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Management of Diabetes in Patients Undergoing Bariatric Surgery

Christopher M. Mulla[1,2] · Harris M. Baloch[1] · Samar Hafida[2]

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Abstract

Purpose of Review The number of bariatric surgeries for patients with type 1 or type 2 diabetes continues to grow. Clinicians are challenged to choose therapies that reach glycemic targets without inducing adverse effects in post-bariatric patients without published guidelines. This review evaluates data supporting the best strategies for diabetes management in patients undergoing bariatric surgery.

Recent Findings Though few clinical trials have evaluated the safety and effectiveness of different glucose-lowering therapies following bariatric surgery, remission of diabetes or reduced medications is an established benefit of bariatric surgery. Adverse events including diabetic ketoacidosis in post-bariatric patients on sodium-glucose co-transporter 2 (SGLT2) inhibitors or inadequate insulin have been reported in patient's with both type 1 and type 2 diabetes. Metformin, glucagon-like peptide-1 (GLP-1) agonists, dipeptidyl peptidase-4 (DPP-4) inhibitors, SGLT2 inhibitors, insulin, and sulfonylureas have been used successfully in the perioperative period for other surgeries and guidelines recommend adjusting the doses of these medications especially in the perioperative period.

Summary Clinicians should favor weight-neutral or weight-loss promoting therapies in post-bariatric surgery patients such as medical nutrition therapy, metformin, GLP-1 agonists, SGLT2 inhibitors, and DPP-4 inhibitors.

Keywords Bariatric surgery · Type 2 diabetes · Type 1 diabetes · Obesity · Weight loss

Introduction

As the prevalence of obesity rises among patients with type 1 and type 2 diabetes, bariatric surgery is becoming increasingly more common. Individuals with type 2 diabetes (T2D) who undergo bariatric surgery have consistently shown superior health outcomes compared with those treated with medical management, as demonstrated by numerous randomized control trials (RCTs) [1, 2]. Fewer data are available for bariatric surgery in patients with type 1 diabetes (T1D). Several retrospective and observational studies and meta-analyses of such studies demonstrate consistent reduction in body weight, but inconsistent improvement of glycemic control [3–8]. From presurgical dietary changes to physiologic alterations occurring after surgery, clinicians should be aware of the challenges and potential pitfalls in diabetes management to achieve safe glucose targets and avoid adverse effects. Though few clinical trials have been performed evaluating management strategies and no guidelines exist, this review will discuss the strategies for managing diabetes perioperatively and postoperatively for bariatric surgery using available data.

This article is part of the Topical Collection on *Obesity*

✉ Christopher M. Mulla
Christopher.mulla@joslin.harvard.edu; mullacm@gmail.com

Harris M. Baloch
Harris.m.baloch.mil@mail.mil

Samar Hafida
Samar.Hafida@joslin.harvard.edu

[1] Division of Endocrinology, Landstuhl Regional Medical Center, US Army, Landstuhl, Germany

[2] Joslin Diabetes Center, Harvard Medical School, Boston, MA, USA

Remission of Type 2 Diabetes

There is abundant evidence for the efficacy of bariatric surgery among patients with overweight/obesity and T2D including improvements in insulin sensitivity, reductions in glucose lowering medications, and complete remission [1], the mechanisms of which are discussed elsewhere [9]. Bariatric surgery has also been associated with lower mortality rates among people with obesity [10, 11]. Furthermore, observational data

from the Swedish Obesity Study demonstrated that bariatric surgery reduces long-term mortality and is an effective tool for diabetes prevention [12]. Clinical trials have demonstrated significant improvements in blood pressure and cholesterol as well as reduced macrovascular [13–16] and microvascular complications in patients with T2D, compared to those treated with medical management [17, 18]. A recent large retrospective observational study involving 13,722 patients with type 2 diabetes showed that patients who received bariatric surgery had a significantly lower risk of incident major adverse cardiovascular events [19].

