Impacts of bariatric surgery on type 2 diabetes mellitus

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ABSTRACT

Objective: **To determine the beneficial effect of bariatric surgery on the treatment of type 2 diabetes mellitus in obese patients.**

Patients and methods: **This prospective study was conducted in Al-Sader teaching hospital and Al-Musawi privet hospital from August 2013 to August 2017 on 332 patients with body mass index between 35-55, their age was range from 30-60 years, and they were 185 (55.7%) females and 147 (44.3%) males. All patients in this study were diabetic type 2 with different stages of the disease, types of medications, C peptide levels, HbA1c and BMI. They were subjected to three different bariatric procedures; laparoscopic sleeve gastrectomy (LSG), mini gastric bypass (MGB), and laparoscopic Roux-en-Y gastric bypass (LRYGB), they were followed for a period of 1-4 years regarding their glycemic control, HbA1c, type and number of medications.**

Results: **Three hundred and thirty two patients were included in this study, 111 patients (33.5%) had MGB, 88 patients (26.5%) had LRYGB, 133 patients (40%) had LSG according to the following selection criteria; duration and severity of DM, C peptide, other comorbidities and the patients preference Resolution of DM was achieved in 100 patient (90%) of MGB, 77 patient (87%) of LRYGB and 75 patient (57%) of LSG while other patients had no improvement.**

Conclusion: **Bariatric surgery for obese diabetic patients resulted in complete resolution in most patients, improvement of diabetes in some and overall improvement in the quality of life in all patients.**

Key words: type 2, diabetes mellitus, bariatric surgery, impacts

تأثير عمليات السمنة على داء السكري النوع الثاني

السمنة في الدراسة: **لتحديد الآثار المفيدة لجراحات السمنة في علاج مرض السكري النوع الثاني للمرضى الذين يعانون من السمنة المفرطة.**

طريقة الدراسة: **أجريت هذه الدراسة في مستشفيات البصرة من آب/أغسطس عام ٢٠١٣ إلى آب/أغسطس ٢٠١٧على ٣٣٢ مريض من المرضى الذين يعانون من ارتفاع مؤشر كتلة الجسم ٣٥–٥٥،و كان على متوسط العمر ٤٥ عاماً، وكان١٨٥(٥٥,٧%) من المرضى إناث و١٤٧ ٤٤,٣(%) من المرضى ذكور. وكان جميع المرضى في هذه الدراسة يعانون من مرض السكري من النوع الثاني مع اختلاف، مراحل المرض، وأنواع الأدوية، مؤشر كتلة الجسم و نسبة الببتيد (سي) مؤشر نسبة السكر التراكمي، وقد خضع جميع المرضى الى احدى عمليات السمنة المختلفة (عملية تكميم المعدة، عملية تحويل مسار المعدة المصغر او عملية تحويل مسار المعدة الكامل) و تمت متابعة المرضى لمدة تتراوح من سنه الى ٤ سنوات عن طريق مراقبة نسبة السكر ونسبة السكر التراكمي.**

نتائج الدراسة: **شارك في هذه الدراسة ٣٣٢ مريض اجريت لهم احدى عمليات السمنة التالية عملية تكميم المعدة١٣٣ مريض عملية تحويل مسار المعدة المصغر ١١١ مريض او عملية تحويل مسار المعدة الكامل ٨٨ مريض وفقا لمعايير خاصه وهي شدة مرض السكري، نسبة السكر التراكمي في الدم ،نوع وعدد الادوية التي يأخذها المريض للسكري نتائج الحث تشير الى ان ٩٠%من الرضى الذين اجريت لهم عملية تحويل مسار المعدة المصغر و ٨٧% من المرضى الذين اجريت لهم عملية تحويل مسار المعدة الكامل و ٥٧% من المرضى الذين اجريت لهم عملية تكميم المعدة اكتسبوا الشفاء من مرض السكري.**

الاستنتاج: **جراحات السمنة لمرضى السكري النوع الثاني الذين يعانون من السمنة المفرطة أدت إلى الشفاء الكامل او التحسن لمرض السكري وتحسن عام في نوعية الحياة.**

