic environment or when taken with meat. If inadequate absorption or intolerance occurs, parenteral iron replacement may be necessary.

A suggested schedule for postoperative biochemical monitoring is listed in Table 4. Patients who develop micronutrient deficiencies may need more frequent monitoring.

Table 4. Schedule for Postoperative Micronutrient Monitoring					
	6	12	18	24	Annually
	months	months	months	months	
Vitamin B ₁₂	Х	Х	Х	Х	Х
Folate	Х	Х	Х	Х	Х
Iron, ferritin	Х	Х	Х	Х	Х
25-hydroxyvitamin D	Х	Х	Х	Х	Х
Calcium	Х	Х	Х	Х	Х
Intact PTH	Х	Х	Х	Х	Х
24-hour urinary calcium	X†	X†		X [†]	X†
Thiamine	Optional	Optional	Optional	Optional	Optional
Vitamin A				Optional	Optional
Zinc	Optional	Optional		Optional	Optional
Copper		Optional [†]			Optional [†]

Table modified from the Endocrine Society Clinical Practice Guideline (30)

Examinations should be performed after RYGB or BPD/DS. All of these could be suggested for patients submitted to restrictive surgery where frank deficiencies are less common. Some surgeons perform additional early biochemical evaluation 3 months postoperatively, and the AACE/TOS/ASMBS Clinical Practice Guidelines suggest evaluation earlier than 6 months for some micronutrients (22).

[†]Recommendation from the AACE/TOS/ASMBS Clinical Practice Guidelines (22)

Oral repletion is often sufficient for correcting micronutrient deficiencies, although parenteral therapy may be required in severe disease. After a repletion course, biochemical testing should be performed and a maintenance dose should be established. Micronutrient deficiencies may co-exist; for example, malabsorptive procedures may result in deficiencies of the fat-soluble vitamins A, E and K.

Table 5. Repletion Recommendations for Micronutrient Deficiencies			
Micronutrient	Repletion recommendation		
Thiamine	Oral: 100 mg 2-3 times daily		
	IM: 250 mg daily for 3-5 days or 100-250 mg monthly		
	IV: 200 mg 2-3 times daily to 500 mg 1-2 times daily for 3-5 days, followed		
	by 250 mg/day for 3-5 days		
	Severe disease: administer thiamine prior to dextrose-containing solutions		
Vitamin B ₁₂	Oral: 1000 mcg/day		
(cobalamin)	IM: 1000 mcg/month to 1000-3000 mcg/6-12 months ⁺		
Folate (folic acid)	1000 mcg/day orally		
Iron	150-200 mg elemental iron/day, up to 300 mg 2-3 times daily		
	Calcium may impair iron absorption		
	Consider co-administration of vitamin C to enhance absorption		
	Consider IV iron infusions for severe/refractory iron deficiency		
Vitamin D	D_3 6000 IU/day or D_2 50,000 IU 1-3 times per week, or more if needed to		
	achieve and maintain 25-hydroxyvitamin D >30 ng/mL		
Calcium	Increase dose and titrate to normalize PTH ± 24-hr urinary calcium level*		
Vitamin A	10,000-25,000 IU/day orally until clinical improvement (1-2 weeks)		
	With corneal changes: 50,000-100,000 IU IM x 3 days, then 50,000 IU/day		
	IM for 2 weeks		
Vitamin E	Optimal therapeutic dose not clearly defined, consider 100-400 IU/day		
Vitamin K	Acute malabsorption: 10 mg parentally		
	Chronic malabsorption: 1-2 mg/day orally or 1-2 mg/week parentally		
Zinc	There is insufficient evidence to make a dose-related recommendation		
Copper	Mild-moderate deficiency: oral copper gluconate or sulfate 3-8 mg/day		
	Severe deficiency: 2-4 mg/day of intravenous copper x 6 days		

Table modified from the ASMBS Integrated Health Nutritional Guidelines (29) IM, intramuscular; IV, intravenous

[†]Recommendation from the AACE/TOS/ASMBS Clinical Practice Guidelines (22)

*In chronic kidney disease, PTH goal should be appropriate for renal function (31,32)

Dumping Syndrome and Post-Gastric Bypass Hypoglycemia

Early and late dumping syndromes are a result of altered gastrointestinal anatomy and hormone secretion after bariatric surgery. The two syndromes have distinct symptomatology and pathophysiology though there is considerable overlap in dietary triggers and treatment approaches. Late dumping syndrome is hallmarked by hypoglycemia and will henceforth be referred to as post-gastric bypass hypoglycemia (PGBH).

