Bariatric Procedure Selection in Diabetics

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5.1 Introduction

Bariatric surgery is the most effective treatment for obesity [1], and often results in Type 2 diabetes (T2DM) remission [2–10]. Of all obesity-related comorbid illnesses, T2DM has the most evidence as an indication for bariatric surgery. T2DM resolution following bariatric surgery likely involves multiple mechanisms, and has yet to be fully elucidated. Complex neuroendocrine and metabolic effects including reductions in glycated hemoglobin (A1C), and concomitant increases in circulating incretin concentrations, insulin sensitivity, and β-cell function have been described [11, 12]. Interestingly, these metabolic effects appear to have weight-independent effects on T2DM and begin to occur prior to discharge from the hospital [13, 14]. Several procedures exist in the modern era of bariatric surgery with important difference in anticipated weight loss, rates of diabetes resolution, and complications, including nutritional deficiencies. The role of the modern bariatric surgeon is to understand the nuances of existing surgical options and guide patients in individualized decision-making based on their unique characteristics and goals. In this chapter, we review existing evidence to guide procedure selection for diabetic patients seeking bariatric surgery.

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5.2 Search Strategy

A comprehensive search of MEDLINE (PubMed), EMBASE, and the Cochrane library databases was conducted for English language publications from 2009 to 2020, and included the following terms: diabetes AND gastric bypass (RYGB), jejunoileal bypass, duodenal switch (DS), gastric sleeve (SG), biliopancreatic diversion (BPD), bariatric surgery, metabolic surgery, obesity surgery, intestinal bypass, along with all relevant related keywords (Table 5.1). We also included papers of historical importance or commonly referenced landmark studies. Bibliographies were cross-referenced to identify additional relevant articles. Recommendations were classified using the GRADE system. Endoscopic and device-based interventions were excluded from this analysis.

5.3 Results

5.3.1 Individualizing Procedure Choice for Diabetic Patients

In patients with obesity, bariatric surgery is superior to maximal lifestyle and medical management of T2DM [2–10]. In general, bariatric procedures that result in more weight lost and higher rates of diabetes remission also carry higher rates of post-procedural and nutritional complications. However, the data suggest a more nuanced appreciation of the various procedures and unique patient factors is required to make appropriate individualized decisions with patients. For diabetic patients, the most common primary goal in pursuing bariatric surgery is the resolution of diabetes [15]. Patient-centered decision-making should weigh the potential of metabolic improvements and diabetes resolution against post-operative and nutritional complications.

SG and RYGB currently make up >90% of primary bariatric procedures performed in the United States, with over half of all procedures being SG [16–18]. Emerging data from randomized controlled trials (RCT) suggests minimal differences in diabetic outcomes comparing RYGB to SG. Aminian, et al. identified four modern RCTs comparing diabetic endpoints in patients with T2DM undergoing RYGB versus SG. The individual studies had small sample size and taken together included 174 patients undergoing RYGB and 175 undergoing SG. Interestingly, no significant difference in diabetes remission was identified in any single study or in

Table 5.1 PICO table

P (Patients)	I (Interventions)	C (Comparator)	O (Outcomes)
Patients with diabetes and obesity	Bariatric surgery as a metabolic intervention	Outcomes of various operative approaches accounting for patient factors	Glycemic control, diabetes remission/resolution, morbidity, mortality, weight loss, cost

Table 5.2 RCTs comparing SG v RYGB (adapted from Aminian, et al. [19])

	RYGB			SG		
	Complete remission	Long-term remission		Complete remission	Long-term remission	
Author (year)	n with remission/n total cohort (%)	n with remission/n total cohort (%)	P value	n with remission/n total cohort (%)	n with remission/n total cohort (%)	P value
Schauer, et al. (2017) [37]	11/49 (22)	7/47 (15)	0.49	15/49 (31)	11/47 (23)	0.57
Salminen, et al. (2018) [41]	10/40 (25)	5/41 (12)	0.23	18/40 (45)	15/41 (37)	0.59
Peterli, et al. (2018) [42]	19/28 (68)	16/26 (62)	0.84	21/28 (75)	20/26 (77)	0.88
Ruiz-Trovar, et al. (2019) [43]	47/59 (79)	48/61 (77)	0.92	51/59 (86)	50/61 (82)	0.67
4 RCTs combined	87/176 (50)	76/175 (43)	0.31	105/176 (60)	96/175 (55)	0.42

pooled analysis (Table 5.2). Primary inclusion criteria in all trials was based on BMI. Thus, diabetic outcomes were secondary endpoints and data came from sub-group analyses. The sub-group analyses were not designed nor powered to detect a difference in diabetes remission between SG and RYGB in any of the individual RCTs. Aminian, et al. performed pooled analyses. *Complete remission* of T2DM (HbA1C < 6%, off diabetic medications) at 5 years was 50% after RYGB and 43% after SG (RR = 0.07, CI-0.2–0.15), while *long-term remission* (HbA1C < 6.5%, off diabetic medications) at 5 years of follow-up was 60% after RYGB and 55% after SG (RR 0.05, CI-0.04–0.14). Because the confidence interval crosses 0, the effect size of 7% for *complete remission* and 5% for *long-term remission* are not statistically significant. These RCT data are underpowered to make strong procedural recommendations regarding differences in diabetic outcomes. However, closely examining the confidence intervals, suggests that at a maximum RYGB might provide a relatively small advantage in complete remission of 15% [19].