Diabetes remission has been defined as a primary outcome in all 12 RCTs reviewed by the latest diabetes surgery summit [1]. However, the definition of remission varied between trials, including hemoglobin A1C (HbA1c) < 6% without the use of medications for ≥ 1 but up to 5 years, fasting plasma glucose < 100 mg/dL (5.6 mmol/L) for ≥ 1 year, and a composite endpoint of HbA1c < 7%, LDL < 100 mg/dL, and systolic blood pressure < 130 mmHg. As there is no consensus on defining diabetes remission, this term implies restoration of normal glucose metabolism after bariatric surgery without medication. However, none of the cutoffs used to define diabetes remission have included parameters occurring below the threshold of impaired fasting glucose or impaired glucose tolerance which are known risk factors for cardiovascular disease (CVD) [20]. This does not, however, diminish the conclusion that bariatric surgery provides substantial metabolic benefits, and in appropriate patients, surpasses medical intervention, regardless of race or gender [21].

Diabetes remission rates varied among the RCTs investigating the effect of bariatric surgery versus medical management, which may be explained by study design, type of procedure, patient population, and study duration. The average percentage of patients meeting study-specific criteria for diabetes remission at the end of the study period was 68% after biliopancreatic diversion [22], 29–90% after Roux-en-Y gastric bypass (RYGB) [22–29], 23–65% after sleeve gastrectomy (SG) [27, 28], and 33–73% after laparoscopic adjustable band (LAGB) [23, 27, 30–32] compared with an average remission rate of 8% in the medical management cohort among all studies [22–32]. Although remission rates decreased over time, surgical intervention was superior to medical management for as long as 5 years post operatively in all but one study using laparoscopic adjustable gastric banding [30].

Individuals with diabetes have a greater risk of developing both microvascular and macrovascular complications, compared with those without. The risk of developing micro- and macrovascular complications increases with prolonged exposure to hyperglycemia, uncontrolled hypertension, and hyperlipidemia. Several trials have shown that intensive glucose control through medical management reduces the progression of microvascular but not macrovascular complications in patients with T2D [33–35]. Conversely, a significant risk of death was observed in the intensive glucose lowering arm in the ACCORD trial, ending it early after 3.5 years [36]. While the glucose lowering effect after metabolic surgery was comparable with that achieved in trials using intensive medical therapy, cardiovascular outcomes were superior and mortality rates were lower in patients with diabetes who received bariatric surgery [11, 13, 16, 37].

Glycemic Targets and Glycemic Monitoring

There is insufficient evidence to support specific glycemic targets prior to bariatric surgery. However, a review of the available evidence suggests that lower preoperative HbA1c predicts improved weight loss [38, 39] and fewer complications. Glycemic targets set by various bariatric surgery programs are often center specific, and extrapolated from non-bariatric surgery data. Higher preoperative HbA1c correlates with poor surgical outcomes, particularly after cardiac surgeries [40]. Preoperative HbA1c > 8% in non-cardiac surgery has been linked with prolonged hospitalization [41]; each percentage point increase over 6.5% was associated with a greater risk of major complications and ICU admissions [42••]. Elevated HbA1c is postulated to increase surgical complications due to long-term hyperglycemia and its impact on vasculature and wound healing. However, one retrospective study did not find an association between pre operative HbA1c and 30-day post operative mortality [43]. Despite the paucity of data in bariatric surgery patients, best practice guidelines endorse the following targets for glucose control in the pre operative period [44]:

i. HbA1c ≤ 8%
ii. Fasting blood glucose ≤ 110 mg/dL
iii. two hour post prandial blood glucose ≤ 140 mg/dL

Glucose monitoring recommendations do not differ pre- or postoperatively except during the perioperative and immediate postoperative period, during which diet and insulin sensitivity will change considerably requiring more frequent assessment. Patients off insulin or only on basal insulin can monitor fasting glucose alone. Those with T1D or T2D requiring prandial insulin should monitor fasting, pre prandial and bedtime glucose levels, and more frequently during illness, stress, or with symptoms of hypo- or hyperglycemia. Some continuous glucose monitors (CGM) have been approved to be used instead of glucometers in insulin dosing. Accuracy of CGM has been evaluated in patients who have had bariatric surgery demonstrating the areas of concern during times of hypoglycemia and following meals. Changes in sensor glucose levels can lag behind venous and capillary glucose significantly during rapid glucose excursions associated with meals [45] and another study demonstrated that sensor

glucose overestimated glucose levels by an average of 18 mg/dL when in the hypoglycemic range [46].