EARLY DUMPING SYNDROME

Early dumping syndrome (DS) typically occurs within 1 hour of eating and is characterized by both gastrointestinal (nausea, abdominal fullness, diarrhea) and vasomotor symptoms (fainting, sleepiness, weakness, diaphoresis, palpitations, and desire to lie down) (33). Dumping syndrome symptoms can appear as early as 6 weeks after surgery and has been reported to affect up to 20% according to large survey studies and up to 40% in smaller prospective studies of individuals who have undergone both restrictive and malabsorptive procedures (34-37). The pathophysiology of DS is not completely understood but is thought to be due to both a rapid delivery of nutrients to the small intestine causing an osmotic shift of intravascular fluid to the intestinal lumen as well as an increased release of gastrointestinal hormones that disrupt motility and hemodynamic status (38-40). There is debate in the literature on whether DS is an adaptive consequence of bariatric surgery that helps restrict food intake and aids weight loss versus an adverse consequence that reduces quality of life and does not contribute to weight loss (34,41,42).

The diagnosis of DS should be made after the exclusion of more serious entities such as intestinal fistulas, adhesions, ischemia, herniation, obstipation, and gallstone disease which may have shared clinical features (39). There are validated questionnaires as well as provocation tests that have been used to confirm DS in research settings. Oral glucose challenge with an increase in heart rate and hematocrit (indicating hemoconcentration) is one such approach (33,43,44).

The first line treatment for DS is to modify the diet so as to avoid foods that worsen symptoms (oftentimes calorie-dense foods with high fat/refined sugar content and low in fiber), eating small volume meals, not eating and drinking at the same time, eating slowly, chewing well, and avoiding alcohol. Indeed, patients often implement these changes on their own and, over time, symptom severity improves or resolves in many (if not most) patients. In addition, lying down for 30 minutes after eating to slow gastric emptying and mitigate symptoms of hypovolemia may be helpful if symptoms occur (45). There are several small interventional studies and case reports that support the use of dietary supplements (e.g., pectin, guar gum) that increase food viscosity and reduced symptoms of DS, however low palatability and potential choking hazard and bowel obstruction are downsides to their use (39). Somatostatin analogs have also been tested in small studies, although this class of drugs are expensive, involve subcutaneous or intramuscular injections, and have gastrointestinal side effects (39). Enteral tube feedings or bariatric surgery reversal have been reported to improve symptoms when all else fails (39).

POST GASTRIC BYPASS HYPOGLYCEMIA

Post-gastric bypass hypoglycemia (PGBH) is a rare complication of bariatric surgery that occurs several months to years after procedures that rapidly pass nutrients through the stomach (or stomach remnant) directly to the small intestine and has not been reported with restrictive procedures. It is defined by the presence of postprandial hypoglycemia (plasma glucose concentration < 55 mg/dL) manifesting with neuroglycopenic symptoms such as confusion or loss of consciousness which resolve when glucose levels are normalized (Whipple's Triad) (46). PGBH is insulin mediated, stimulated by a carbohydrate containing meal, and is distinct from dumping syndrome in that it occurs 1-3 hours after eating without vasomotor symptoms (39).

The reported prevalence of PGBH varies widely in the literature depending on the methodology of measurement. In a retrospective nationwide cohort study performed in Sweden, involving >5000 individuals who had undergone bariatric surgery, the rate of hypoglycemia (and related symptoms such as dizziness. visual disturbances, syncope and seizures) as ascertained by diagnosis codes was low but significantly higher in patients without diabetes who had undergone RYGB (0.2%) compared to the general reference population (0.04%) (47). A large cross-sectional database analysis of 145,582 US subjects who underwent RYGB and 29,930 who underwent SG showed that only 0.1% and 0.02% had self-reported hypoglycemia as a postoperative complication (48). Another US study involving mailed

questionnaires to subjects who had undergone bariatric surgery reported that 11% had experienced severe or medically confirmed hypoglycemia though, interestingly, the only significant correlate of these severe postoperative hypoglycemic episodes was a history of pre-operative hypoglycemic symptoms (49).