الكلمات المفتاحية:مرض السكري النوع الثاني، عمليات السمنة، تأثير

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INTRODUCTION

The increasing prevalence of obesity in adult population triggered a concomitant rise in type 2 diabetes mellitus (T2DM).[1,2] Obesity and insulin resistance are the main components of metabolic syndrome and result in impaired glucose metabolism. Of the various treatment options, bariatric surgery remains the most effective method to achieve a long-term weight loss. [3,4] Post-surgical weight loss improves all obesity-related comorbidities with a good quality of life and decreased overall mortality rate. [5,6] There are several bariatric procedures currently available including laparoscopic sleeve gastrectomy (LSG), mini gastric bypass (MGB), laparoscopic Roux-en-Y gastric bypass (LRYGB), laparoscopic adjustable gastric band (LAGB), and biliopancreatic diversion with duodenal switch (LBPD-DS). [7] Remission or improvement of T2DM can be predicted by considering a number of factors. The ABCD score which is also called the diabetes surgery score, is a simple multifactorial grading system that can predict the success of bariatric surgery on T2DM remission (Table-1). The score contains four hubs, (1) patient age (2) the degree of obesity (BMI), (3) islet cell mass (C-peptide level) and (4) competence of B cell function (T2DM duration), [8,9]

Table 1. ABCD grading system.

Factor	Score
1. Age (years)	
< 40	**1**
≥ 40	**0**
2. BMI (kg/m^2)	
< 27	**0**
27-34.9	**1**
35-41.9	**2**
≥ 42	**3**
3. C-peptide (mg/ml)	
< 2	**0**
2-2.9	**1**
3-3.9	**2**
≥ 5	**3**
4. Duration of DM (years)	
> 8	**0**
4-8	**1**
1-3.9	**2**
< 1	**3**
Total score calculated by adding each of the four variables	**0-10**

The benefit of bariatric surgery in diabetic patients with BMI < 27 kg/m^2 is reduced, and the procedure is not recommended for diabetes treatment. [10,11] There is another scoring system named as DiaRem score which is used to predict the success of bariatric surgery on T2DM reemission, the score include the following factors,[12] as shown in (Table-2)

Table 2. DiaRem score.

Factor	Score
1.Age (years)	
< 40	**0**
40-49	**1**
50-59	**2**
≥ 60	**3**
2.HbA1c	
< 6.5	**0**
6.5-6.9	**2**
7-8.9	**4**
≥ 9.0	**6**
3.Other diabetes drugs	
No sulfonylureas or insulin-sensitizing agents other than metformin	**0**
Sulfonylureas and insulin-sensitizing agents other than metformin	**3**
4.Treatment with insulin	
No	**0**
Yes	**10**
Total score	**0-22**

The mechanism of T2DM remission after bariatric surgery is still not fully elucidated.[13] Numerous studies postulated that intestinal hormonal changes after bariatric surgery play an important role in T2DM remission and developed two hypotheses: the hindgut and the foregut hypotheses. The hindgut hypothesis 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 glucagon like peptide-1(GLP-1) and peptide YY.[14,15] This hypothesis focuses on

GLP-1 because its effects on B-cells proliferation and insulin production.[16] The foregut hypothesis states that bypassing the proximal small intestine, the secretion of anti-incretin hormones is diminished and blood glucose control is improved.[15] Gastric inhibitory peptide (GIP) is another incretin responsible for increased postprandial insulin release after bypass surgery.[17] Ghrelin is 28 amino acid polypeptide hormone produced mainly by endocrine A like cell in the gastric (mainly fundus) and duodenal epithelia being responsible for appetite stimulation; its concentration is reduced after bypass surgery as a result of lack of food stimulation. [18] Changes are also seen in adipocyte derived hormones, leptin is correlated with insulin resistance whereas adeponectin enhance insulin sensitivity, after bypass surgery, a decrease in leptin and increase in adeponectin level are observed.[19]
This study aimed to determine the valuable effects of bariatric surgery on the treatment of type 2 diabetes mellitus in obese patients.