Nutrition Goals and Recommendations

A critical component of diabetes management is medical nutrition therapy, and these dietary recommendations evolve in relation to the pre- and postoperative time period for bariatric surgery. Patients entering bariatric surgery programs in the USA undergo rigorous nutrition education as well as medical and behavioral assessments preoperatively. However, the duration of preoperative management varies widely due to regional differences in wait times, often dictated by insurance-mandated preoperative weight loss requirements. Increased wait times in patients with complex medical histories had similar outcomes to patients with shorter wait times according to one study in Medicaid patients [47]. Although benefits of preoperative weight loss remain controversial, several studies demonstrated that following a low calorie diet for 2–6 weeks prior to the surgery date is associated with superior short- and long-term outcomes [48]. A systematic review of 15 studies including 942 participants using preoperative meal replacements for the intent of weight loss revealed that the most consistent impact of weight loss was on improvements in glucose control [49]. There is no consensus among experts regarding the best macronutrient composition, calories consumed, or duration of weight loss efforts preoperatively. However, most institutions recommend a "low-calorie" diet.

Postoperatively, patients undergo reintroduction of food in stages: liquid, pureed, and soft, followed by regular solids. The duration of each stage varies by type of surgery, institutional protocol, and individual response to the prior dietary stage. Achieving a regular solid diet can take up to three months postoperatively [50]. Patients are counseled to avoid sugary drinks and high glycemic index carbohydrates which can cause dumping syndrome; to drink water in-between instead of during meals; and to take vitamin and mineral supplements including iron, vitamin D, calcium, and vitamin B12; this is often managed with an experienced nutritionist [51]. Because calories and carbohydrates consumed differ significantly during the perioperative period, patients and physicians must be vigilant in assessing the glycemic response to pharmacotherapy and modify the medical regimen in order to safely achieve appropriate glycemic targets.

Medication Adjustments

Diabetes medication adjustments are necessary to achieve target glucose levels in the setting of the reduced calorie intake and altered insulin sensitivity. Most bariatric surgery programs recommend medically supervised weight loss with the intent of achieving a 5–10% reduction in body weight, reduction in liver size, improving metabolic markers including glucose profile, blood pressure, and lipids, and reducing postoperative complications [52, 53]. During this period as well as the period after surgery, patients taking medications to lower glucose may be at risk of hypoglycemia; therefore, we recommend the following adjustments (Table 1):

Insulin

A significant number of patients with T2D and all patients with T1D require insulin, either as basal insulin only, basal and bolus (prandial), mixed insulin, or continuous subcutaneous infusion of insulin via insulin pumps [58]. For insulin-requiring patients, a dose reduction should be implemented corresponding to dietary changes, subsequent weight loss, and improved insulin sensitivity [59]. When initiating preoperative reduced calorie intake, we recommend a 20% initial insulin dose reduction, and frequent adjustments at regular intervals should be made thereafter to avoid hypoglycemia.

Patients should be educated on self-titration of basal insulins to achieve fasting blood glucose of 80–110 mg/dL. The dose of basal insulin should be increased by two units every three days, or decreased by two to four units if hypoglycemia occurs. Basal insulin in patients with T2D with fasting blood glucose levels < 80 mg/dL may be discontinued if the dose drops to < 0.1–0.2 units/kg. Patients with T1D should never discontinue basal insulin.

Rapid-acting insulin analogues administered prior to food intake or in response to hyperglycemia are typically favored over regular human insulin due to pharmacokinetic properties and lower hypoglycemia rates [60]. A reduced calorie and carbohydrate intake leading to weight loss should improve insulin sensitivity; therefore, mealtime and corrective dosages would need to be reduced to avoid hypoglycemia. For patients on fixed doses of prandial insulin, we recommend a 20% or greater reduction in their dose with frequent adjustments based on blood glucose levels measured two hours after caloric intake.