The exact pathophysiology of PGBH is not entirely understood. In one case series, six individuals with biochemical confirmation of PGBH underwent selective arterial calcium stimulation testing followed by partial pancreatectomy (50). Pathological analysis of pancreatic samples confirmed an insulinoma in one, while five had evidence for beta cell hyperplasia and hypertrophy compared to obese controls who had undergone pancreatectomy for pancreatic cancer. The authors of a subsequent study using the same pathology samples taken from the affected post-RYGB patients but compared to otherwise healthy lean and obese controls found no evidence for post-RYGB islet hypertrophy or "nesidioblastosis" and postulated that hyperinsulinemia may instead be due to hyper functioning of existing beta cells (51). A commonly proposed mechanism for such beta cell "hyperfunction" is the large increase in GLP-1 response to meals that occurs after gastric bypass (52-54). In two separate studies, individuals with PGBH had higher levels of GLP-1 that were generated in response to a mixed meal challenge compared to bariatric patients without symptoms (52,53). However, similar symptoms and effects have not been reported with long-term use of GLP-1 agonists used for the management of type 2 diabetes and obesity. Interestingly, despite large increases in GLP-1 secretion, post-prandial glucagon levels are not suppressed in both non-symptomatic patients after RYGB and PGBH patients, nor does glucagon treatment readily reverse this condition.

Alternatively, a reasonable explanation for the state of post-prandial hyperinsulinemic-hypoglycemia after RYGB in some patients may come down to a mismatch between the clearance of glucose and insulin after the meal. Gastric emptying is accelerated after RYGB leading to earlier and higher peaks of both glucose and insulin compared to non-surgical controls. Without a pyloric valve regulating nutrient entry to the gut, however, glucose levels also fall quickly. Since insulin clearance occurs at a fixed rate, insulin levels may not be able to fall commensurate with the drop in glucose levels, and without a pyloric valve to provide a more piecemeal entry, a mismatch may ensue.

If suspected, a careful history of symptoms consistent with PGBH should be ascertained and other etiologies of hypoglycemia should be ruled out (e.g., medication-induced hypoglycemia and rarely an insulinoma can be unmasked when insulin resistance improves after surgically induced weight loss). Although there is no standardized test to confirm PGBH, a mixed-meal tolerance test with confirmatory serum glucose levels both before and at 30-minute intervals after the meal is commonly used Alternatively, 3-day continuous (55). glucose monitoring performed in the context of an individual's normal eating pattern has been demonstrated to be sensitive in detecting PGBH (56). Oral glucose tolerance testing is less useful as individuals who have undergone RYGB commonly experience low glucose levels following an oral glucose load without symptoms of hypoglycemia (57,58).

Suggested treatments for PGBH ranging from dietary modification to more extreme measures such as gastric bypass reversal have been reported. Recommended dietary modifications consist of small frequent meals that do not result in large, rapid carbohydrate delivery to the small intestine. These meals should be high in fiber and protein and very low in simple carbohydrates (59). Successful use of medications such as acarbose, nifedipine, somatostatin, and diazoxide has been described in case reports and small series (60-63). As a last resort, symptoms have been shown to resolve with re-introduction of nutrient flow through the stomach and duodenum either by gastric-tube feedings or reversal of the gastric bypass. Due to future risk of diabetes and frequent symptom recurrence, PGBH treatment involving distal pancreatectomy is no longer recommended (55).

Cholelithiasis

Rapid weight loss after bariatric surgery promotes gallstone formation by increasing the lithogenicity of bile, with hypersaturation of the bile with cholesterol and with increased mucin production (64,65). Gallbladder hypomotility contributes to this process (66). Further, additional risk factors for cholelithiasis, including obesity, female sex, and premenopausal status, are already prevalent in the bariatric surgery patient population. Indeed, after RYGB, reported incidence of cholelithiasis ranges from 7% to 53%, with most figures around 30%, substantially higher than in the general population (67). A recent study of patients undergoing SG documented a similarly elevated incidence of radiographic cholelithiasis (68).

Ursodeoxycholic acid, commonly known as ursodiol, can successfully reduce risk of postoperative cholelithiasis. In a multicenter randomized controlled trial of RYGB patients, ursodiol at any of 3 doses decreased risk compared to placebo, with 43% of patients in the placebo group forming gallstones on ultrasound by the 6-month postoperative time point, vs. 8% of patients in a 300 mg twice daily group. The efficacy of prophylactic ursodiol after bariatric surgery was subsequently confirmed in a meta-analysis of this and 4 other RCTs (69), and a recent randomized controlled trial demonstrated that ursodiol decreased cholelithiasis incidence 6 months after SG (68). As a result of these data, a common practice is to treat bariatric surgery patients with ursodiol 300 mg twice daily for the 6 months following surgery.

