**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 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 dyslipidemia, 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 the risk of cholelithiasis, which can be mitigated by ursodiol. After 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. In summary, given dramatic physiologic changes with bariatric surgery, clinicians should be prepared to taper treatments for chronic metabolic diseases, and to manage postoperative medical and nutritional complications. For complete coverage of this and all related areas of Endocrinology, please visit our FREE on-line web-textbook, [www.endotext.org](http://www.endotext.org).

**INTRODUCTION**

Bariatric surgery is a highly effective treatment for obesity, inducing substantial and durable weight loss and improvement in obesity-related comorbidities ([1](#_ENREF_1)). Moreover, it reduces mortality ([2-4](#_ENREF_2)). The surgical treatment of obesity is discussed in the chapter “Surgical Treatment of Obesity”, 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). Chapter “Surgical Treatment of Obesity” also addresses the benefits of bariatric surgery on obesity-related conditions including type 2 diabetes.

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 conditions, focusing on type 2 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

|  |
| --- |
| Complication |
| 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, the primary care provider 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 loss-independent, with weight loss-independent effects likely mediated by alterations in gut hormones, gastrointestinal tract nutrient sensing, bile acid metabolism, and the gut microbiome ([5](#_ENREF_5),[6](#_ENREF_6)). Due to these complex factors and the effects of postoperative calorie restriction, improvement in glucose homeostasis is evident within days to weeks following RYGB ([7](#_ENREF_7),[8](#_ENREF_8)). 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](#_ENREF_1)). Of participants in the Longitudinal Assessment of Bariatric Surgery-2 (LABS-2) study with T2D, 69% of RYGB participants and 30% of LAGB participants were in diabetes remission 3 years after surgery ([9](#_ENREF_9)). Even after controlling for differences in amount of weight lost, the diabetes remission rate after RYGB was almost double that after LAGB. The newer SG procedure appears to be positioned between RYGB and LAGB in T2D effectiveness ([10-12](#_ENREF_10)). Effects of surgery on T2D are discussed at greater length in the chapter “Surgical Treatment of Obesity”.

The endocrinologist or primary care provider caring for a bariatric surgery patient with T2D must anticipate a quick and potentially dramatic improvement in glycemic status. Typically, oral insulin secretagogues (sulfonylureas 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 hypoglycemia. Metformin is often continued postoperatively, with appropriate caution exercised in patients with reduced kidney function, until blood glucose levels and hemoglobin A1c 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 insulin sensitivity and volume status. 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 A1c 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, certain patients are at higher risk for not going into remission or for having recurrence of their diabetes over time, including older patients, those with a longer-duration of diabetes, and those who required more than one non-insulin medication or were using insulin ([9](#_ENREF_9),[13](#_ENREF_13)). 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 ([13](#_ENREF_13)). In the LABS-2 study, 7 years after surgery, 60% of RYGB participants and 20% of LAGB participants were in diabetes remission ([14](#_ENREF_14)).

In patients not reaching glycemic targets or experiencing relapse, therapies can be resumed or added. A rational 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 ([15](#_ENREF_15)), suggesting weight loss-dependent and weight loss-independent mechanisms ([16](#_ENREF_16)). An early systematic review and meta-analysis of bariatric surgery outcomes demonstrated that, of patients with preoperative hypertension, hypertension resolved completely after surgery in 62% and resolved or improved in 79% ([1](#_ENREF_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 often yielded less impressive but still very favorable results ([16](#_ENREF_16),[17](#_ENREF_17)). 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 ([18](#_ENREF_18)), and 33% of RYGB participants and 17% of LAGB participants had complete remission after 7 years ([14](#_ENREF_14)). The newer SG procedure also has a substantial effect on hypertension, with resolution or improvement in the majority of cases ([19](#_ENREF_19)), although a recent meta-analysis concluded that the odds of resolution of hypertension was greater after RYGB than SG ([20](#_ENREF_20)). Effects of bariatric surgery on hypertension are also discussed in the chapter “Surgical Treatment of Obesity”..

Because the effect of bariatric surgery on blood pressure is thought to be variable and potentially less durable than the effect 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 ([21](#_ENREF_21)). 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 ([22](#_ENREF_22)). 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 improved in 71%, and hypertriglyceridemia improved in 82% ([1](#_ENREF_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 ([18](#_ENREF_18)), and percentages were generally similar 7 years after surgery ([14](#_ENREF_14)). Regarding the SG, a systematic review confirmed its effectiveness for the treatment of dyslipidemia ([23](#_ENREF_23)). 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 ([11](#_ENREF_11)). Change in LDL level was not different between groups, although the number of medications needed to treat hyperlipidemia was lower in the surgical groups than the medical therapy group. Effects of bariatric surgery on dyslipidemia are also discussed in the chapter “Surgical Treatment of Obesity”..