For patients who are proficient with calculating prandial and corrective doses based on insulin-to-carbohydrate ratios and insulin sensitivity ratios, we recommend a similar adjustment (reduction of insulin to carbohydrate ratio and insulin sensitivity factors by 20%). For patients on prandial insulin, it is imperative to monitor blood glucose levels two hours after eating in order to titrate their prandial dose for a target of 120–140 mg/dL and to avoid hypoglycemia. Patients should be advised to increase the prandial dose by one to two units if remaining above target, or reduce by two units if experiencing hypoglycemia. In patients with T2D who consistently have blood glucose < 140 mg/dL two hours after eating, or if prandial insulin dose has dropped to < 10 units per meal to avoid hypoglycemia, consider discontinuing prandial insulin. Patients with T1D

Table 1 Pharmacotherapy for management of type 2 diabetes after bariatric surgery: factors to consider in choice of therapy for glucose management

	Insulin	Metformin	GLP-1 agonists	SGLT2-i	AG-i	Sulfonylureas	DPP-4-i
Causes hypoglycemia	Yes	No	No	No	No	Yes	No
Weight	Gain	Slight loss	Loss	Loss	Neutral	Gain	Neutral
Renal	Dose adjustment required	Contraindicated if eGFR< 30 mL/min/1.73 m^2	Exenatide not indicated for GFR < 30	Dose adjustment required	Dose adjustment required	Dose adjustment required	Dose adjustment required
CVD Benefits	–	No	Yes for liraglutide	Yes for dapagliflozin, empagliflozin, and canagliflozin	Neutral	Uncertain	Use with caution
Major Adverse Effects	Hypoglycemia, difficult to administer	GI upset, lactic acidosis	Nausea, vomiting, diarrhea	Increased urinary tract infections, euglycemic DKA,	Flatulence, diarrhea, abdominal discomfort	Hypoglycemia	Headaches, upper respiratory tract infections
Average A1C reduction	–	1%**	1%*	0.8–1.0***	1%**	1.25%**	0.75%**

AG-i, alpha-glucosidase inhibitors; *DKA*, diabetic ketoacidosis; *DPP-4-i*, dipeptidyl peptidase-4 inhibitors; *eGFR*, estimated glomerular filtration rate; *GI*, gastrointestinal; *GLP-1*, glucagon-like peptide-1; *SGLT2-i*, sodium-glucose co-transporter 2 inhibitors

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***[57]

should not discontinue prandial insulin. Pre-mixed insulins are another option for patients who require both prandial and basal insulin coverage. They are best suited for patients who are unable to implement a complex regimen with two different insulins; however, it should be noted that these insulins lack ability to adjust long and short acting insulins independent of each other and may lead to more weight gain than other insulin formulations [61]. However, this formulation may be appropriate for some patients who struggle with the complexity of basal-bolus regimens but have prandial requirements that cannot be met with basal insulin alone [62]. The dose of mixed insulin should be reduced by at least 20%, as with other insulin formulations, and patients should attempt to adjust dose to the same fasting and post-prandial blood glucose targets.

Clinicians should be vigilant in the postoperative period for the risk of diabetic ketoacidosis (DKA), including euglycemic ketoacidosis in their patients on insulin, especially patients with T1D. One retrospective cohort analysis in two hospitals determined that 21% of patients with T1D developed DKA within the first month after surgery [63], supported by similar findings in a larger retrospective study of 107 patients [3]. Patients with T2D on insulin preoperatively have also developed DKA, especially if insulin is omitted [64–66]. Risk factors for development of DKA include poor oral intake, dehydration, post operative infection, and insulin omission including both accidental and iatrogenic. Screening for post operative DKA is important because symptoms of DKA including abdominal pain, nausea, and emesis can mirror those of postoperative complications such as gastric stenosis, intestinal obstruction, leak, or infection and can lead to unnecessary imaging studies [64].

