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Al-Nahrain University
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كلية الطب
جامعة النهرين
تأسست عام ١٩٨٧

(Diabetic control after Bariatric surgery)

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M.B.ch.B F.I.B.M.S

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بِسمِ اللهِ الرَّحمنِ الرَّحيم

الَّذِي خَلَقَنِي فَهُوَ يَهْدِينِ (78) وَالَّذِي هُوَ يُطْعِمُنِي
وَيَسْقِينِ (79) وَإِذَا مَرِضْتُ فَهُوَ يَشْفِينِ(80)

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I would like to convey my thanks to my dear father and mother for support, patience and encouragement

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Abstract

Objective

Evaluate the long-term effects of bariatric surgery on type 2 diabetes (T2DM) remission and metabolic risk factors.

Background

Although the impressive antidiabetic effects of bariatric surgery have been shown in short- and medium-term studies, the durability of these effects is uncertain. Specifically, long-term remission rates following bariatric surgery are largely unknown.

Methods

Clinical outcomes of 30 patients with T2DM who underwent bariatric surgery between 2017 and 2019 and had at least 6 month- follow-up were assessed. Complete remission was defined as *glycated hemoglobin*(A1C) less than 6% and fasting blood glucose (FBG) less than 100 mg/dL off diabetic medications. Changes in other metabolic comorbidities, including hypertension, dyslipidemia, and diabetic nephropathy, were assessed.

Results

At a median follow-up of 1 years (range: 6month–3 years) after surgery (Roux-en-Y gastric bypass, $n = 30$; sleeve gastrectomy, $n = 11$ a mean excess weight loss (EWL) of 55% was associated with mean reductions in A1C from 7.5% ± 1.5% to 6.5% ± 1.2% ($P < 0.001$) and FBG from 155.9 ± 59.5 mg/dL to 114.8 ± 40.2 mg/dL ($P < 0.001$).

Discussion : Our data are consistent with other studies who have demonstrated that RYGB has a higher long-term rate of diabetes remission than restrictive procedures

Conclusions

Bariatric surgery can induce a significant and sustainable remission and improvement of T2DM and other metabolic risk factors in severely obese patients. Surgical intervention within 5 years of diagnosis is associated with a high rate of long-term remission.

Keywords: bariatric, diabetes, gastric banding, gastric bypass, LAGB, long term, metabolic, nephropathy, RYGB, sleeve gastrectomy

Introduction

The prevalence of obesity and type 2 diabetes mellitus in North America and across the world has been increasing at alarming rates. Obesity is a critical risk factor for the development of type 2 diabetes. The relative risk for type 2 diabetes in individuals with obesity (body mass index [BMI] ≥ 30 kg/m^2) is 10 times greater than in those with normal BMIs (≥18.5 to ≤24.9 kg/m^2). In addition, 90% of all individuals with type 2 diabetes are overweight or obese (1). Although intensive lifestyle modification, with diet-induced weight loss, exercise and intensive medical therapy can result in good control and even remission (2,3) of type 2 diabetes, the majority of patients find it difficult to achieve sustained control of blood glucose. In addition, intensification of medical therapy can lead to hypoglycemia and weight gain.

Therefore, many have turned to bariatric surgery (BS) or metabolic surgery for treatment of obesity and type 2 diabetes. Surgical weight loss provides marked improvement in glycemic control, with the rate of type 2 diabetes remission varying from 24% to 95% at 2 years, depending on the type of surgery, the definition of remission and the type of subjects enrolled (2,4-6). The definition of remission varies from study to study but is generally defined as normoglycemia and glycated hemoglobin (A1C) levels below 6%, without the need for glucose-lowering medications for at least 1 year (7). Recent long-term data, however, suggest that relapse of type 2 diabetes is common in the years following BS. Here we review clinical studies of type 2 diabetes relapse after BS and discuss pathophysiology and determinants of type 2 diabetes relapse and its clinical implications.

HOW DOES BARIATRIC SURGERY IMPROVE TYPE 2 DIABETES?

Three major mechanisms have been proposed to explain how bariatric surgery reverses diabetes. [9,10] TABLE 1 summarizes the effects of the different procedures on factors involved.