Unlike insulin and antihypertensive medications, which must be decreased or discontinued when no longer needed in order to acute the acute dangers of overtreatment, lipid-lowering medications may be continued during the metabolically dynamic early postoperative period. Moreover, 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 ([24](#_ENREF_24)) and National Lipid Association recommendations ([25](#_ENREF_25)). With this in mind, for many patients, endocrinologists and primary care providers should be careful preoperatively 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 ([26](#_ENREF_26)). In many bariatric centers, proton pump inhibitor therapy is prescribed postoperatively, as evidence from cohort studies suggests that it may decrease ulcer risk ([27](#_ENREF_27)). 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 is often the provider to identify and manage 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 a 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 ([28](#_ENREF_28)), Clinical Practice Guidelines from the combined American Association of Clinical Endocrinologists (AACE), The Obesity Society (TOS), and ASMBS ([21](#_ENREF_21)), and The Endocrine Society Clinical Practice Guidelines ([29](#_ENREF_29)). These recommendations for adults reflect general guidelines, and patients with specific diseases may require further evaluation and closer monitoring. For example, nutritional anemias resulting 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 B12 (cobalamin) | All | Vitamin B12 (optional: MMA)  |
| Folate (folic acid) | All | Folate (optional: RBC folate, homocysteine, MMA) |
| 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 ([28](#_ENREF_28))

\*Recommendation from the Endocrine Society Clinical Practice Guideline ([29](#_ENREF_29))

Universal postoperative supplementation (Table 3) is an important component of postoperative care. For example, vitamin B12 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 B12 (cobalamin) | Oral or sublingual: 350-500 mcg/day Intranasal: 1000 mcg/week\*Intramuscular: 1000 mcg/month |
| Folate (folic acid) | 400-800 mcg/dayWomen of childbearing age: 800-1000 mcg/day |
| Iron | 18 mg/day elemental ironRYGB, SG, BPD/DS or menstruating women: 45-60 mg/dayTake separately from calcium supplements |
| Vitamin D | D3 3000 IU/day |
| Vitamin A | LAGB: vitamin A 5000 IU/day RYGB or SG: vitamin A 5,000-10,000 IU/dayBPD/DS: vitamin A 10,000 IU/day |
| Vitamin E | 15 mg/day |
| Vitamin K | LAGB, SG or RYGB: 90-120 mcg/dayBPD/DS: 300 mcg/day |
| Zinc | SG or LAGB: 8-11 mg/dayRYGB: 8-22 mg/dayBPD/DS: 16-22 mg/day |
| Copper | SG or LAGB: 1 mg/dayRYGB or BPD/DS: 2 mg/day |
| As separate supplementation |
| 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 ([28](#_ENREF_28))

\*Recommendation from the Endocrine Society Clinical Practice Guideline ([29](#_ENREF_29))

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 months | 12 months | 18 months | 24 months | Annually |
| Vitamin B12  | X | X | X | X | X |
| Folate | X | X | X | X | X |
| Iron, ferritin | X | X | X | X | X |
| 25-hydroxyvitamin D | X | X | X | X | X |
| Calcium | X | X | X | X | X |
| Intact PTH | X | X | X | X | X |
| 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 ([29](#_ENREF_29))

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 ([21](#_ENREF_21)).

†Recommendation from the AACE/TOS/ASMBS Clinical Practice Guidelines ([21](#_ENREF_21))

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 dailyIM: 250 mg daily for 3-5 days or 100-250 mg monthlyIV: 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 daysSevere disease: administer thiamine prior to dextrose-containing solutions |
| Vitamin B12 (cobalamin) | Oral: 1000 mcg/dayIM: 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 dailyCalcium may impair iron absorptionConsider co-administration of vitamin C to enhance absorptionConsider IV iron infusions for severe/refractory iron deficiency |
| Vitamin D | D3 6000 IU/day or D2 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/daySevere deficiency: 2-4 mg/day of intravenous copper x 6 days |

Table modified from the ASMBS Integrated Health Nutritional Guidelines ([28](#_ENREF_28))

IM, intramuscular; IV, intravenous

†Recommendation from the AACE/TOS/ASMBS Clinical Practice Guidelines ([21](#_ENREF_21))

\*In chronic kidney disease, PTH goal should be appropriate for renal function ([30](#_ENREF_30),[31](#_ENREF_31))

**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) ([32](#_ENREF_32)). 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 ([33-36](#_ENREF_33)). 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 ([37-39](#_ENREF_37)). 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 ([33](#_ENREF_33),[40](#_ENREF_40),[41](#_ENREF_41)).

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 ([38](#_ENREF_38)). 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 ([32](#_ENREF_32),[42](#_ENREF_42),[43](#_ENREF_43)).

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 ([44](#_ENREF_44)). 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 ([38](#_ENREF_38)). 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 ([38](#_ENREF_38)). Enteral tube feedings or bariatric surgery reversal have been reported to improve symptoms when all else fails ([38](#_ENREF_38)).

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) ([45](#_ENREF_45)). 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 ([38](#_ENREF_38)).