PATIENTS AND METHODS

This prospective study included 332 morbidly obese patients who are a known cases of type 2 diabetes who underwent bariatric procedures by the same surgeon in both Al-Sader Teaching Hospital and Al-Musawi Privet Hospital from August 2013 to August 2017. Their mean age was 45 years old (from 35-60) they were 147 male and 185 female with BMI range from 35 to 55 km/m^2. They underwent; laparoscopic sleeve gastrectomy in 133 patients, mini gastric bypass in 111 cases and Roux-en-Y gastric bypass in 88 patients. The type of bariatric procedure depend on severity of DM, age of patient, presence of comorbidities in which patient could not tolerate long operation and patient's preference. The severity of diabetes was classified according to; impaired fasting blood sugar (FBS), HbA1c, type of treatment (oral hypoglycemic drug, insulin, and diet control) and C peptide. All patients met the criteria for bariatric surgery which includes; (1) BMI more than 40, (2) BMI more than 35 with obesity related life threatening co-morbidities like DM, hypertension, and obstructive sleep apnea, (3) failure of weight reduction with noninvasive method like diet and exercise, and (4) psychologically stable. Candidates were excluded if they have; (1) diabetes secondary to specific disease like pancreatitis, and drug or alcohol addiction, (2) recent vascular event (MI, strock within 6 month), (3) malignancy, (4) inability to cooperate in long term follow-up, and (5) mental impairment. Pre-operative evaluation for all patients included; history and physical examination, nutritional, cardiovascular and endocrine evaluation, pre-operative abdominal ultrasound, and oesophageo-gastro-duodenoscopy (OGD) for those patients with symptoms of gastro esophageal reflux disease (GERD). Pre-operative preparation also included; detailed explanation of surgery, benefit and risk (short and long term complications), nutritional squeal and possible conversion to open surgery. A written informed consent was obtained for all patients. All operations were done under general anesthesia, with a reversed trendelenberg position. Four to five ports were inserted; 15 mm port above and to the left of the umbilicus, 12 mm port in the left upper quadrant of abdomen, 5 mm port in the right upper quadrant, and 5 mm port in the epigastric region for liver retractor and 5 mm port in left subcostal region. All procedures were done in the classical way as described previously. After recovery from anesthesia, they were transmitted to the ward unless they required intensive care unit monitoring. Blood sugar was checked 6 hourly in the first 48 hour and the patients were started oral fluid in the first post-operative day and if there was no complication, patients are usually discharged on the second postoperative day. All patients were advised to check their blood sugar twice daily and continue on their medication if their blood sugar is more than 160

mg/dl and they were followed-up at 7, 30, 90 days and then every 3 months in the outpatient clinic. For all the patients, the mean post-operative follow-up was 2 years (from 1-4 years).

RESULTS

Patients participating in this study were 332 cases. The age range was 30-58 year for LSG group, 38-60 for MGB group and 36-52 for RYGB group. Patients were 147 males and 185 females and were divided according to groups as demonstrated in (Table-3).

Table 3. Age and gender distribution.

Type of surgery	No. of Patients	Male	Female	Age
LSG	133	43	90	30-58 y
MGB	111	71	40	38-60 y
RYGB	88	33	55	36-52 y
Total number	332	147	185	

All the 332 morbidly obese patients with type 2 diabetes were divided into 3 groups according to their type of surgery; LSG group included 133 patients (40 patients on insulin, 88 patients on oral hypoglycemic drug and 5 patients who were newly diagnosed), MGB group included 111 patients (92 patients on insulin, 9 patients on oral hypoglycemic drug and 10 patients who were newly diagnosed), and LRYGB group included 88 patients (44 patients on insulin, 40 patients on oral hypoglycemic drug and 4 patients who were newly diagnosed), as shown in (Table-4).

Table 4. The types of bariatric surgeries.

