Effect of Laparoscopic Sleeve Gastrectomy on Type II Diabetes Mellitus in Morbidly Obese Patients

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ABSTRACT

Morbid obesity, a newly perceived epidemic, is notoriously associated with numerous co-morbidities. Type 2 diabetes mellitus is an important issue in this context. Laparoscopic Sleeve Gastrectomy (LSG) is now a universally accepted stand-alone bariatric procedure with encouraging results.The objective of this study was to identify the impact of this weight losing procedure on patients with type 2 diabetes mellitus (T2DM). Twenty patients were included in this study, their mean fasting blood sugar(FBS)was 208±69.58 mg/dl and their mean glycosylated hemoglobin (HbA1c) was 8±0.78.signicant changes have been reported in all patients after 6 and 12months postoperatively, FBS fell to a mean of 95.4mg/dl and HbA1c fell to a mean of 6.32±0.38 after 12 months. This is to conclude that LSG is effective , as a stand-alone procedure , in inducing improvement of T2DM in obese patients.

Key Words: LSG – T2DM

INTRODUCTION

Type 2 diabetes (T2DM) is a public health problem that threatens to spiral out of control in the twenty-first century. Early intervention can greatly mitigate the serious socioeconomic impact of the disease, driven largely by disabling microvascular complications and cardiovascular disease. Morbid obesity is affecting 2/3 of adults and reaching alarming rates in children in modern society. The understanding of adipose tissue has evolved drastically in the past decade being now viewed as a dynamic "endocrine organ" responsible for the development or worsening of insulin resistance and "lipotoxicity" in obese individuals. "Lipotoxicity" describes the damage that occurs when chronic energy supply exceeds metabolic needs and lipid accumulates in tissues that would not normally store large amounts of lipid.

Lipid is redirected into harmful pathways of nonoxidative metabolism, with accumulation of toxic metabolites that activate inflammatory pathways and eventually lead to apoptosis. It affects organs responsible for maintaining normal energy homeostasis, such as the liver, skeletal muscle, and pancreatic beta-cells, but also the vascular bed [(1)].

However, it was not until relatively recently that our perception of adipose tissue shifted from a rather "passive" fuel storage depot to a highly complex endocrine organ with an important role in causing systemic inflammation in obesity-related states. Because this topic has been the subjects of a number of recent in-depth reviews, this is considered just briefly a few aspects of the link between abnormal fat cells and inflammation.[(2)]

Type 2 diabetes is characterized by insulin resistance (at the level of skeletal muscle, adipose tissue, and liver) and by impaired β -cell function .

Both genetic and acquired defects have been shown to play a role in affecting insulin action and insulin secretion. Among the acquired defects, obesity and glucotoxicity have received special attention as both are believed to worsen insulin resistance and possibly contribute to the decline in β -cell function. [(3)]

Liver and muscle insulin resistance are both central to the pathogenesis of T2DM. Hepatic insulin resistance per se may drive a chronic increase in insulin secretion aimed at refraining excessive rates of hepatic glucose production and prevent subsequent hyperglycemia. Hepatic insulin resistance is frequently associated with a fatty liver, diminished insulin clearance, and peripheral hyperinsulinemia. [(4)]

Finally, it is well established that there is an intrinsic defect in insulin action in skeletal muscle of patients with T2DM. Skeletal muscle insulin resistance has been well documented in muscle

biopsy studies from lean normal glucose-tolerant and, otherwise, healthy subjects genetically predisposed to T2DM (without the confounding factor of obesity and elevated plasma FFA levels), long before the development of frank lipo- and/or gluco-toxicity observed in T2DM.

It is unquestionable that cardiorespiratory fitness reduces the risk of cardiovascular diseases and that low rates of physical activity are associated with a greater risk of developing insulin resistance, obesity and T2DM.

In the midst of the problem of morbid obesity and diabetes, renewed interest has developed in understanding the molecular pathways by which exercise appears to reverse defects associated with insulin resistance. **(5)**

The aim of the study is to evaluate the impact of laparoscopic sleeve gastrectomy on type II DM in terms of blood sugar level, HBA1c at 0, 6, 12 months postoperatively.

PATIENTS AND METHODS

This is a prospective study based on follow up of 20 patients underwent Laparoscopic Sleeve Gastrectomy.

Inclusion criteria:

1. Male and female between 18 and 65 years.
2. Patients with BMI > 35 .
3. Type 2 diabetic patients on oral anti-diabetic agents and/or insulin treatment for a minimum of 12 months prior to the enrollment. s
4. Diagnosis of T2DM for at least 12 months.
5. HbAlc ≥ 7 preoperatively.
6. Compliance for regular follow up.