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%) ([46](#_ENREF_46)). 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 post-operative complication ([47](#_ENREF_47)). 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 post-operative hypoglycemic episodes was a history of pre-operative hypoglycemic symptoms ([48](#_ENREF_48)).

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 ([49](#_ENREF_49)). Pathological analysis of pancreatic samples confirmed an insulinoma in one, while five had enlarged beta cell nuclear diameter compared to obese controls ([50](#_ENREF_50)). The authors of this study postulate that hyperinsulinemia may be due to hyper functioning of existing beta cells, rather than islet hypertrophy or “nesidioblastosis.” A commonly put forth mechanism for such beta cell “hyperfunction” is the large increase in GLP-1 response to meals that occurs after gastric bypass ([51-53](#_ENREF_51)). In two separate studies, individuals with PGBH had higher levels of GLP-1 generated in response to a mixed meal challenge compared to bariatric patients without symptoms ([51](#_ENREF_51),[52](#_ENREF_52)). 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. While the etiology is poorly understood, what may ultimately be 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 ([54](#_ENREF_54)). Alternatively, 3-day continuous glucose monitoring done in the context of an individual's normal eating pattern has been demonstrated to be sensitive in detecting PGBH ([55](#_ENREF_55)). Oral glucose tolerance testing is less useful as individuals who have undergone RYGB commonly generate abnormally low glucose levels when provoked by an oral glucose load without symptoms of hypoglycemia ([56](#_ENREF_56),[57](#_ENREF_57)).

The treatments for PGBH from dietary modification to more extreme measures such as gastric bypass reversal have been reported. 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 ([58](#_ENREF_58)). Successful use of medications such as acarbose, nifedipine, somatostatin, and diazoxside has been described in case reports and small series ([59-62](#_ENREF_59)). 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 ([54](#_ENREF_54)).

**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 ([63](#_ENREF_63),[64](#_ENREF_64)). Gallbladder hypomotility contributes to this process ([65](#_ENREF_65)). 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 ([66](#_ENREF_66)). A recent study of patients undergoing SG documented a similarly elevated incidence of radiographic cholelithiasis ([67](#_ENREF_67)).

Ursodeoxycholic acid, commonly known as ursodiol, can successfully reduce the risk of postoperative cholelithiasis. In a multicenter RCT 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 ([68](#_ENREF_68)), and a recent RCT demonstrated that ursodiol decreased cholelithiasis incidence 6 months after SG ([67](#_ENREF_67)). 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 ([66](#_ENREF_66)). 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. Risk is procedure-specific, with greatest risk following the most malabsorptive procedures including BPD/DS, moderately elevated risk following RYGB, and risk similar to the nonsurgical population following SG and LAGB ([69-71](#_ENREF_69)). 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 ([70](#_ENREF_70)).

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) ([69](#_ENREF_69),[72](#_ENREF_72),[73](#_ENREF_73)). 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 ([69](#_ENREF_69),[72](#_ENREF_72),[73](#_ENREF_73)).

Therapeutic strategies to mitigate nephrolithiasis risk after bariatric surgery (Table 7) are similar to those for the general population ([74](#_ENREF_74)). 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 has been 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 ≥ 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 bone turnover state. After RYGB, for example, biochemical markers of bone resorption have been shown to double in the first postoperative year ([75-78](#_ENREF_75)). Bone mineral density (BMD) assessed by dual-energy X-ray absorptiometry (DXA) decreases ([75-78](#_ENREF_75)), and while there has been concern about potential unreliability of DXA assessment in the setting of marked weight loss and changing soft tissue composition ([79](#_ENREF_79),[80](#_ENREF_80)), 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 ([81-85](#_ENREF_81)). Decline in BMD has been most consistently reported after RYGB ([76](#_ENREF_76),[77](#_ENREF_77),[83](#_ENREF_83)), but also after BPD/DS ([86](#_ENREF_86),[87](#_ENREF_87)) and SG ([85](#_ENREF_85),[88-90](#_ENREF_88)). After LAGB, DXA-assessed BMD decreases modestly at the proximal hip but not at the spine ([76](#_ENREF_76),[77](#_ENREF_77)), with reductions in hip density smaller than those after RYGB ([91](#_ENREF_91)). 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 ([82](#_ENREF_82),[89](#_ENREF_89),[92](#_ENREF_92)) and mild weight regain ([92](#_ENREF_92)).

Ultimately, the important question is whether risk of fracture increases after bariatric surgery. Recent studies have now indicated that fracture risk is indeed higher after bariatric surgery in comparison to obese ([93](#_ENREF_93),[94](#_ENREF_94)), non-obese ([94](#_ENREF_94)), and general population ([95](#_ENREF_95)) nonsurgical controls. Fracture risk is higher after RYGB than LAGB ([96](#_ENREF_96)).