	Patients No. (%)	Insulin	Oral hypoglycemic drug	Newly Diagnosed
LSG	133 (40)	40	88	5
MGB	111 (33.5)	92	9	10
RYGB	88 (26.5)	44	40	4

The mean BMI was 39 kg/m2 for the LSG group, 45kg/m2 for the MGB group and 44kg/m2 for the RYGB group. The mean pre-operative random plasma glucose (RPG) was 140mg/dL for the LSG group, 133mg/dL for the MGB group and 160 mg/dL for the RYGB group. The mean HbA1c was 9 for the LSG group, 12 for the MGB group and 12 for the RYGB group as shown in (Table-5).

Table 5. Preoperative parameters.

type of Surgery	No. of Patients	Mean RPG (mg/dl)	BMI	Mean Hba1c
LSG	133	140	39	9
MGB	111	133	45	12
RYGB	88	160	44	12

There were no major intraoperative complications or conversion to open surgery. The mean operative time was 45 min for the LSG group, 60 min for the MGB group and 100 min for the RYGB group. Postoperatively there were no major complications apart from 2 patients developed intra-abdominal bleeding and they were treated conservatively. There was no leak, no DVT, no pulmonary embolism and no mortality. The mean hospital stay was 48 hours (1.5-4 days). During the first 6 months after surgery, the mean BMI fell from 39 to 33 kg/m2 for the LSG group, from 45 to 38kg/m2 for the MGB group, and from 44 to 36 kg/m2 for the RYGB group. The mean HbA1c fell from 9 to 7 for the LSG group, 12 to 9 for the MGB group, and from 12 to 10 for the RYGB group and then continued to decrease slowly after that as shown in (Figure-1).

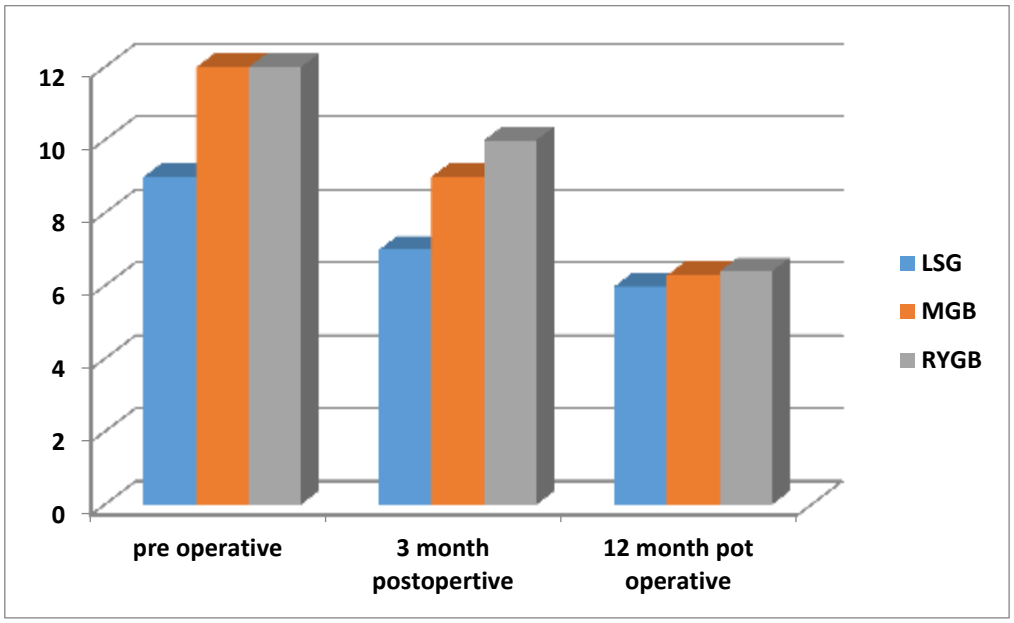
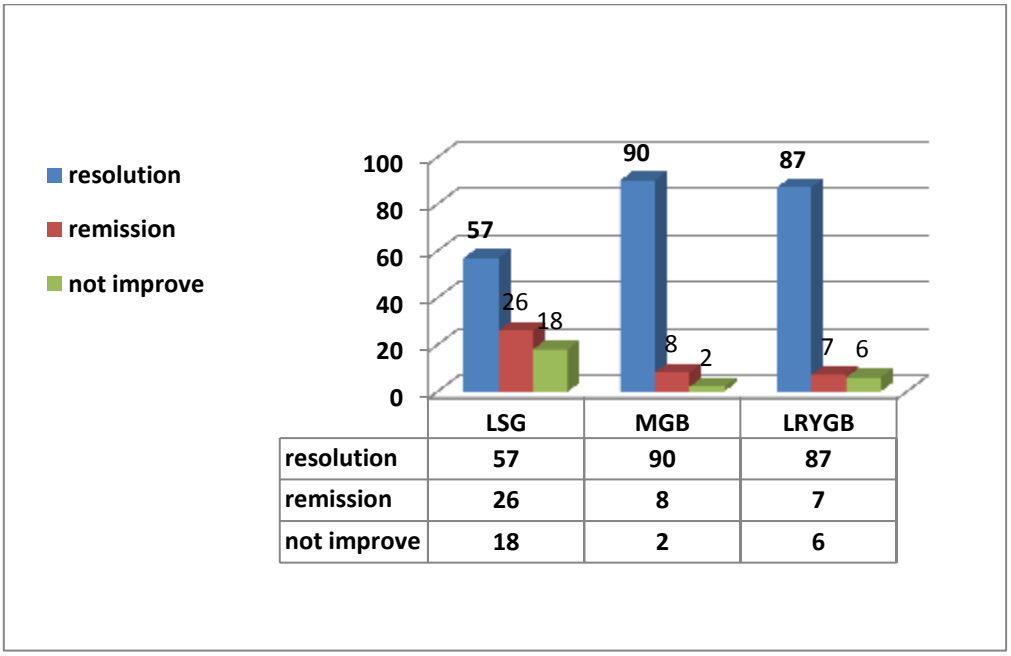