Metformin

Metformin is a first-line pharmacotherapy for new onset T2D [58] and is beneficial in the prevention of progression of prediabetes to T2D [67]. It has multiple mechanisms of action including decreasing hepatic gluconeogenesis, increasing gut glucose utilization, increasing glucagon-like peptide-1 (GLP-1) [68], altering the gut microbiome [69] and enhancing insulin sensitivity via effects on fat metabolism [70]. GLP-1 increases following bariatric surgery [71] and is associated with postoperative weight loss [9]. Addition of metformin following bariatric surgery can improve glycemic control and contribute to sustained weight loss [72].

Metformin is contraindicated in severe chronic kidney disease (CKD) stage 4 (eGFR < 30 mL/min/1.73 m^2) due to the risk of metformin accumulation and high anion gap lactic acidosis type B, a potentially fatal complication [73]. Starting

metformin in patients with eGFR between 30 and 45 mL/min/1.73 m^2 is not recommended. It is also recommended to temporarily discontinue metformin before an iodinated contrast imaging procedure in patients with an eGFR < 60 mL/min/1.73 m^2, excessive acute or chronic alcohol use, hepatic insufficiency, or heart failure. However, the actual risk of lactic acidosis in patients who underwent bariatric surgery is unclear as limited and conflicting data exists regarding the actual levels of lactic acid in the perioperative period. Increased ketone levels and risk of lactic acidosis was reported [74], while other studies demonstrated no differences in patients taking metformin compared with patients not on metformin [75].

Despite widespread use of metformin, few studies have assessed its safety and efficacy perioperatively for bariatric surgery. Surgical guidelines recommend discontinuing metformin the day of surgery due to risks of metformin-associated lactic acidosis [76, 77]. These recommendations should be extrapolated to use in bariatric patients; metformin can be discontinued on the day of surgery. Administering metformin in the perioperative period requires careful dosing since metformin absorption has been shown to increase by up to 50% in patients who had bariatric surgery [78]. Metformin does not cause hypoglycemia and can be continued during the low-caloric diet phase prior to surgery.

One of the main reasons for non-adherence to metformin is gastrointestinal distress which can occur in up to 53% of patients [79]. Gastrointestinal discomfort is also common in patients who have undergone bariatric surgery; therefore, metformin should not be initiated during the immediate recovery period from surgery.

AACE/TOS/ASMBS guidelines for perioperative bariatric care recommend continuing metformin until resolution of diabetes is fully documented [44], although the recommendation is based on Grade D (low quality) evidence. Most surgeons tend to hold metformin for three days following a major surgery as the drug is not suitable to be used among those experiencing postoperative complications such as sepsis and acute renal failure, and those needing iodine-based diagnostic imaging. Therefore, it may be prudent to wait until tolerating a solid diet before resuming or initiating metformin in a patient with persistent T2D after surgery.

GLP-1 Agonists

GLP-1 agonists are a newer class of medications used to treat diabetes and obesity. GLP-1 agonists work through multiple signaling targets, leading to decreased glucagon concentrations, slowed gastric emptying, increased satiety, and decreased free fatty acid concentrations; all which contribute to improved insulin sensitivity, decreased HbA1c and decreased body weight [80, 81]. Liraglutide has been demonstrated to improve glycemic control along with weight loss in patients with T2D, and also to promote significant weight loss in overweight and obese patients without T2D [82]. The American Diabetic Association recommends GLP-1 agonists as one of the first medications after initiation of metformin for the treatment of T2D [58].

Since GLP-1 agonists can promote weight loss through multiple signaling mechanisms, they may be considered for post-bariatric surgery patients. Several studies have previously demonstrated a significant increase in GLP-1 concentrations in post-bariatric patients with post-prandial levels rising significantly after bariatric surgery, a physiologic state similar to GLP-1 agonist administration [83]. In non-bariatric patients, GLP-1 agonists have also been used perioperatively and compared with insulin with positive outcomes including more stable glucose levels requiring less sliding-scale corrective insulin in the perioperative period [84•].