TABLE 1

Antidiabetic effects of bariatric procedures

	LAPAROSCOPIC ADJUSTABLE GASTRIC BANDING	ROUX-EN-Y GASTRIC BYPASS	BILIOPANCREATIC DIVERSION
Tempo of diabetes remission	Slow	Rapid	Rapid
Insulin sensitivity	Improved	Improved	Supranormal
Insulin secretion	Reduced	Increased	Reduced
Glucagon-like peptide-1 levels	No change	Increased	Increased
Peptide YY levels	No change	Increased	Increased
Glucose-dependent insulinotropic peptide levels	No change	No change or increased	Reduced

Hypothesis 1: Weight loss increases insulin sensitivity

The enforced caloric restriction, negative energy balance, and weight loss after bariatric surgery reduce insulin resistance. Consequently, the beta cells can rest because they don't need to produce as much insulin. These effects have been observed after both gastric restrictive procedures and gastric bypass procedures.

Hypothesis 2: Less lipotoxicity, inflammation

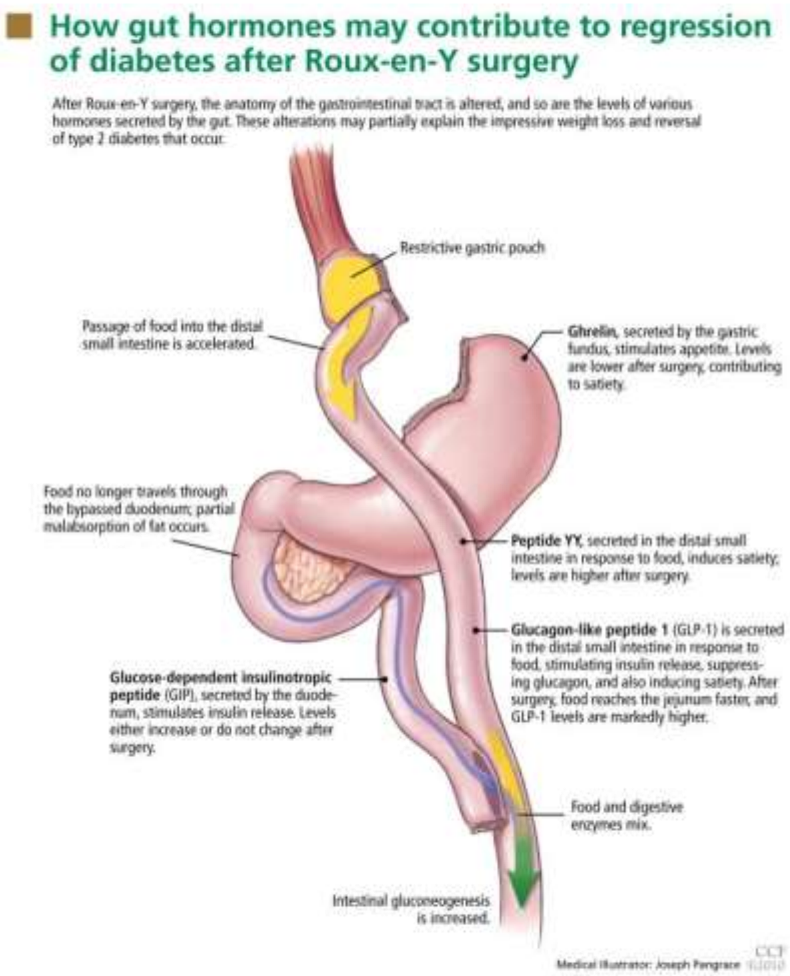
Another theory is that bariatric surgery lessens insulin resistance by reducing "lipotoxicity," a condition related to dysregulated fatty acid flux, lipid metabolites in tissues, and direct and indirect effects of hormones secreted by adipocytes.

The strongest evidence for this theory comes from Bikman et al,[26] who found that insulin sensitivity increased after Roux-en-Y surgery more than expected from weight loss alone. One year after surgery, even though they remained anthropometrically obese (BMI > 30 kg/m^2), the patients had insulin sensitivity levels similar to those in a control group of lean people (BMI < 25 kg/m^2).

Insulin sensitivity begins to improve within 1 week of intestinal bypass procedures,[15,27] suggesting that these procedures are doing something more than simply forcing weight loss via caloric restriction, as gastric restrictive procedures do.