Cholecystectomy is sometimes performed at the time of bariatric surgery, but in whom it should be performed is controversial and variable between surgeons (67). Some surgeons perform prophylactic cholecystectomy at the time of surgery; some perform cholecystectomy if preoperative ultrasound reveals gallstones, even if asymptomatic; and some perform concomitant cholecystectomy only if both pathology and symptoms exist.

Nephrolithiasis

Bariatric surgery increases risk for new-onset nephrolithiasis. This increased risk is procedurespecific and is proportionate to the degree of procedure-induced malabsorption: greatest after BPD/DS, moderate following RYGB, and risk similar to the nonsurgical population following SG and LAGB (70-72). For example, in one recent retrospective cohort study, the comorbidity-adjusted relative hazard of nephrolithiasis was 4.15 (2.16-8.00) after the most malabsorptive procedures and 2.13 (1.30-3.49) after RYGB; the risk after SG and LAGB was similar to that of obese controls (71).

The pathophysiologic mechanisms of kidney stone formation after RYGB and BPD/DS include low urinary volume and low urinary citrate, but the driving mechanism relates to high urinary oxalate in the setting of malabsorption (enteric hyperoxaluria) (70,73,74). Normally, dietary calcium binds dietary oxalate, precipitates out as calcium oxalate, and is excreted in the feces. In the setting of malabsorption. non-absorbed fatty acids preferentially bind calcium in the intestine, leaving high concentrations of unbound oxalate that can passively diffuse into the blood, where it is filtered and excreted by the kidneys. Under predisposing conditions—such as low urinary volume—urinary oxalate may precipitate with urinary calcium to form kidney stones. Further, colonic permeability to

oxalate may increase with exposure to unconjugated bile salts and long chain fatty acids, both of which increase after bariatric surgery. Finally, it is speculated that postoperative alterations in gut microbiota, and particularly in the oxalate-degrading *Oxalobacter formigenes*, might also contribute to hyperoxaluria (70,73,74).

Therapeutic strategies to mitigate nephrolithiasis risk after bariatric surgery (Table 7) are similar to those for the general population (75). Fluid intake to achieve a urine volume of at least 2.5 L/day can be a challenge when a small stomach pouch restricts overall intake and a patient should be counseled to drink fluids between rather than with meals. This highlights the need for the sipping of water throughout the day. A registered dietitian can help a patient achieve a diet low in oxalate-rich foods that also meets the patient's other dietary needs. Some patients may assume that consumption of calcium will increase kidney stone risk and thus may benefit from teaching that adequate calcium consumption (from diet and calcium citrate supplements) is necessary to limit oxalate absorption and avoid enteric hyperoxaluria.

Table 7. Therapeutic Strategies to Decrease Risk of Kidney Stones			
Strategy	Rationale		
Hydration to achieve urine volume of \geq 2.5 L/day	Dilute urine		
Limitation of oxalate-rich foods (e.g., spinach, nuts, vitamin C)	Limit oxalate absorption		
Low fat diet	Limit oxalate absorption		
Adequate calcium consumption (diet ± calcium citrate supplements)	Limit oxalate absorption		
Low salt and low non-dairy animal protein diet	Increase urinary citrate		
Potassium citrate therapy if urinary citrate low	Increase urinary citrate		

Bone Loss and Fracture Risk

Bariatric surgery has a significant impact on bone metabolism. All bariatric procedures induce a high postoperative bone turnover state. For example, after RYGB biochemical markers of bone resorption have been shown to double in the first postoperative year (76-79). Bone mineral density (BMD) assessed by dual-energy X-ray absorptiometry (DXA) decreases (76-79), and while there has been concern about potential unreliability of DXA assessment in the setting of marked weight loss and changing soft tissue composition (80,81), declines in BMD have now been demonstrated clearly using quantitative computed tomography (QCT) at the axial skeleton and high-resolution peripheral QCT at the appendicular skeleton (82-86). Decline in BMD has been most consistently reported after RYGB (77,78,84), but also after BPD/DS (87,88) and SG

(86,89-91). After LAGB, DXA-assessed BMD decreases modestly at the proximal hip but not at the spine (77,78), with reductions in hip density smaller than those after RYGB (92). While some loss of bone mass may be an appropriate physiological response to weight loss, BMD has been shown to decline progressively after RYGB, even after weight stabilization (83,90,93) and mild weight regain (93).