Exclusion criteria:

1. Previous abdominal surgery, except laparoscopic surgeries.
2. Severe COPD (chronic obstructive lung disease).
3. Obese due to a clinically diagnosed endocrine disorder.
4. Subjects with impaired liver functions.
5. History of malignant disease.
6. Pregnant or planning on pregnancy while enrolled in study.
7. Inability to gain informed consent.
8. Inaccessibility for follow up .
9. Type 1 D.M

Procedure assessment:

Our proposed approach is evaluated by gathering the following data in the 20 patients undergoing Laparoscopic Sleeve Gastrectomy .

Preoperative data:

- Weight, height and BMI (Body Mass Index).
- Preoperative Fasting Blood Sugar.
- Preoperative HBAlc in Blood.

Operative Technique:

The operation was performed under general anesthesia. A Veress needle was inserted in the left upper quadrant with insufflation of the abdominal cavity to a pressure of 15 mmHg. Five laparoscopic ports were inserted, two 5 mm, one 10 mm and two 12 mm ports. The lesser sac was entered by opening the gastrocolic ligament. A point on the greater curve, on the antrum, is chosen as the starting point approximately 4-6 cm from the pylorus. The short gastric vessels are taken down along the greater curvature of the stomach with ultrasonic dissection using a Harmonic® scalpel (Ethicon Endo-Surgery, Inc.) extending cephalad, taking the short gastric vessels down around the fundus of the stomach.

Once freed, a 34-Fr bougie is inserted by anesthesiologist. This is guided to hug the lesser curvature. Once bougie is placed, sequential firings of the Echelon® 60™ Endopath stapler (Ethicon Endo-Surgery, Inc.) with the blue cartridge (3.5-mm staple height), were used to transect the lateral stomach to create a vertical gastrectomy. Before each firing, adequate tension was ensured to avoid excess tissue under the sleeve that is measured against a 34-Fr bougie. A small margin of gastric tissue was left at the angle of His. At this point, approximately 75% to 80% of the stomach has been separated.

Once the gastrectomy is complete, The specimen was removed by enlarging one of the 12 mm ports. A drain was then placed alongside the staple line.

Postoperative data:

- Follow up weight documentation 6 and 12 months after the operation .
- Fasting blood sugar 6 and 12 months after the operation .
- HbAlc in blood 6 & and 12 months after the operation .

Primary outcomes:

1. Laparoscopic Sleeve Gastrectomy is effective in controlling Type 2 Diabetes Mellitus.

2. Laparoscopic Sleeve Gastrectomy is not effective in controlling Type 2 Diabetes Mellitus.

Secondary outcome parameters:

Improvement of BMI after Laparoscopic Sleeve Gastrectomy .

Statistical Analysis

The data was coded and entered using the statistical package SPSS version 15. The data was summarized using descriptive statistics: mean standard deviation and range for quantitative variables. The changes of the studied variables overtime were tested using repeated measurement ANOVA (analysis of variance) with post Hoc Bonferroni test for quantitative variables and correlations. P-values less than or equal to 0.05 were considered statistically significant.

RESULTS

This study shows 20 patients with a mean age 33.2 ± 8.13 with a range of median of 34,with a minimum of 21 and maximum of 46.

A mean height 159.15 cm ± 6.28 with a median of 160.5 cm ,with a range of minimum of 150 cm and maximum of 172cm .

P value index indicate difference between 3 groups :

- PI indicate difference between basal BMI and 6 months BMI . Mean Difference: 8 ± 0.541
- P2 indicate difference between basal BMI and 12 months BMI. Mean Difference: 13.316 ± 0.991
- P3 indicate difference between 6 months BMI and 12 months BMI Mean Difference: 5.316 ± 0.607