Hypothesis 3: An effect on gut hormones

The third theory is likely the most relevant and relates to various hormones secreted by the gut in response to food (FIGURE 1). Surgical exclusion of the duodenum in the Roux-en-Y procedure and exclusion of the duodenum and jejunum in biliopancreatic diversion result in altered sites—or at least altered relative distribution—of carbohydrate and fat absorption.



Mechanisms of T2DM Remission after Bariatric Surgery

Several studies suggested that a decrease in plasma glucose level in T2DM patients after bariatric surgery is a result of a caloric restriction, not of a significant weight loss. Even though any decrease in caloric intake can improve plasma glucose levels and liver fat content, the mechanism of T2DM remission after bariatric surgery is still not fully elucidated (26). Numerous studies postulated that intestinal hormonal changes after bariatric surgery play an important role in T2DM remission and developed two hypotheses: the hindgut hypothesis and the foregut hypothesis. The hindgut hypothesis of T2DM remission proposes that following bypass surgery, there is a rapid delivery of nutrients to the distal intestine stimulating L-cell secretion of anorexigenic and antidiabetic peptides, including GLP-1 and peptide YY (27, 28). This hypothesis focuses on GLP-1 because its effects on B-cells proliferation and insulin production (29). The foregut hypothesis states that bypassing the proximal small intestine the secretion of anti-incretin hormones is diminished and blood glucose control is improved (28). Gastric inhibitory peptide (GIP) is another incretin responsible for increased postprandial insulin release after bypass surgery (30).

Ghrelin is a 28-amino acid polypeptide hormone produced mainly by endocrine A-like cells in the gastric and duodenum epithelia being responsible for appetite stimulation; its concentration is reduced after bypass surgery as a result of lack of food stimulus (31).

Changes are also seen in adipocyte-derived hormones, leptin is correlated with insulin resistance whereas adiponectin enhances insulin sensitivity (32). After bypass surgery, a decrease in leptin level and a rise in adiponectin concentration are noted (33, 34). A recently published study investigating adipocyte-derived exosomal microRNAs after gastric bypass showed that there are major changes in these microRNAs which correlated to improvement of insulin resistance and metabolomic changes consistent with improved glucose homeostasis (34).

A randomized controlled trial comparing RYGB to a lifestyle intervention included Taiwanese and American patients published in 2016 by Chong et al. found that RYGB was associated with better improvement and remission of diabetes in both ethnicities (35).

As the aforementioned findings indicate, success of T2DM *via* bariatric surgery can be predicted and that the actual mechanism supporting these phenomena appears multifactorial and may involve changes in gut- and adipocyte-derived hormones (31).

INDICATIONS FOR BARIATRIC SURGERY IN PATIENTS WITH DIABETES

According to guidelines from the National Institutes of Health,[23] the current indications for bariatric surgery include a BMI of 40 kg/m^2 or higher, or a BMI between 35 and 40 kg/m^2 with at least two obesity-related comorbidities. Diabetes is considered a key comorbidity that justifies the risk of surgery. The guidelines suggest that bariatric surgery be discussed with all severely obese patients (BMI > 35 kg/m^2) with type 2 diabetes who have not been able to lose weight with other weight-control approaches.

Since type 2 diabetes mellitus is a progressive disease characterized by relentless deterioration of beta-cell function, many endocrinologists favor aggressive weight-loss approaches early in the course of the disease. bariatric surgery should be considered early, as it may help preserve pancreatic beta-cell function and slow the progression of microvascular and macrovascular complications.

Short-term risks

An important concern about using bariatric surgery to treat type 2 diabetes is the risk of morbidity and death associated with these procedures.

Buchwald et al[13] performed a meta-analysis of 136 bariatric studies that included 22,094 patients. The 30-day operative death rates were 1.1% with biliopancreatic diversion, 0.5% with Roux-en-Y surgery, and 0.1% with restrictive procedures.

Laparoscopic adjustable gastric banding is considered the safest of the current bariatric procedures. It does not involve bowel anastomosis, and the risks of major hemorrhage, gastric perforation, and pulmonary embolism are less than 1%. Late complications requiring reoperation include band slippage or prolapse (5%–10%) and band erosion (1%–3%). The entire intestinal tract is left intact, so subsequent nutritional deficiencies are rare.[32]

Roux-en-Y gastric bypass carries an overall risk of major complications of 10% to 15%. Anastomotic leak (1%–5%), pulmonary embolism (< 1%), and hemorrhage (1%–4%) can be life-threatening but are rare if the staff are experienced. Late complications such as ulcer or stricture formation at the gastrojejunostomy site occur in 5% to 10% of cases and are managed nonoperatively.