Negative skeletal effects appear to be multifactorial ([78](#_ENREF_78),[97-99](#_ENREF_97)). Potential mechanisms include the decreased skeletal loading with weight loss; loss of muscle mass; changes in levels of fat-secreted hormones (adipokines), sex steroids, and gut-derived hormones; changes in bone marrow adipose tissue ([100](#_ENREF_100)); 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 ([83](#_ENREF_83)), presumably because the bypassed duodenum and proximal jejunum are the usually predominant sites of active, transcellular, 1,25-dihydroxyvitamin D-mediated 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-PTH-mediated 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 ([101](#_ENREF_101)), 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 ([21](#_ENREF_21)) and Endocrine Society Clinical Practice Guidelines ([29](#_ENREF_29)), as well as in an additional position statement from the ASMBS ([102](#_ENREF_102)). 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 ([103](#_ENREF_103)) or the United States Preventive Services Task Force ([104](#_ENREF_104)); 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 in their recommendations 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 muscle-loading 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 ([90](#_ENREF_90)).

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 as bisphosphonates 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 hypocalcemia ([105](#_ENREF_105)). If pharmacotherapy 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.

**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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**REFERENCES**

1. Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: A systematic review and meta-analysis. *JAMA*. 2004; 292**:**1724-1737.

2. Adams TD, Gress RE, Smith SC, et al. Long-term mortality after gastric bypass surgery. *N Engl J Med*. 2007; 357**:**753-761.

3. Sjostrom L, Narbro K, Sjostrom CD, et al. Effects of bariatric surgery on mortality in Swedish obese subjects. *N Engl J Med*. 2007; 357**:**741-752.

4. Arterburn DE, Olsen MK, Smith VA, et al. Association between bariatric surgery and long-term survival. *JAMA*. 2015; 313**:**62-70.

5. Laferrere B, Teixeira J, McGinty J, et al. Effect of weight loss by gastric bypass surgery versus hypocaloric diet on glucose and incretin levels in patients with type 2 diabetes. *J Clin Endocrinol Metab*. 2008; 93**:**2479-2485.

6. Batterham RL, Cummings DE. Mechanisms of diabetes improvement following bariatric/metabolic surgery. *Diabetes Care*. 2016; 39**:**893-901.

7. Isbell JM, Tamboli RA, Hansen EN, et al. The importance of caloric restriction in the early improvements in insulin sensitivity after Roux-en-Y gastric bypass surgery. *Diabetes Care*. 2010; 33**:**1438-1442.

8. Martinussen C, Bojsen-Moller KN, Dirksen C, et al. Immediate enhancement of first-phase insulin secretion and unchanged glucose effectiveness in patients with type 2 diabetes after Roux-en-Y gastric bypass. *Am J Physiol Endocrinol Metab*. 2015; 308**:**E535-544.

9. Purnell JQ, Selzer F, Wahed AS, et al. Type 2 diabetes remission rates after laparoscopic gastric bypass and gastric banding: results of the Longitudinal Assessment of Bariatric Surgery study. *Diabetes Care*. 2016; 39**:**1101-1107.

10. Cho JM, Kim HJ, Lo Menzo E, Park S, Szomstein S, Rosenthal RJ. Effect of sleeve gastrectomy on type 2 diabetes as an alternative treatment modality to Roux-en-Y gastric bypass: systemic review and meta-analysis. *Surg Obes Relat Dis*. 2015; 11**:**1273-1280.

11. Schauer PR, Bhatt DL, Kirwan JP, et al. Bariatric surgery versus intensive medical therapy for diabetes - 5-year outcomes. *N Engl J Med*. 2017; 376**:**641-651.

12. Hutter MM, Schirmer BD, Jones DB, et al. First report from the American College of Surgeons Bariatric Surgery Center Network: Laparoscopic sleeve gastrectomy has morbidity and effectiveness positioned between the band and the bypass. *Ann Surg*. 2011; 254**:**410-420; discussion 420-412.

13. Adams TD, Davidson LE, Litwin SE, et al. Weight and metabolic outcomes 12 years after gastric bypass. *N Engl J Med*. 2017; 377**:**1143-1155.

14. Courcoulas AP, King WC, Belle SH, et al. Seven-year weight trajectories and health outcomes in the Longitudinal Assessment of Bariatric Surgery (LABS) study. *JAMA Surg*. 2017;

15. Ahmed AR, Rickards G, Coniglio D, et al. Laparoscopic Roux-en-Y gastric bypass and its early effect on blood pressure. *Obes Surg*. 2009; 19**:**845-849.

16. Owen JG, Yazdi F, Reisin E. Bariatric surgery and hypertension. *Am J Hypertens*. 2017;

17. Schiavon CA, Drager LF, Bortolotto LA, et al. The role of metabolic surgery on blood pressure control. *Curr Atheroscler Rep*. 2016; 18**:**50.

18. Courcoulas AP, Christian NJ, Belle SH, et al. Weight change and health outcomes at 3 years after bariatric surgery among individuals with severe obesity. *JAMA*. 2013; 310**:**2416-2425.