Fig 1. Pre and postoperative changes in HbA1c

Resolution from diabetes (HbA1c less than 6.5) without anti-diabetic medication was observed in 57% of the LSG group, 90% of the MGB group and 87% of the RYGB group. Remission of DM was observed in 26% in LSG group, 8% in MGB group, and 7% in RYGB group, in those patients there was normal HbA1c that can be achieved with oral hypoglycemic drugs only without need of insulin. In 18% of the LSG group, 2% of the MGB and 6% of the RYGB group there was very little improvement regarding their blood sugar, as shown in (Figure-2).



	LSG	MGB	LRYGB
resolution	57	90	87
remission	26	8	7
not improve	18	2	6

Fig 2. The percentage of cure and remission of DM after bariatric surgery.

DISCUSSION

The close relationship between type2 diabetes mellitus (T2DM) and obesity is well documented.[20] All obese patients have some level of insulin resistance and risk of development of T2DM that grows with increased weight [21,22] and about 90% of all patient with T2DM either are overweight or obese. The national health and nutrition examination survey data demonstrated that risk of DM is approximately 50% with BMI greater than or equal to 30 and over 90% with BMI of 40 or more. Lifestyle changes will often improve diabetes, however the changes are not sustained.[23,24] Most nonsurgical treatments can control hyperglycemia, but they cannot induce remission of diabetes.[25] Bariatric surgery can result in resolution of both obesity and diabetes. Restrictive versus malabsorptive operations offers deferent degrees of resolution of T2DM and insulin resistance.[25-27] This study showed that average level of HbA1c, fasting blood glucose and clinical outcome of comorbidities are much better than conventional and intensive medical therapy. In this study, there is complete resolution of T2DM in 90%, 87%, and 56% of patients who underwent MGB, RYGB, and LSG respectively as they had normal blood glucose and HbA1c without the need of any medication. Improvement of diabetes after LRYGB and MGB surgery occur after early days of surgery independent to weight loss, surgically induce hormonal changes and post-operative diet restriction are the proposed mechanisms while after LSG surgery, the glycemic control tooks longer time. Improvement of glycemic control observed in 26%, 8%, and 7% of patients with LSG, MGB and RYGB groups respectively. Most of those patients have good glycemic control and normal HbA1c (below 6.5) with oral medication only (without need of insulin) and there is a marked decrease in number of medication use in these groups than before surgery. About (18%) of LSG, (6%) of LRYGB, and (2%) of MGB showed very little improvement after surgery, most of these patients have DM for long duration more than 10 years with sever impairment of blood sugar before surgery. An important factor in the improvement of T2DM after bariatric surgery is the preoperative severity of T2DM, the most important factors that determine the severity of diabetes are duration of T2DM, elevated HbA1c and insulin use. Patients with these 3 factors are less likely to achieve resolution. In contrast, the important parameters that increase the chance of remission of diabetes includes; use of oral hypoglycemic drug instead of insulin and short duration of diabetes (less than 5 years).[28] To explain the mechanism underlying the effectiveness of bariatric surgery in normalizing blood glucose, it has been suggested that removal of gut may play a major role in diabetes remission especially because there are an important hormones secreted from this region. In 2009 Cummings D.E reviewed the existing hypothesis regarding the mechanisms underlying diabetes remission, based on this review the main hypotheses included: the Ghrelin hypothesis, upper intestinal hypothesis, and lower intestinal hypothesis.