Nutritional deficiencies

Nutritional deficiencies, including protein-calorie malnutrition and deficiencies of iron, other minerals, and vitamins A, E, D, and B_{12}, occur in 30% to 70% of patients Patients at high risk of developing severe nutritional deficiencies include those who have lost more than 10% of their body weight by 1 month, those with anastomotic stenosis, those undergoing surgical revision, and those with persistent vomiting.[35]

Protein-calorie malnutrition is recognized by signs such as edema, hypoalbuminemia, anemia, and hair loss. To minimize this problem after Roux-en-Y surgery, we suggest that patients take in 60 to 80 g of protein and 700 to 800 kcal a day.

Vitamin deficiencies can lead to Wernicke encephalopathy (due to thiamine deficiency), peripheral neuropathy (due to vitamin B_{12} deficiency),[45,46] and metabolic bone disease (due to long-term deficiencies of vitamin D and calcium). Often, vitamin deficiencies are present before surgery and require prompt supplementation to avoid exacerbation of these deficiencies afterward.

Aim of the study :

Aim of this study is to assess effects of bariatric surgery in a type 2 diabetic control.

Patients and methode :

2.1 study settings:

This is retrospective study undertaken using previous medical record data of a group of Iraqi patients with obesity and T2DM.

In this study, thirty cases of obese adult patient ,different ages, from those who referred for Al-imamain Al-kadhumain Medical City department of surgery, Baghdad city, Capital of Iraq, selected as case group after diagnosis and confirmation their diabetes mellitus by HA1c and fasting blood sugar and undergoes bariatric surgery, . The study performed In Al-imamain Al-kadhumain Medical City in Baghdad, during the years of 2018-2019.

2-2. Inclusion and exclusion criteria

Inclusion criteria were patients have D.M type 2 and obesity BMI > 30 and they did bariatric surgery whether sleeve surgey or gastric bypass surgery .

The exclusion criteria were those who have no D.M. and those have D.M but they didn’t undergo any type of bariatric surgery.

2-3 Methodology:

A cross-sectional study was conducted at Immamain Alkadymain teaching hospital at Baghdad city. The study was conducted for 4 months (1-11-2018) to (1-3-2019). After obtaining informed consent, a total of 30 patients, those fulfilled the inclusion and exclusion criteria, were recruited for the study. All patients were referred for surgery department.

Results

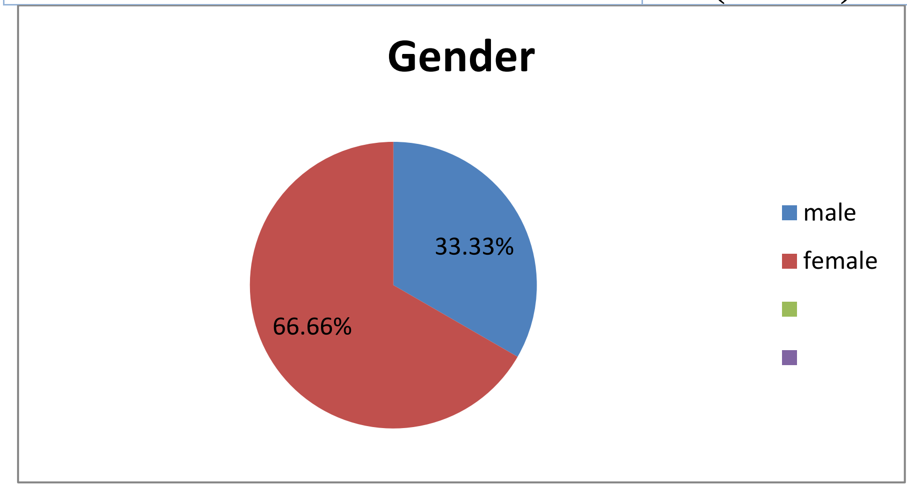
Of the 30 patients with T2DM who had bariatric surgery between 2017 and 2019, 102 reoperative bariatric surgery cases and 72 patients were excluded on the basis of initial eligibility criteria.

In this study, the medical record of 30 patients were studied. The age of the patients ranged from (38- 100) years old.