19. Sarkhosh K, Birch DW, Shi X, Gill RS, Karmali S. The impact of sleeve gastrectomy on hypertension: a systematic review. *Obes Surg*. 2012; 22**:**832-837.

20. Li J, Lai D, Wu D. Laparoscopic Roux-en-Y gastric bypass versus laparoscopic sleeve gastrectomy to treat morbid obesity-related comorbidities: a systematic review and meta-analysis. *Obes Surg*. 2016; 26**:**429-442.

21. Mechanick JI, Youdim A, Jones DB, et al. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient--2013 update: Cosponsored by American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic & Bariatric Surgery. *Endocr Pract*. 2013; 19**:**337-372.

22. Bays HE, Jones PH, Jacobson TA, et al. Lipids and bariatric procedures part 1 of 2: Scientific statement from the National Lipid Association, American Society for Metabolic and Bariatric Surgery, and Obesity Medicine Association: executive summary. *J Clin Lipidol*. 2016; 10**:**15-32.

23. Al Khalifa K, Al Ansari A, Alsayed AR, Violato C. The impact of sleeve gastrectomy on hyperlipidemia: a systematic review. *J Obes*. 2013; 2013**:**643530.

24. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association task force on practice guidelines. *Circulation*. 2014; 129**:**S1-45.

25. Jacobson TA, Ito MK, Maki KC, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: Part 1 - executive summary. *J Clin Lipidol*. 2014; 8**:**473-488.

26. Coblijn UK, Lagarde SM, de Castro SM, Kuiken SD, van Wagensveld BA. Symptomatic marginal ulcer disease after Roux-en-Y gastric bypass: incidence, risk factors and management. *Obes Surg*. 2015; 25**:**805-811.

27. Ying VW, Kim SH, Khan KJ, et al. Prophylactic PPI help reduce marginal ulcers after gastric bypass surgery: a systematic review and meta-analysis of cohort studies. *Surg Endosc*. 2015; 29**:**1018-1023.

28. Parrott J, Frank L, Rabena R, Craggs-Dino L, Isom KA, Greiman L. American Society for Metabolic and Bariatric Surgery integrated health nutritional guidelines for the surgical weight loss patient 2016 update: micronutrients. *Surg Obes Relat Dis*. 2017; 13**:**727-741.

29. Heber D, Greenway FL, Kaplan LM, Livingston E, Salvador J, Still C. Endocrine and nutritional management of the post-bariatric surgery patient: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2010; 95**:**4823-4843.

30. Ketteler M, Block GA, Evenepoel P, et al. Executive summary of the 2017 KDIGO chronic kidney disease-mineral and bone disorder (CKD-MBD) guideline update: what's changed and why it matters. *Kidney Int*. 2017; 92**:**26-36.

31. Isakova T, Nickolas TL, Denburg M, et al. KDOQI US commentary on the 2017 KDIGO clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). *Am J Kidney Dis*. 2017;

32. Laurenius A, Olbers T, Naslund I, Karlsson J. Dumping syndrome following gastric bypass: validation of the dumping symptom rating scale. *Obes Surg*. 2013; 23**:**740-755.

33. Banerjee A, Ding Y, Mikami DJ, Needleman BJ. The role of dumping syndrome in weight loss after gastric bypass surgery. *Surgical endoscopy*. 2013; 27**:**1573-1578.

34. Nielsen JB, Pedersen AM, Gribsholt SB, Svensson E, Richelsen B. Prevalence, severity, and predictors of symptoms of dumping and hypoglycemia after Roux-en-Y gastric bypass. *Surg Obes Relat Dis*. 2016; 12**:**1562-1568.

35. Papamargaritis D, Koukoulis G, Sioka E, et al. Dumping symptoms and incidence of hypoglycaemia after provocation test at 6 and 12 months after laparoscopic sleeve gastrectomy. *Obes Surg*. 2012; 22**:**1600-1606.

36. Tzovaras G, Papamargaritis D, Sioka E, et al. Symptoms suggestive of dumping syndrome after provocation in patients after laparoscopic sleeve gastrectomy. *Obes Surg*. 2012; 22**:**23-28.

37. MacGregor I, Parent J, Meyer JH. Gastric emptying of liquid meals and pancreatic and biliary secretion after subtotal gastrectomy or truncal vagotomy and pyloroplasty in man. *Gastroenterology*. 1977; 72**:**195-205.

38. van Beek AP, Emous M, Laville M, Tack J. Dumping syndrome after esophageal, gastric or bariatric surgery: pathophysiology, diagnosis, and management. *Obes Rev*. 2017; 18**:**68-85.

39. Lawaetz O, Blackburn AM, Bloom SR, Aritas Y, Ralphs DN. Gut hormone profile and gastric emptying in the dumping syndrome. A hypothesis concerning the pathogenesis. *Scand J Gastroenterol*. 1983; 18**:**73-80.