Ultimately, the important question is whether fracture risk increases after bariatric surgery. Recent studies have now indicated that fracture risk is indeed higher after bariatric surgery in comparison to obese (94-96), non-obese (95), and general population (97) nonsurgical controls. There may be bias introduced when studies identify obese nonsurgical controls based on the assignment of diagnostic codes for morbid obesity, as those nonsurgical patients may be sicker. However, recent studies with BMI-matching also demonstrate an increase in fracture risk (98,99). Fracture risk after bariatric surgery appears to vary by bariatric procedure, with the risk most clearly defined for RYGB (98). Fracture risk is higher after RYGB than LAGB (100,101). Risk for fracture might be lower after SG (96,102), although longer-term data are needed for SG, the newer procedure, before conclusions should be drawn.

Negative skeletal effects resulting from bariatric surgery appear to be multifactorial (79,103-105). Potential mechanisms include the decreased skeletal loading with weight loss; loss of muscle mass: in levels fat-secreted changes of hormones (adipokines), sex steroids. and gut-derived hormones; changes in bone marrow adipose tissue (106); and, importantly, nutritional factors including vitamin D deficiency, inadequate calcium intake, and calcium malabsorption. Intestinal calcium absorption has been shown to decrease after RYGB even in the setting of optimized vitamin D status (84), presumably because the bypassed duodenum and proximal jejunum are the usually predominant sites of transcellular, 1,25-dihydroxyvitamin active. Dmediated calcium uptake, and the distal intestine is unable to compensate. In response to calcium malabsorption after RYGB, parathyroid hormone (PTH) secretion increases, and the effects of PTH include an increase in bone resorption in order to maintain serum calcium concentration. Meanwhile, bone resorption also increases due to non-PTHmediated processes like mechanical unloading and changes in the hormonal milieu. This mobilization of calcium from the skeleton may actually dampen the need for greater PTH secretion (Figure 1).



Figure 1. Effects of RYGB on calcium homeostasis. Reprinted from J Steroid Biochem Mol Biol, Schafer AL, Vitamin D and intestinal calcium transport after bariatric surgery, 173:202-210, 2017 (107), with permission from Elsevier.

Strategies that aim to decrease the risk of postoperative skeletal complications have been included in the AACE/TOS/ASMBS Clinical Practice Guidelines (22) and Endocrine Society Clinical Practice Guidelines (30), as well as in an additional position statement from the ASMBS (108). A reasonable approach is described in Table 8.

Preoperatively, testing of 25-hydroxyvitamin D level with treatment of vitamin D deficiency is recommended for patients preparing to undergo any bariatric surgical procedure. DXA scanning should be performed based on age-appropriate recommendations of the National Osteoporosis Foundation (109) or the United States Preventive Services Task Force (110); other patients with risk factors for osteoporosis or fracture could also undergo baseline BMD assessment, although there is no evidence to support that approach.

Postoperatively, universal supplementation with calcium and vitamin D are necessary after any bariatric surgical procedure; even after procedures without a malabsorptive component since restricted food intake and variety poses a risk for micronutrient deficiencies. After RYGB, SG, and LAGB, a total calcium intake of 1200-1500 mg/day from diet and supplements (as needed) is recommended. After BPD/DS, a higher calcium intake may be necessary. Supplemental calcium should be provided as chewable calcium citrate in divided doses. An initial postoperative vitamin D supplement of 3000 IU/day is

reasonable for most patients regardless of procedure. Postoperative laboratory monitoring should include 25-hydroxyvitamin D, calcium. albumin, phosphorus, and PTH levels. The vitamin D supplement dose can be titrated to achieve and maintain a 25-hydroxyvitamin D level of at least 30 ng/mL. If secondary hyperparathyroidism is present despite an optimized 25-hydroxyvitamin D level, the most likely cause is inadequate calcium intake or absorption; a low 24-hour urinary calcium level would support this. Increased calcium intake would be appropriate, with follow-up laboratory testing to confirm normalization of PTH level. (PTH level should, of course, be interpreted and targeted based on renal function.) Professional organizations have differed recommendations in their about postoperative DXA, in light of the absence of evidence about the utility of such screening.