The study shown that 20 out of 30 patient were female (66.66%) and 10 were male(33.33%) ,((as shown in table (1) and graph (1)).

Table (2) Gender distribution of the patients

Gender	Number of patients
Male	10 (33.33%)
Female	20 (66.66%)



Graph (1) gender distribution

According to age, we divided the data into four groups, the first age group ranged

from (30-40) year which involve 4 patients about (13.33%) , the second group (40-50) years old which involve 16 patients (53.33%) and it's the most group affected, the third one from (50-60) years old have 8 patients (26.66%),and the fourth group (above 60) years old involve 2 patients (6.66%)

The mean of age was 51,006 ±12 years old, ((as shown table (2))

Table(3) Age of distribution of patients:

Age	Male	Female	Total
20-30	0	0	0
30-40	1	3	4
40-50	5	11	16
50-60	4	4	8
Above 60	0	2	2

According to BMI kg/m2 (body mass index) we divided obese patients into three groups ,first group (30-35) obese class 1,second group (35-40) obese class 2,and the third group (above 40)obese class 3

Table(4) BMI distribution

BMI	30-35	35-40	>40
Male	0	3	10
Female	0	5	12

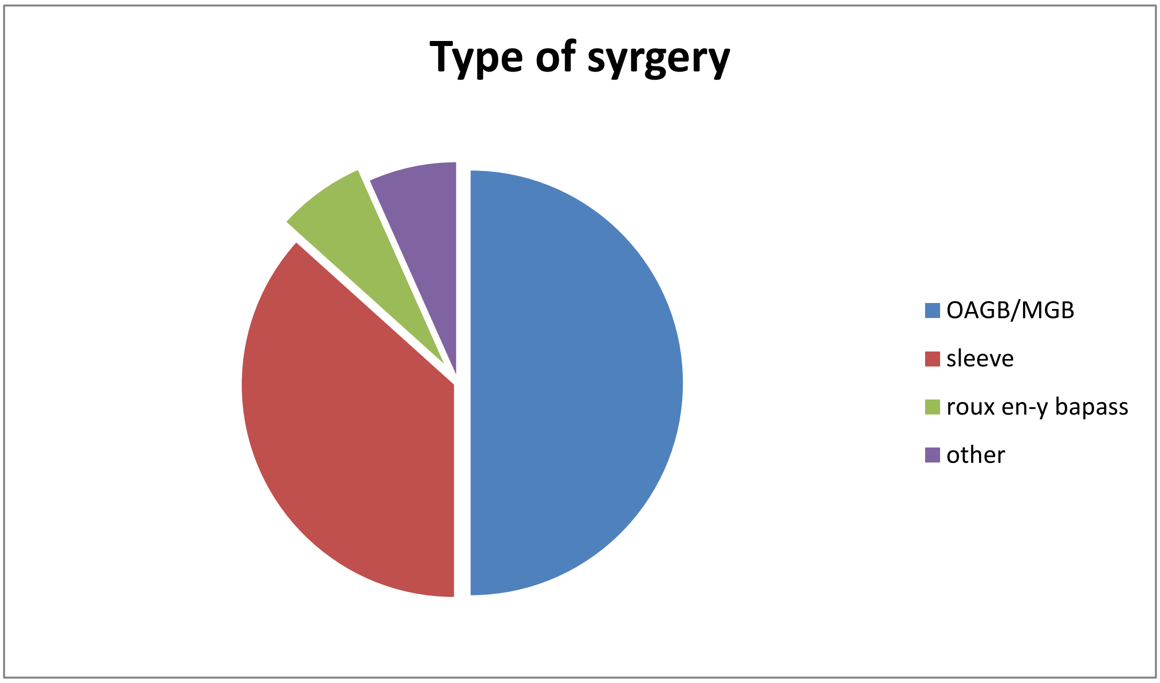
According to the types of the procedures we divided the cases into four groups ,

Sleeve surgery (11cases) , OAGB/MGB (15 cases) which was the most common , Roux en y

Bypass (2 cases), and sasi 2 cases.