40. Miras AD, le Roux CW. Mechanisms underlying weight loss after bariatric surgery. *Nat Rev Gastroenterol Hepatol*. 2013; 10**:**575-584.

41. Emous M, Wolffenbuttel BHR, Totte E, van Beek AP. The short- to mid-term symptom prevalence of dumping syndrome after primary gastric-bypass surgery and its impact on health-related quality of life. *Surg Obes Relat Dis*. 2017;

42. Sigstad H. A clinical diagnostic index in the diagnosis of the dumping syndrome. Changes in plasma volume and blood sugar after a test meal. *Acta Med Scand*. 1970; 188**:**479-486.

43. Linehan IP, Weiman J, Hobsley M. The 15-minute dumping provocation test. *Br J Surg*. 1986; 73**:**810-812.

44. Ukleja A. Dumping syndrome: pathophysiology and treatment. *Nutr Clin Pract*. 2005; 20**:**517-525.

45. Rariy CM, Rometo D, Korytkowski M. Post-gastric bypass hypoglycemia. *Curr Diab Rep*. 2016; 16**:**19.

46. Marsk R, Jonas E, Rasmussen F, Naslund E. Nationwide cohort study of post-gastric bypass hypoglycaemia including 5,040 patients undergoing surgery for obesity in 1986-2006 in Sweden. *Diabetologia*. 2010; 53**:**2307-2311.

47. Sarwar H, Chapman WH, 3rd, Pender JR, et al. Hypoglycemia after Roux-en-Y gastric bypass: the BOLD experience. *Obes Surg*. 2014; 24**:**1120-1124.

48. Lee CJ, Clark JM, Schweitzer M, et al. Prevalence of and risk factors for hypoglycemic symptoms after gastric bypass and sleeve gastrectomy. *Obesity (Silver Spring)*. 2015; 23**:**1079-1084.

49. Service GJ, Thompson GB, Service FJ, Andrews JC, Collazo-Clavell ML, Lloyd RV. Hyperinsulinemic hypoglycemia with nesidioblastosis after gastric-bypass surgery. *New Engl J Med*. 2005; 353**:**249-254.

50. Meier JJ, Butler AE, Galasso R, Butler PC. Hyperinsulinemic hypoglycemia after gastric bypass surgery is not accompanied by islet hyperplasia or increased beta-cell turnover. *Diabetes Care*. 2006; 29**:**1554-1559.

51. Goldfine AB, Mun EC, Devine E, et al. Patients with neuroglycopenia after gastric bypass surgery have exaggerated incretin and insulin secretory responses to a mixed meal. *J Clin Endocrinol Metab*. 2007; 92**:**4678-4685.

52. Salehi M, Prigeon RL, D'Alessio DA. Gastric bypass surgery enhances glucagon-like peptide 1-stimulated postprandial insulin secretion in humans. *Diabetes*. 2011; 60**:**2308-2314.

53. Korner J, Bessler M, Inabnet W, Taveras C, Holst JJ. Exaggerated glucagon-like peptide-1 and blunted glucose-dependent insulinotropic peptide secretion are associated with Roux-en-Y gastric bypass but not adjustable gastric banding. *Surg Obes Relat Dis*. 2007; 3**:**597-601.

54. Eisenberg D, Azagury DE, Ghiassi S, Grover BT, Kim JJ. ASMBS position statement on postprandial hyperinsulinemic hypoglycemia after bariatric surgery. *Surg Obes Relat Dis*. 2017; 13**:**371-378.

55. Kefurt R, Langer FB, Schindler K, Shakeri-Leidenmuhler S, Ludvik B, Prager G. Hypoglycemia after Roux-en-Y gastric bypass: detection rates of continuous glucose monitoring (CGM) versus mixed meal test. *Surg Obes Relat Dis*. 2015; 11**:**564-569.

56. Roslin M, Damani T, Oren J, Andrews R, Yatco E, Shah P. Abnormal glucose tolerance testing following gastric bypass demonstrates reactive hypoglycemia. *Surg Endosc*. 2011; 25**:**1926-1932.

57. Kim SH, Liu TC, Abbasi F, et al. Plasma glucose and insulin regulation is abnormal following gastric bypass surgery with or without neuroglycopenia. *Obes Surg*. 2009; 19**:**1550-1556.

58. Kellogg TA, Bantle JP, Leslie DB, et al. Postgastric bypass hyperinsulinemic hypoglycemia syndrome: characterization and response to a modified diet. *Surg Obes Relat Dis*. 2008; 4**:**492-499.

59. Guseva N, Phillips D, Mordes JP. Successful treatment of persistent hyperinsulinemic hypoglycemia with nifedipine in an adult patient. *Endocr Pract*. 2010; 16**:**107-111.

60. Spanakis E, Gragnoli C. Successful medical management of status post-Roux-en-Y-gastric-bypass hyperinsulinemic hypoglycemia. *Obes Surg*. 2009; 19**:**1333-1334.