The PCORnet Bariatric Study included a cohort of 9710 adults with T2DM who underwent bariatric surgery between 2010 and 2014 in the United States (US). In this unmatched surgical cohort, 64.2% underwent RYGB and 35.8% had SG, although pre-operative diabetes severity was similar between groups. The majority of diabetes remission occurred in the first 2 years following surgery. Patients who underwent RYGB had slightly higher T2DM remission rates compared to SG (HR 1.10 [95% CI, 1.04–1.16]). At each time point, there was higher T2DM remission following RYGB compared with SG, 59.2% vs 55.9% at 1 year, 84.3% vs 81.5% at 3 years, and 86.1% vs 83.5% at 5 years. The authors conclude that in a real world setting RYGB results in small, but improved long-term T2DM outcomes compared to SG [20].

Existing data for diabetes remission following RYGB and SG vary widely and depend on multiple factors including the severity and duration of pre-existing diabetes, as well as the study's definition of *resolution* and/or *remission*. Overall, studies consistently favor RYGB over SG for diabetic endpoints, but the differences are small. Existing data encompass only 5 years of follow-up, and longer-term data are needed, especially when considering possible differences in recidivism.

Duodenal switch (DS) comprises less than 1% of bariatric procedures performed in the US [16]. DS causes more pronounced post-operative metabolic changes and higher rates of immediate and delayed complications [21–25]. Long-term rates of diabetes remission following DS are 83–93%, higher than published rates in RYGB and SG [26–28]. No RCTs or prospective trials were identified comparing diabetic outcomes of DS versus RYGB and/or SG. However, limited retrospective data suggests higher rates of diabetes remission, lower HbA1C, and decreased need for antidiabetic medications for DS compared to SG [22–26]. A systematic review performed by Buchwald, et al. in 2009 identified 103 treatment arms with 3188 patients measuring diabetic resolution. This study primarily identified single-arm series and only 1.6% of studies contributed class I evidence. However, in this analysis, DS demonstrated complete T2DM remission of 95% compared to 80% after RYGB. Rates of complications were not compared [21]. As minimally invasive techniques improve, more comparative data and risk/benefit analyses are needed to determine the role for DS in obese diabetic patients.

5.3.2 Use of Decision-Aid Tools for Procedure Selection

While there does not appear to be large differences in diabetic outcomes based on broad population data, patient specific factors are also important to consider when selecting an appropriate bariatric procedure. A shared decision-making model informs patients about anticipated benefits and complications, and elicits patient's preference and desires. Diabetic outcomes are dependent on pre-existing factors such as duration of disease, severity of insulin resistance, insulin use, and ability to achieve adequate glycemic control [29–32]. Several evidenced-based decision-aid tools now exist to support shared-decision making conversations. These tools take into account specific patient and procedure factors and can help with procedure selection for diabetic patients.

The ABCD [29] and DiaRem [30] scores are validated tools to predict remission of T2DM following RYGB at 12 and 14 months respectively. The ABCD score incorporates age, BMI, C-peptide levels, and duration of diabetes, whereas the DiaRem score incorporates use of insulin, age, HbA1C, and type of antidiabetic medications. These two scores have similar performance characteristics overall [32].

The Individualized Metabolic Surgery (IMS) score helps frame anticipated outcomes when considering RYGB versus SG operations for diabetic patients. This validated online calculator utilizes accessible patient information including, the number of pre-op T2DM medications, insulin use, and HbA1C, as well as duration of T2DM, to guide expectations for diabetes remission. The tool was developed

from retrospective data of 659 patients undergoing RYGB or SG, and validated in 241 patients at a second center. Short- and long-term complication rates are not explicitly considered in this model. Follow-up data was captured out to 5 years. This tool divides patients into mild, moderate, and severe diabetic catagories, which corresponds to 15%, 51%, and 34% of the study population respectively. For patients with mild diabetes, RYGB and SG are both highly effective, but RYGB was significantly better at achieving diabetes resolution (92% vs. 74%, p = 0.04) and decreasing the need for diabetic medication at 5 years. Patients with moderate diabetes, which comprised 51% of the study cohort, experienced a significant and dramatic difference in remission rates at 5 years favoring RYGB over SG (60% v. 25%, p = <0.001). Additionally, RYGB patients with moderate T2DM were significantly more likely to achieve a HbA1C <7, take less anti-diabetic medications, or remain off all diabetic medications. The authors suggest a clear advantage of RYGB over SG for moderate diabetics. In patients with severe diabetes there was no difference in rates of diabetes remission (12% in both SG and RYGB groups). However, the validation cohort of severe diabetics did demonstrate a difference in remission rates of 8% in the RYGB arm versus 3% in the SG arm. Given that SG has potentially less post-operative and nutritional complications, the authors favor SG in severe diabetics, and argue this avoids the slightly increased risk of complications associated with RYGB [31]. More data are needed to understand the true difference in diabetes remission rates in severe diabetics.