Table(5) types of procedure have been done:

Type of surgery	Sleeve	OAGB/MGB	Roux en y By bass	Other(sasi)
Number	11	15	2	2



Graph (2) types of surgery

The outcome of the surgery at at least 6 month follow up according to the HA1c and fasting blood glucose measurement as the following:

Table(6) outcome For sleeve surgery:

Case No.	HA1c%	p-value	FBG(mg/dl)	p-value
1	6.2	0.03	110	0.04
2	5.8		95	
3	6.8		122	
4	6.9		111	
5	6.4		140	
6	5.9		88	
7	6.3		98	
8	7		110	
9	5.6		99	
10	7.1		117	
11	6		90	

Table(7) outcome of Roux en-y bypass :

Case NO.	HA1c%	p-value	FBG(mg/dl)	p-value
1	6.2	0.05	95	0.03
2	5.9		89	

Table(8) outcome for other(sasi) :

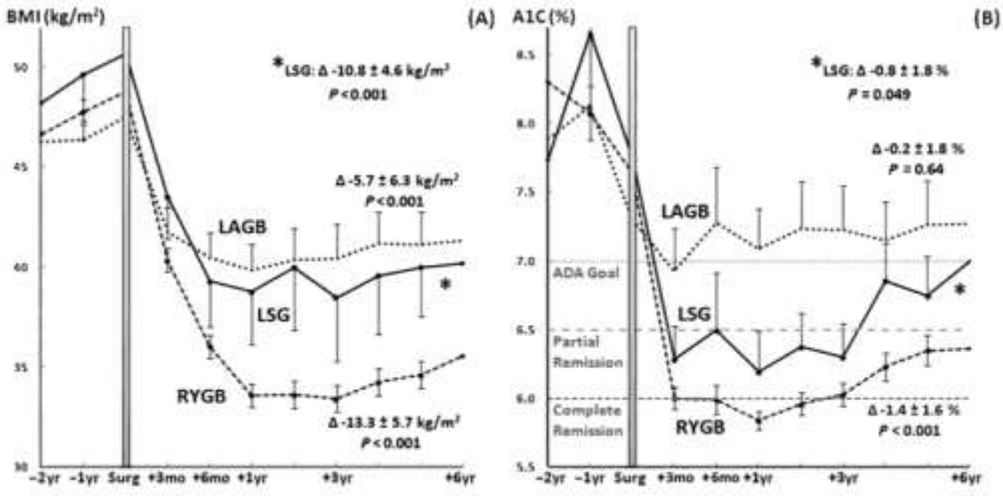
Case NO.	HA1c%	p-value	FBG(mg/dl)	p-value
1	5.9	0.001	97	0.023
2	6.2		108	

mini (one anastomosis) gastric bypass; RYGB, Roux-en-Y gastric bypass.

Table(9) outcome for OAGB/MGB:

Case No.	HA1c%	p-value	FBG(mg/dl)	p-value
1	6.3	<0.001	122	0.001
2	5.7		116	
3	6.3		90	
4	5.4		95	
5	5.8		98	
6	5.4		99	
7	6		86	
8	6.2		100	
9	5.5		90	
10	5.7		82	
11	5.8		78	
12	5.89		92	
13	5.6		99	
14	5.9		79	
15	6		110	

p-value less than 0.05 consider significant.



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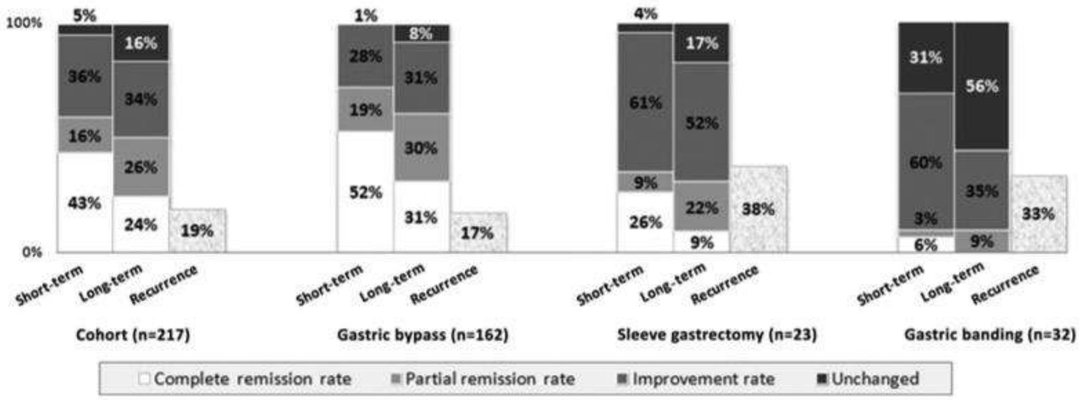
[Figure 1](#)

Changes in BMI (A) and A1C (B) according to procedure type. Δ: Mean ± SD at the last follow-up point—baseline at time of surgery.