61. Ritz P, Vaurs C, Bertrand M, Anduze Y, Guillaume E, Hanaire H. Usefulness of acarbose and dietary modifications to limit glycemic variability following Roux-en-Y gastric bypass as assessed by continuous glucose monitoring. *Diabetes Technol Ther*. 2012; 14**:**736-740.

62. Mordes JP, Alonso LC. Evaluation, medical therapy, and course of adult persistent hyperinsulinemic hypoglycemia after Roux-en-Y gastric bypass surgery: a case series. *Endocr Pract*. 2015; 21**:**237-246.

63. Gustafsson U, Benthin L, Granstrom L, Groen AK, Sahlin S, Einarsson C. Changes in gallbladder bile composition and crystal detection time in morbidly obese subjects after bariatric surgery. *Hepatology*. 2005; 41**:**1322-1328.

64. Shiffman ML, Sugerman HJ, Kellum JM, Moore EW. Changes in gallbladder bile composition following gallstone formation and weight reduction. *Gastroenterology*. 1992; 103**:**214-221.

65. Bastouly M, Arasaki CH, Ferreira JB, Zanoto A, Borges FG, Del Grande JC. Early changes in postprandial gallbladder emptying in morbidly obese patients undergoing roux-en-y gastric bypass: correlation with the occurrence of biliary sludge and gallstones. *Obes Surg*. 2009; 19**:**22-28.

66. Grover BT, Kothari SN. Biliary issues in the bariatric population. *Surg Clin North Am*. 2014; 94**:**413-425.

67. Adams LB, Chang C, Pope J, Kim Y, Liu P, Yates A. Randomized, prospective comparison of ursodeoxycholic acid for the prevention of gallstones after sleeve gastrectomy. *Obes Surg*. 2016; 26**:**990-994.

68. Uy MC, Talingdan-Te MC, Espinosa WZ, Daez ML, Ong JP. Ursodeoxycholic acid in the prevention of gallstone formation after bariatric surgery: a meta-analysis. *Obes Surg*. 2008; 18**:**1532-1538.

69. Bhatti UH, Duffy AJ, Roberts KE, Shariff AH. Nephrolithiasis after bariatric surgery: a review of pathophysiologic mechanisms and procedural risk. *Int J Surg*. 2016; 36**:**618-623.

70. Lieske JC, Mehta RA, Milliner DS, Rule AD, Bergstralh EJ, Sarr MG. Kidney stones are common after bariatric surgery. *Kidney Int*. 2015; 87**:**839-845.

71. Upala S, Jaruvongvanich V, Sanguankeo A. Risk of nephrolithiasis, hyperoxaluria, and calcium oxalate supersaturation increased after Roux-en-Y gastric bypass surgery: a systematic review and meta-analysis. *Surg Obes Relat Dis*. 2016; 12**:**1513-1521.

72. Canales BK, Hatch M. Kidney stone incidence and metabolic urinary changes after modern bariatric surgery: review of clinical studies, experimental models, and prevention strategies. *Surg Obes Relat Dis*. 2014; 10**:**734-742.

73. Sakhaee K, Poindexter J, Aguirre C. The effects of bariatric surgery on bone and nephrolithiasis. *Bone*. 2016; 84**:**1-8.

74. Pearle MS, Goldfarb DS, Assimos DG, et al. Medical management of kidney stones: AUA guideline. *J Urol*. 2014; 192**:**316-324.

75. Liu C, Wu D, Zhang JF, et al. Changes in bone metabolism in morbidly obese patients after bariatric surgery: a meta-analysis. *Obes Surg*. 2016; 26**:**91-97.

76. Yu EW. Bone metabolism after bariatric surgery. *J Bone Miner Res*. 2014; 29**:**1507-1518.

77. Stein EM, Silverberg SJ. Bone loss after bariatric surgery: causes, consequences, and management. *Lancet Diabetes Endocrinol*. 2014; 2**:**165-174.

78. Scibora LM. Skeletal effects of bariatric surgery: examining bone loss, potential mechanisms and clinical relevance. *Diabetes Obes Metab*. 2014; 16**:**1204-1213.

79. Tothill P, Hannan WJ, Cowen S, Freeman CP. Anomalies in the measurement of changes in total-body bone mineral by dual-energy X-ray absorptiometry during weight change. *J Bone Miner Res*. 1997; 12**:**1908-1921.

80. Van Loan MD. Is dual-energy X-ray absorptiometry ready for prime time in the clinical evaluation of body composition? *Am J Clin Nutr*. 1998; 68**:**1155-1156.

81. Stein EM, Carrelli A, Young P, et al. Bariatric surgery results in cortical bone loss. *J Clin Endocrinol Metab*. 2013; 98**:**541-549.

82. Yu EW, Bouxsein ML, Putman MS, et al. Two-year changes in bone density after Roux-en-Y gastric bypass surgery. *J Clin Endocrinol Metab*. 2015; 100**:**1452-1459.