Table 8. Pre- and Postoperative Skeletal Health Strategies				
Preoperative strategies				
	Check 25-hydroxyvitamin D and replete low levels			
	DXA based on age-appropriate screening			
	Consider DXA in select patients			
Postoperative strategies				
Supplementation	Calcium, as calcium citrate, to achieve total daily calcium intakes:			
	LAGB, SG, RYGB: Calcium 1200-1500 mg/day from diet + supplements			
	BPD/DS: Calcium 1800-2400 mg/day from diet + supplements			
	Vitamin D 3000 IU, titrate to ≥30 ng/mL			
Lab monitoring	Calcium, albumin, phosphorus, PTH, 25-hydroxyvitamin D after 3 months,			
	then every 6-12 months			
	24-hour urinary calcium if additional data is needed (e.g., elevated PTH)			
BMD monitoring	DXA based on age-appropriate screening; consider in others after 2 years			

Other strategies which may benefit the skeletal health of the bariatric surgery patient include exercise—particularly weight-bearing and muscleloading exercise—and higher protein intake, as these mitigate loss of bone mass during non-surgical weight loss in older adults. A randomized controlled trial of a multipronged intervention of exercise, calcium, vitamin D, and protein supplementation was shown to attenuate—although not entirely prevent postoperative increases in bone turnover markers and declines in BMD after RYGB and sleeve gastrectomy (91).

For those who have had bariatric surgery and are found to be osteoporotic, there are very few data to guide management. Antiresorptive osteoporosis medications such bisphosphonates as and denosumab should only be considered after appropriate therapy for calcium and vitamin D insufficiency and confirmation that adequate calcium and vitamin D status are maintained. Otherwise, there is a meaningful risk of medication-induced (111). lf pharmacotherapy hypocalcemia is prescribed, a parenterally administered agent is recommended due to concerns about adequate gastrointestinal absorption and potential anastomotic ulceration with orally administered bisphosphonates. Research is needed to guide osteoporosis management in postoperative bariatric surgery population.

WEIGHT REGAIN AFTER BARIATRIC SURGERY

Given that obesity is a chronic disease and sustained weight loss requires ongoing management, understanding the durability of weight loss after bariatric of critical surgery is importance. Unfortunately, published studies reporting weight loss after bariatric surgery thus far tend to be short-term (many with < 5 years follow-up), and longer studies often lack high retention rates and/or adequate control groups (112,113). Additionally, the literature on long-term weight loss mostly addresses LAGB and RYGB, and the literature on SG is just emerging. Furthermore, methods of quantifying weight change vary across studies, including percentage excess weight loss (%EWL) and percentage weight loss (%WL) (Table 9), making comparisons between studies challenging. Percentage weight loss (%WL) may be the best method for measuring weight change after bariatric surgery (114), as it is least confounded by preoperative BMI and allows surgical studies to be compared to non-surgical interventions. However, this method is not widely used in the surgical literature.

Table 9. Hypothetical Comparison of Anthropometrics, Including Total Weight Loss,				
Excess Weight Loss, and Percentage Weight Loss, Following Bariatric Surgery.				
Example patient	Baseline	Scenario 1:	Scenario 2:	
		Post-op BMI 30	Post-op BMI 35	
		kg/m²	kg/m²	
Weight	120 kg (264 lbs)	79 kg (175 lb)	93 kg (204 lb)	
Height	163 cm (64 in)			
BMI	45 kg/m²	30 kg/m ²	35 kg/m²	
1 + 1 = 1 + 1 + 1 + 1 + 1 + 1 + 1 + 1 +				
Ideal Weight (If BIVII 25 kg/m²)	66 KG (145 IDS)			
	E4 kg (110 kg)	11 km (20 lb)	0.7 km (50 lb)	
	54 Kg (119 lbs)	14 Kg (30 lb)	27 Kg (59 lb)	
(Weight above ideal weight)				
Excess BMI	20 kg/m ²	5 kg/m ²	10 kg/m²	
(BMI above 25 kg/m ²)				
Total Weight Loss		40 kg (89 lbs)	27 kg (60 lbs)	
(baseline weight - post op				
weight)				

% Weight Loss	 44%	33%
(Total weight loss/baseline		
weight x 100)		
% Excess Weight Loss	75%	50%
(Total weight loss/excess weight		
x 100)		
% Excess BMI Loss	75%	50%
(Excess BMI - total BMI loss)		

Using RYGB as an example, several studies with long-term follow-up and high retention rates highlight expected weight trajectories (Figure 2 and Table 10). It is important for patients to understand that the amount of weight loss can be highly variable between people, and that soon after achieving a postoperative weight loss nadir, it is not unusual to have a slight weight regain before achieving a new weight stabilization. These findings were highlighted recently in an analysis from the Longitudinal Assessment of Surgery (LABS) Study, Bariatric a 10-center observational cohort study in the U.S. that followed 2,348 participants after RYGB (n=1,738) or LAGB (n=610). Serial weight measurements were obtained in person for 82.9% of participants up to 7 years after surgery (10). The weight nadir was typically achieved between 6 months and 2 years after this procedure, with a mean weight loss 7 years after RYGB of 28.4% (95%CI, 27.6-29.2) with 3.9% weight regain having been observed between years 3-7. Grouping individuals by similarly modeled weight-loss trajectories identified six distinct patterns (Figure 2). Roughly 75% of individuals achieved a 7-year weight loss of 25% or more from baseline (Groups 3 to 6). Less than 5% of patients lost less than 10% of their initial weight while 13.3% lost 45% or more. These patterns of weight loss closely mirrored achieved weight loss by 6 months and all but one group experienced some weight rebound between postoperative years one to six (10).