[Figure 2](#)

Short- and long-term diabetes remission and recurrence rates according to procedure type.

Discussion:

The outcome of all the cases was better than before the surgery in the follow up by the evidence of decreasing the FBG and HA1c and the no need for the anti-diabetic medications and all these as a reflect of the metabolic and the absorptive changes of the gut after the bariatric syrgery.

There is now a substantial body of evidence describing the short- and medium-term effects of bariatric surgery on T2DM, including 3 recent randomized trials.[8,17,18] The percentage of patients who achieve T2DM remission after surgery in these studies depends on the type of procedure performed, the duration and severity of T2DM at the time of surgery, the length of follow-up, and, importantly, the definitions of remission and improvement used by the authors. There is generally agreement among the published studies that gastrointestinal bypass procedures achieve higher rates of remission than procedures involving restriction of the gastric fundus only and that patients who have long-standing T2DM or require insulin at the time of surgery have lower remission rates.[7,19–22] Currently, though, there are relatively few studies reporting long-term T2DM remission rates after bariatric surgery and fewer still that report long-term biochemical evidence of remission .

Our data are consistent with other studies who have demonstrated that RYGB has a higher long-term rate of diabetes remission than restrictive procedures.[14] Although there is evidence that sleeve gastrectomy is a metabolic operation with incretin effects resulting in excellent short-term diabetes control,[20,23] long-term data on the metabolic effects of LSG are scarce. At a mean follow-up period of 73 months after LSG, Eid et al[24] reported 77% remission or improvement in diabetes of 35 patients, but long-term biochemical data were not reported and further studies are necessary with regard to the long-term effects of LSG on metabolic disease. Similarly, there are few long-term studies reporting biochemical evidence of T2DM remission after gastric banding.[25,26] A study by Sultan et al[25] reported 5-year diabetes outcomes in 95 patients who had LAGB with a reduction of A1C from 7.5% to 6.6% and a complete remission rate of 40% among the 58 patients with long-term biochemical data. Buchwald et al's[14] meta-analysis of diabetic patients undergoing bariatric surgery found an overall T2DM remission rate of 56.7% after LAGB with no difference in studies reporting more than 2 year follow-up.

Conclusion

Diabetes remission, improvement of blood glucose control, and reduction of antidiabetic medications after bariatric surgery can be sustained for many years with a decrease in overall morbidity and mortality. There are grading systems to predict T2DM remission success and that while the mechanisms supporting this are not fully understood there are a number of hormonal changes that may play a significant role in stabilizing blood glucose levels, improving insulin sensitivity, and regulating appetite which overall have a beneficial effect on T2DM. Restrictive-malabsorptive procedures are known to improve glucose homeostasis, insulin sensitivity, and B-cells secretory function. Bariatric surgery can be considered as a second-line therapy in non-obese diabetic patients. In non-diabetic morbidly obese patients, bariatric surgery may prevent the development of T2DM and other comorbidities. PBH is a serious complication, dysregulation of insulin secretion with hyperinsulinemic state being the most important predicting factor for this group of surgical patients. Food restriction is the first-line therapy for this condition and if failed, pharmacological management should be considered. Pancreatectomy may be required for limited cases. Further research should identify the patient population at risk for post-bariatric hypoglycemia and elaborate on the effective treatment. The metabolic benefits, as well as short- and long-term surgical complications, should be considered when the patient is advised to proceed with surgery.

Recommendations:

We carefully look at body composition of fat and muscle mass in our postoperative patients. Do you have any evidence to show that the patients that really do well with the diabetes lose more fat mass while maintaining their lean muscle mass?

In terms of body composition in this particular study, we have no evidence to support the effect of body composition changes related to changes in glycemic control. Those types of data are coming from other prospective mechanistic studies.

We did not present any data in this retrospective study on insulin resistance, but that is something that we are looking at in our prospective studies. I think it is important, particularly when we are talking to endocrinologists, that we provide that type of data as well.

Limitation of the study:

1. Sample size
2. Lack of previous studies in the research area.
3. Data Collection Process
4. Timing of Study
5. Equipment
6. Access to Literature

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