[29] Ghrelin hypothesis maintains that Ghrelin regulation may be disturbed following RYGB. Ghrelin is a hormone secreted by stomach and proximal small bowel particularly before meal, its main physiological effect is to increase appetite and fat mass. [30] Several studies have shown that ghrelin level are very low following RYGB, decreased ghrelin can decreases appetite and food intake and also may have a role in increasing glucose tolerance as it can stimulate counter regulatory hormones.[31] The lower intestinal hypothesis suggests that increase in transit of concentrated nutrient particularly glucose to the distal intestine results in increase GLP1, this hormone is an incretion that increase insulin secretion and in addition it also increase the proliferation and decrease the apoptosis of beta cell of pancreas. [32] The upper intestinal

hypothesis maintains that avoiding of nutrient contact with duodenum is responsible for diabetes improvement, the basis of this hypothesis is that there are unknown factors from duodenum influence glucose hemostasis.[29] Data from many observational studies as well as meta-analyses showed that bariatric surgery is useful in marked improvement in diabesity parameters. The Surgical Treatment and Medications Potentiall. Eradicate Diabetes Efficiently (STAMPEDE) trial investigators found that after the first year of randomization, gastric bypass and sleeve gastrectomy were superior to intensive medical therapy alone in achieving glycemic control and reducing cardiovascular risk factors.[33] The STAMPEDE trial gives a 3-year follow up analysis of bariatric surgery from a single center involving 150 obese patients in a 3-groups randomized controlled design, the 3 arms of the trial were: Intensive medical treatment group compared with sleeve gastrectomy or gastric bypass groups. The primary endpoint of HbA1c of less than 6% was attained by only 5% of patients in the intensive medical control arm while 38% of the patients in the surgery arms. Also the glucose lowering medications and insulin use was significantly reduced in the 2 groups of patients in the surgical arms. At 3 years, reduction in body weight, and BMI, was greater after gastric bypass and sleeve gastrectomy than after intensive medical therapy. There were also significant improvements in other diabesity parameters in patients of the surgical arms such as reduction of triglyceride levels and increase in high density lipoprotein levels. There was no excessive weight loss or hypoalbuminemia and no life-threatening complications or deaths in any of these groups. Comparable results were reported in a more recent trials with a 5-year follow-up data by Mingrone, et al[34] showed remarkable improvements in the diabesity parameters and possible cardiovascular morbidity and mortality benefits that make these clinical trials unique. The long-term follow-up results of these major clinical trials should give us better insight into the morbidity and mortality benefits of metabolic surgery. While the gold standard for DM remission remains the RYGB surgery because all mechanisms of DM remission are present. The MGB could be a good alternative, this is supported by our results that encourage and support MGB as an effective treatment strategy for DM remission. Further studies are needed to reach definitive conclusion regarding the ideal procedure for obtaining DM

In Conclusion, bariatric surgery results in a complete resolution, improvement of blood glucose control, reduction in anti-diabetic medication and decrease in overall morbidity and mortality in morbidly obese patients with type 2 diabetes.

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