Up to 50% of individuals taking GLP-1 agonists develop nausea, vomiting, and diarrhea, with the majority experiencing transient symptoms which resolve over time [55]. As these symptoms may overlap with symptoms of immediate postoperative complications, it would be prudent to hold GLP-1 agonists until the patient has progressed to tolerate a solid food, stage 5 diet. At the market introduction of these medications, there was concern regarding potential pancreatitis with several cases of acute pancreatitis reported via MedWatch system. However, overtime, these concerns have not been validated with sufficient evidence to confirm an increased risk [85].

Based on data from studies of perioperative glycemic control among patients undergoing non-bariatric surgery [84•], GLP-1 agonists are presumed to be suitable for use in patients with persistent or recurrent T2D after bariatric surgery, especially given their ability to promote weight loss. However, there is limited direct evidence to recommend their use. Further studies are needed to determine the safety of GLP-1 agonists in the postoperative period. Studies evaluating postoperative GLP-1 use in sleeve gastrectomy patients are underway to evaluate for potentially increased weight loss [86, 87].

DPP-4 Inhibitors

Dipeptidyl peptidase-4 (DPP-4) inhibitors block the enzyme that normally degrades GLP-1 by prolonging the half-life of circulating GLP-1 and thereby enhancing endogenous GLP-1 effect on glucose-stimulated insulin secretion, delayed gastric emptying, and inhibited post-prandial glucagon secretion [88]. The different DPP-4 inhibitors including alogliptin, linagliptin, saxagliptin, and sitagliptin lower HbA1c up to 0.7% in clinical trials [89, 90]. DPP-4 inhibitors are generally well tolerated, do not cause hypoglycemia and are weight neutral. They should be avoided in patients with a history of pancreatitis due to possible risk of exacerbation. FDA has

issued warnings for increased risk of hospitalization for heart failure (HF) in patients with a history of HF, specifically for alogliptin and saxagliptin, so they should also be avoided in such patients. Dose adjustment is required in CKD for eGFR < 45 except for linagliptin which is cleared through the enterohepatic system. The benefit-risk profile of DPP-4 inhibitors has led clinicians to regard these as second-line therapeutic agents for T2D.

Preoperatively, sitagliptin has been demonstrated to be safe in inpatient general medicine and surgical patients in combination with basal insulin [91]. With regard to use of this class of drugs postoperatively, one RCT of 4 weeks duration which evaluated efficacy of sitagliptin in patients with T2D after RYGB surgery reported glucose-lowering benefit without significant adverse events [92].

Due to their relatively benign side effect profile, DPP-4 inhibitors are suitable agents for post-bariatric patients with mild hyperglycemia; however, they would not be appropriate as monotherapy for significant hyperglycemia or to induce weight loss given only modest improvement in A1c of 0.7% and no impact on weight.

SGLT2 Inhibitors

Sodium-glucose co-transporter 2 (SGLT2) inhibitors including canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin, are being increasingly used to treat T2D, obesity, CVD, HF, and CKD. Recent clinical trials have demonstrated benefits of SGLT2 inhibitors in reducing major adverse cardiovascular events, preserving renal function in CKD and reducing hospitalizations in patients with T2D and HF [54]. SGLT2 inhibitors have recently become first-line therapy for patients with T2D and an HbA1c above goal with a history of HF, CKD or a compelling need to promote weight loss [58, 93]. SGLT2 inhibitors increase urinary glucose excretion independent of insulin, leading to reduced blood glucose and blood pressure as well as modest weight loss. Other benefits of SGLT2 inhibitors include oral administration, once-daily dosing, and low hypoglycemia risk. Because SGLT inhibitors are not associated with weight gain or hypoglycemia, they may be suitable agents for post-bariatric surgery patients with persistent or new T2D [94].