While rates of diabetes remission is an important factor to consider when counseling bariatric patient on procedure choice, other factors such as weight loss, risk profile of post-operative and nutritional complications, and options for revision surgery are important to consider. Additionally, co-morbid conditions such as gastroesophageal reflux or Barrett's esophagus, inflammatory bowel disease, abdominal hernias, and psychiatric disease may influence procedure selection.

5.3.3 Recidivism and Incident Diabetes

It is important to recognize that 35–50% of patients who achieve remission of T2DM following bariatric surgery experience recurrence within 5 years [33–35]. In the PCORnet Bariatric Study, T2DM relapse rate was lower for RYGB than SG (HR 0.75 [95% CI, 0.67–0.84)]. The proportion of patients who experienced diabetes recidivism after RYGB was lower at each time point compared to SG, (8.4% vs 11% at 1 year, 21.2 vs 27.2% at 3 years, and 33.1% vs 41.6% at 5 years) [20]. However, with or without relapse, patients who undergo surgery maintain substantial improvement in glycemic control from baseline for at least 5–15 years [36]. Predictors of a more durable anti-diabetic response to bariatric surgery include, shorter duration of diabetes, no insulin requirement, and better preoperative glycemic control, possibly related to preservation of beta cell function [34, 35, 37, 38]. The Individualized Diabetes Relapse (IDR) score has been developed to calculate the risk of diabetes relapse in patients who have experienced early remission [39]. These data are not

yet robust enough to inform procedure selection, but may become important as more long-term data are reported.

Metabolic surgery may additionally have a role in the prevention of diabetes in obese, at-risk patients. The Swedish Obese Subjects (SOS) trial is the largest and longest multi-center prospective bariatric trial and includes secondary diabetic endpoints. Recruitment occurred from 1987 to 2001 with 20 years of follow-up data, and included 1658 surgical patients (311 underwent gastric banding, 1140 underwent vertical banded gastroplasty, and 207 underwent RYGB), matched with 1771 obese controls. In the post-surgical arm, T2DM developed with an incidence rate of 6.8 cases per 1000 person-years versus 28.4 cases per 1000 person-years in controls, representing a nearly 80% risk reduction of incident diabetes following bariatric surgery. Assessment of incident diabetes in at-risk obese patients following bariatric surgery is an important outcome to consider in future bariatric studies [40].

5.4 Recommendations Based on the Data

1. Sleeve gastrectomy and Roux-en-Y gastric bypass are both effective procedures to induce remission of T2DM.	High	Strong
2. Roux-en-Y gastric bypass and sleeve gastrectomy have similar rates of diabetes remission over 5 years of follow-up.	High	Strong
3. Individual patient factors are important for appropriate procedure selection.	High	Strong
4. Patients with moderate diabetes have superior outcomes after RYGB compared to SG.	Moderate	Moderate
5. DS leads to increased rates of T2DM remission and complications compared to RYGB and SG.	Low	Weak
6. Despite rates of recidivism, diabetic patients still have significant benefit compared to baseline following bariatric surgery, and recidivism should not be considered a “failure”.	Moderate	Moderate

5.5 A Personal View of the Data

It is well established that bariatric surgery is superior to the best medical management for the treatment of T2DM. As surgeons, we must help guide our patients to an optimal outcome using the best available evidence. Currently, we can be confident that the majority of patients with T2DM will experience diabetes remission after bariatric surgery. However, it is important to acknowledge a moderate rate of long-term relapse.

Procedure selection involves understanding individual patients’ priorities and goals, as well as comorbidities and prior surgery that may influence surgical decision-making. If diabetes resolution is the highest priority to the patient, RYGB will offer superior results to SG. This relationship is most pronounced in those with moderate disease. The metabolic benefits of RYGB to patients with mild or severe disease is more controversial. The use of the IMS online prediction tool can help

guide preoperative discussions with diabetic patients. Of note, minimally invasive variations of the duodenal switch are increasingly performed in the US and may offer another strong anti-diabetic operation, but high quality comparative studies are needed.

Moderate rates of long-term relapse of T2DM exist. However, these cases should not be considered a failure as patients still have improved long-term outcomes despite recidivism. In a patient-centered shared-decision making model, patient specific factors and preferences should be accounted for, including thoughtful discussions of risks and benefits, in order to guide procedure selection.

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