Figure 2. Weight change trajectory groups following RYGB. Lines indicate modeled group trajectories; data markers and median values; bars, interquartile range (IQR) of observed data. Negative value indicates weight loss from baseline (10).

Table 10. Observational Studies of Long-Term Weight Loss Following RYGB				
Author (Year)	Study size (% follow up)	Weight loss at follow up		
Study Type				
Courcoulas (2018)	N=1130 (86%)	28.4% WL at 7 years		
Prospective				
Adams (2012)	N=417 (92.6%)	27.7% WL at 6 years		
Prospective				
Maciejewski (2016)	N=688 (81.9%)	28% WL at 10 years		
Retrospective				
Christou (2006)	N=288 (83%)	68.1% EWL at 12 years		
Retrospective				
Carbajo (2017)	N=1200 (87% at 6 years, 74%	77% EWL at 6 years		
Retrospective	at 8 years, 72% at 10 years,	73% EWL at 8 years		
	70% at 12 years)	70% EWL at 10 years		
		70% EWL at 12 years		
Pories (1995)	N=574 (96%)	55% EWL at 10 years		
Retrospective				

In the LABS study, 7-year weight loss after LAGB averaged only 15% with 25% losing \leq 5% of baseline weight and another 5% regaining all their lost weight and more (10). Data on weight loss following SG is still emerging, but typically runs roughly 2% to 5% less than RYGB by either %EWL or %TWL criteria, with greater variability between patients (13,120-123).

Adams et al. prospectively followed a cohort of 417 subjects undergoing RYGB at a Utah-based surgical group (115) for 6 years, 92.6% of whom had followup weights, mostly obtained via in person measurement or medical chart review. Weight change was compared to 2 control groups: those who sought but did not undergo surgery (72.9% follow-up) and matched controls from a local healthcare database (96.9% follow-up). The RYGB group had the greatest mean adjusted weight loss from baseline to postoperative year 2 at 34.9%, decreasing to 27.7% in postoperative year 6. The authors report the absolute difference between these two figures as "percent weight regain" of 7.2%. Additionally, among RYGB patients, 94% had lost >20% of baseline weight at year 2, though 76% had maintained >20% weight loss at year 6. The control groups experienced negligible weight change.

A Veterans Administration (VA) retrospective cohort study evaluated 10-year weight loss outcomes among 1787 individuals who underwent RYGB, comparing these to 5,305 non-surgical matches derived from the VA electronic health record (116). Among eligible patients, 81.9% of RYGB patients and 67.4% of non-surgical matches had follow-up data at 10 years. Percentage weight loss in the RYGB group was 31% (n= 1,755) at year 1 and 28% (n=564) at year 10. The control group had lost only modest amounts of weight in follow-up, and the difference in weight loss between RYGB and controls was calculated at 30% and 21% in postoperative years 1 and 10, respectively.

Christou *et al.* of McGill University retrospectively studied 272 patients who had undergone RYGB, 83% of whom were available for in-person or phone follow-up (117). Among all patients, the greatest %EWL was 89% at the 2.5 years postoperative timepoint, and this reduced to 68.1% at the 12 years postoperative time-point. Thus, approximately 18% of excess weight loss in the second year was regained by year 12. At 10 years, among patients with a starting BMI <50 kg/m², "excellent" surgical response (postoperative BMI <30 kg/m²) and "good" surgical response (postoperative BMI 30-35 kg/m²) were achieved in 51% and 29%, respectively. Among those with a baseline BMI >50 kg/m², the results were less positive: 13% achieved an excellent response, and 29% achieved a good response. Rates of follow-up were similar between the two groups.

Carbajo *et al.* of Spain performed a database analysis of 1,200 patients who underwent oneanastomosis gastric bypass (a modification of RYGB) and had at least 6 years follow-up (118). Mean preoperative BMI was 46 kg/m² (range, 33-86 kg/m²). Among the 1,200, follow-up rates at 6, 8, 10 and 12 years were 87% (n=233), 74% (n=607), 72% (n=759) and 70% (n=839), with roughly half followed up in person and half via electronic correspondence. %EWL was 77% for 6-year follow-up, 73% for 8-year follow-up, and 70% for 10- and 12-year follow-up. Percentage weight loss in the first 5 years of operation was not reported.