Adverse effects of SGLT2 inhibitors include acute kidney injury, increased risk of distal extremity amputations, fractures, genitourinary tract infections, hypotension, DKA in addition to high cost that should be considered and which may limit their use in the peri- and postoperative periods. FDA has issued warnings regarding the risks of DKA, and serious urinary tract infections with rare cases of necrotizing fasciitis of the perineum, called Fournier's gangrene with use of SGLT2 inhibitors [95, 96]. Among bariatric surgery patients, there are several case reports of postoperative DKA while taking an SGLT2 inhibitor [65, 97–99]. SGLT2 inhibitors may also increase the risk of DKA or euglycemic ketoacidosis in patients with T1D and ketosis-prone T2D [100–102]. In patients requiring insulin or with prior DKA, SGLT2 inhibitors should be used with caution, if at all, during the preoperative and early postoperative period. The American College of Endocrinology (ACE) and American Association of Clinical Endocrinologists (AACE) recommend holding SGLT2 inhibitors for > 24 h prior to elective surgery and until the patient has progressed to a solid diet; this strategy is reasonable to apply to patients undergoing bariatric surgery as well [103].

Though uncommon in adults with T2D before bariatric surgery, there is an increased risk of dehydration and orthostatic hypotension when SGLT2 inhibitors are used in combination with loop or thiazide diuretics, especially in patients over the age of 75 years [104]. Dehydration is the most-common cause for emergency room visits and hospital re-admissions following bariatric surgery [105, 106]. In addition to hypotension, cases of acute kidney injury were reported after dapagliflozin or canagliflozin use prompting the FDA to issue a series of safety warnings [107]. However, further analysis has determined that although SGLT2 inhibitors may cause an initial rise in serum creatinine levels, continued use does not lead to permanent kidney disease [108, 109]. An RCT in patients with T2D and kidney disease revealed reduced rates of kidney failure or CV events with canagliflozin compared with placebo [108].

There has been conflicting data on fracture risk after use of SGLT2 inhibitors, specifically canagliflozin, along with an association of reduced 1,25-dihydroxyvitamin D3, increased serum phosphate and reduced bone mineral density [110, 111]. One large population-based new-user cohort study of over 150,000 patients found no difference in fracture incidence of the humerus, forearm, pelvis, or hip in patients who had started canagliflozin compared with those who started a GLP-1 agonist; however, the follow-up period was only 200–264 days [112]. Because post-bariatric surgery patients often have deficiencies of vitamin D, calcium, and other micronutrients, careful monitoring of bone density and fracture risk is advised when using SGLT2 inhibitors in these patients.

Alpha-Glucosidase Inhibitors

Alpha-glucosidase (AG) inhibitors, including acarbose and miglitol, are another class of medications which delay the absorption of glucose and stabilize post-prandial peak glucose. They may be used in diabetes management for patients with mild hyperglycemia and residual beta cell function. They reduce post-prandial insulin levels, are weight-neutral, do not cause hypoglycemia, and are taken at the start of meals [113]. AG inhibitor-associated gastrointestinal adverse effects including flatulence, diarrhea, and abdominal discomfort lead to low

compliance with use of these drugs [114]. Since gastrointestinal disturbances are common after bariatric surgery [115], use of AG inhibitors may further exacerbate these problems.

Sulfonylureas

Sulfonylureas (SUs), which block potassium-ATP channels in beta cells of the pancreatic islets eventually leading to increased plasma levels of insulin independent blood glucose levels, remain commonly prescribed medications for the management of T2D [116]. They are only utilized in patients with preserved beta-cell function.

The major concern with SUs is hypoglycemia, especially with long-acting formulations. SUs are also associated with weight gain, which limits use of these drugs in patients who plan to or have undergone bariatric surgery. No studies have been performed on using SU in patients who have had bariatric surgery. Due to the availability of several other medications for T2D that do not induce weight gain or increase the risk of hypoglycemia, SUs are not preferred for management of T2D in the perioperative or postoperative period.

Conclusion

Bariatric surgery is an increasingly utilized therapy for obesity, including in patients with either T2D or T1D. Management of patients with pre-existing diabetes or a new diagnosis of diabetes following bariatric surgery requires careful attention to the potential adverse effects and strengths of available pharmacotherapy. Therapies should be targeted to reduce hyperglycemia with the least adverse effects including avoidance of weight gain. Clinicians should pay careful attention during the early post operative period when the risk of dehydration, ketoacidosis, and hypoglycemia are the greatest.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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- • Of importance
- •• Of major importance

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