83. Schafer AL, Weaver CM, Black DM, et al. Intestinal calcium absorption decreases dramatically after gastric bypass surgery despite optimization of vitamin D status. *J Bone Miner Res*. 2015;

84. Shanbhogue VV, Stoving RK, Frederiksen KH, et al. Bone structural changes after gastric bypass surgery evaluated by HR-pQCT: a two-year longitudinal study. *Eur J Endocrinol*. 2017; 176**:**685-693.

85. Bredella MA, Greenblatt LB, Eajazi A, Torriani M, Yu EW. Effects of Roux-en-Y gastric bypass and sleeve gastrectomy on bone mineral density and marrow adipose tissue. *Bone*. 2017; 95**:**85-90.

86. Tsiftsis DD, Mylonas P, Mead N, Kalfarentzos F, Alexandrides TK. Bone mass decreases in morbidly obese women after long limb-biliopancreatic diversion and marked weight loss without secondary hyperparathyroidism. A physiological adaptation to weight loss? *Obes Surg*. 2009; 19**:**1497-1503.

87. Marceau P, Biron S, Lebel S, et al. Does bone change after biliopancreatic diversion? *J Gastrointest Surg*. 2002; 6**:**690-698.

88. Carrasco F, Basfi-Fer K, Rojas P, et al. Changes in bone mineral density after sleeve gastrectomy or gastric bypass: Relationships with variations in vitamin D, ghrelin, and adiponectin levels. *Obes Surg*. 2014; 24**:**877-884.

89. Maghrabi AH, Wolski K, Abood B, et al. Two-year outcomes on bone density and fracture incidence in patients with T2DM randomized to bariatric surgery versus intensive medical therapy. *Obesity (Silver Spring)*. 2015; 23**:**2344-2348.

90. Muschitz C, Kocijan R, Haschka J, et al. The impact of vitamin D, calcium, protein supplementation, and physical exercise on bone metabolism after bariatric surgery: the BABS study. *J Bone Miner Res*. 2016; 31**:**672-682.

91. Hsin MC, Huang CK, Tai CM, Yeh LR, Kuo HC, Garg A. A case-matched study of the differences in bone mineral density 1 year after 3 different bariatric procedures. *Surg Obes Relat Dis*. 2015; 11**:**181-185.

92. Vilarrasa N, San Jose P, Garcia I, et al. Evaluation of bone mineral density loss in morbidly obese women after gastric bypass: 3-year follow-up. *Obes Surg*. 2011; 21**:**465-472.

93. Lu CW, Chang YK, Chang HH, et al. Fracture risk after bariatric surgery: a 12-year nationwide cohort study. *Medicine (Baltimore)*. 2015; 94**:**e2087.

94. Rousseau C, Jean S, Gamache P, et al. Change in fracture risk and fracture pattern after bariatric surgery: nested case-control study. *BMJ*. 2016;

95. Nakamura KM, Haglind EG, Clowes JA, et al. Fracture risk following bariatric surgery: a population-based study. *Osteoporos Int*. 2014; 25**:**151-158.

96. Yu EW, Lee MP, Landon JE, Lindeman KG, Kim SC. Fracture risk after bariatric surgery: Roux-en-Y gastric bypass versus adjustable gastric banding. *J Bone Miner Res*. 2017;

97. Hage MP, El-Hajj Fuleihan G. Bone and mineral metabolism in patients undergoing Roux-en-Y gastric bypass. *Osteoporos Int*. 2014; 25**:**423-439.

98. Brzozowska MM, Sainsbury A, Eisman JA, Baldock PA, Center JR. Bariatric surgery, bone loss, obesity and possible mechanisms. *Obes Rev*. 2013; 14**:**52-67.

99. Folli F, Sabowitz BN, Schwesinger W, Fanti P, Guardado-Mendoza R, Muscogiuri G. Bariatric surgery and bone disease: From clinical perspective to molecular insights. *Int J Obes (Lond)*. 2012; 36**:**1373-1379.

100. Kim TY, Schwartz AV, Li X, et al. Bone marrow fat changes after gastric bypass surgery are associated with loss of bone mass. *J Bone Miner Res*. 2017;

101. Schafer AL. Vitamin D and intestinal calcium transport after bariatric surgery. *J Steroid Biochem Mol Biol*. 2017; 173**:**202-210.

102. Kim J, Brethauer S, ASMBS Clinical Issues Committee. Metabolic bone changes after bariatric surgery. *Surg Obes Relat Dis*. 2014; 11:406-411.

103. Cosman F, de Beur SJ, LeBoff MS, et al. Clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Int*. 2014; 25**:**2359-2381.

104. Screening for osteoporosis: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2011; 154**:**356-364.

105. Rosen CJ, Brown S. Severe hypocalcemia after intravenous bisphosphonate therapy in occult vitamin D deficiency. *N Engl J Med*. 2003; 348**:**1503-1504.