Pories *et al.* of East Carolina University School of Medicine retrospectively evaluated %EWL in patients who underwent RYGB from 1980-1994 (119). Among the 608 operated on, 574 were alive at the time analysis, and 553 of those remained in contact (i.e., 96% follow-up). Among the 553, 49% were examined in person, and the remainder were interviewed by telephone. Mean %EWL values at years 1, 2, 10, and 14 were 69% (n=506), 58% (n=407), 55% (n=158), and 49% (n=10), respectively. Thus, the average excess weight loss at 14 years is 20% less than at year 1.

Overall, among RYGB studies with high retention rates, the greatest average weight loss (nadir) is typically reported in the first two years with %EWL ranging from 69-89% and %WL of 31-35%. In general, about 10-20% of the maximum weight lost after surgery is regained when patients are followed for six years or longer. However, %EWL remains between 49-70% and %WL nearly 30%, which far exceeds any non-surgical weight loss interventions.

Medical Management of Postoperative Weight Regain

In observational studies, clinical predictors of insufficient weight loss or weight regain after bariatric surgery have identified specific diet and exercise practices, female sex, older age, higher initial BMI, presence of T2D, psychological factors, and non-white race, although the influence of any individual factor is relatively small (10,124,125). While the actual physiology that explains the long-term weight rebound following both RYGB and SG or why some individuals achieve 50% weight loss (or more) and others regain all their lost weight remains unknown at present, it is possible traditional influencers of body weight are playing a role, including genetics (126,127) and the postoperative use of medications that promote weight gain (128).

Interventions to stabilize or restore weight loss that have compared lifestyle or psychological support to usual care after surgery have shown (with some exceptions) to be minimally effective, but the studies conducted thus far have been relatively small (124). Several observational studies suggest that medical (drug) weight loss therapy may be a promising modality to aid in weight loss after bariatric surgery. The largest published study to date on the use of pharmacologic agents to reverse weight regain or weight loss plateau came from 319 patients who underwent RYGB (n=258) or SG (n=61) at 2 academic centers and had been prescribed one or more weight loss medications (129) with at least 1 year of follow-up (130). The medications included FDA-approved weight-loss rugs (e.g., phentermine,

liraglutide, lorcaserin, orlistat) and off-label use of medications with potential weight-lowering effects topiramate monotherapy, (e.g., metformin, pramlinitide, and canagliflozin). The medications were more often started for weight regain (78.5%) than weight loss plateau (21.5%), and the mean start time of a medication was earlier after SG (mean of 23.2 months) than RYGB (mean of 59.3 months). Overall, 54% of patients lost at least 5% of weight, 30% lost at least 10%, and 15% lost more than 15%. Topiramate use was associated with highest success, with a 1.9 odds ratio of achieving at least 10% weight loss. Other small observational studies have shown efficacy of topiramate, liraglutide, phentermine, and phentermine/topiramate combination for post bariatric surgery weight loss (131-135). A recent randomized, controlled trial of liraglutide 1.8 mg given to patients with persistent or recurrent T2DM after RYGB or SG for six months showed an additional 4 kg weight loss compared to placebo (136).

While historically weight loss variability or regain after weight-loss surgery has been attributed to "poor habits" or "failure" on the patient's part to adhere to recommended food intake, it is now recognized that such variability is similar to other chronic diseases where some individuals respond well to certain therapies while others do not or in which progression of the underlying disease state necessitates combination therapies (such as in T2DM as the islet

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cell impairment progresses over time). It is therefore important to continue to support the patient who experiences postoperative weight regain by emphasizing continued healthy lifestyle practices, identifying medical conditions or medications that might be contributing to their weight gain and either stopping them or switching to weight neutral medications, and considering adding in weight loss medications.

CONCLUSIONS

The postoperative management of the bariatric surgery patient requires an interdisciplinary team, including the surgeon, dietitian, and endocrinologist and/or primary care provider. It is critical that endocrinologists and primary care providers have the training and tools required to meet the population's medical needs, which include the management of chronic metabolic conditions and the prevention and treatment of postoperative medical and nutritional complications during lifelong follow-up. The teamwork of informed and experienced clinicians can optimize the long-term benefits of bariatric surgery.

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