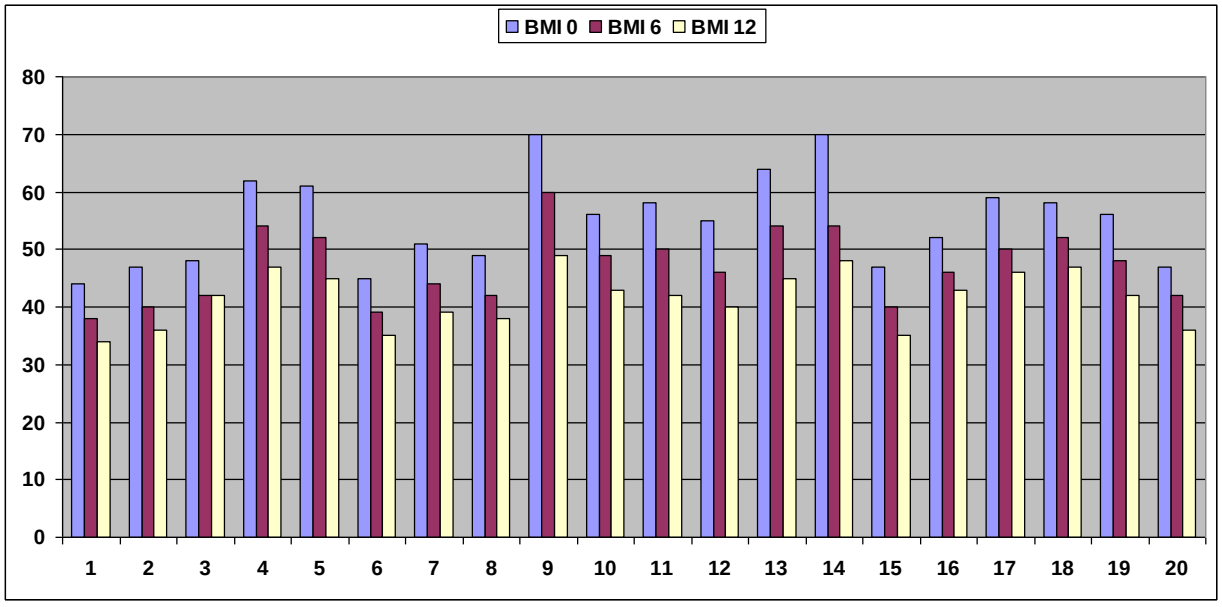

Fig. (1): Diagram illustrating change in BMI 0, 6 & 12 months

P value index indicate difference between 3 groups :

- PI indicate difference between Basal Wt and 6 months Wt. Mean Difference: 19.211 ± 0.929
- P2 indicate difference between Basal Wt and 12 months Wt. Mean Difference: 34.158 ± 2.19
- P3 indicate difference between 6 months Wt and 12 months Wt Mean Difference: 14.947 ± 1.559

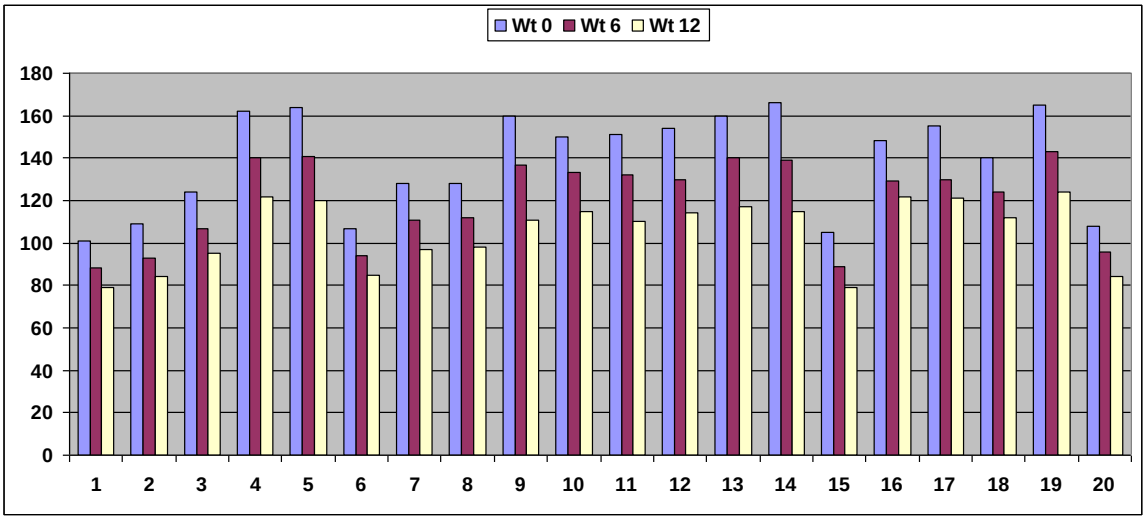

Fig. (2): Diagram illustrating change in Weight 0, 6 & 12 months

P value index indicate difference between 3 groups :

- PI indicate difference between Basal FBS and 6 months FBS . Mean Difference: 82.895 ± 8.936
- P2 indicate difference between Basal FBS and 12 months FBS . Mean Difference: 96.947 ± 12.003
- P3 indicate difference between 6 months FBS and 12 months FBS Mean Difference: 14.53 ± 3.441

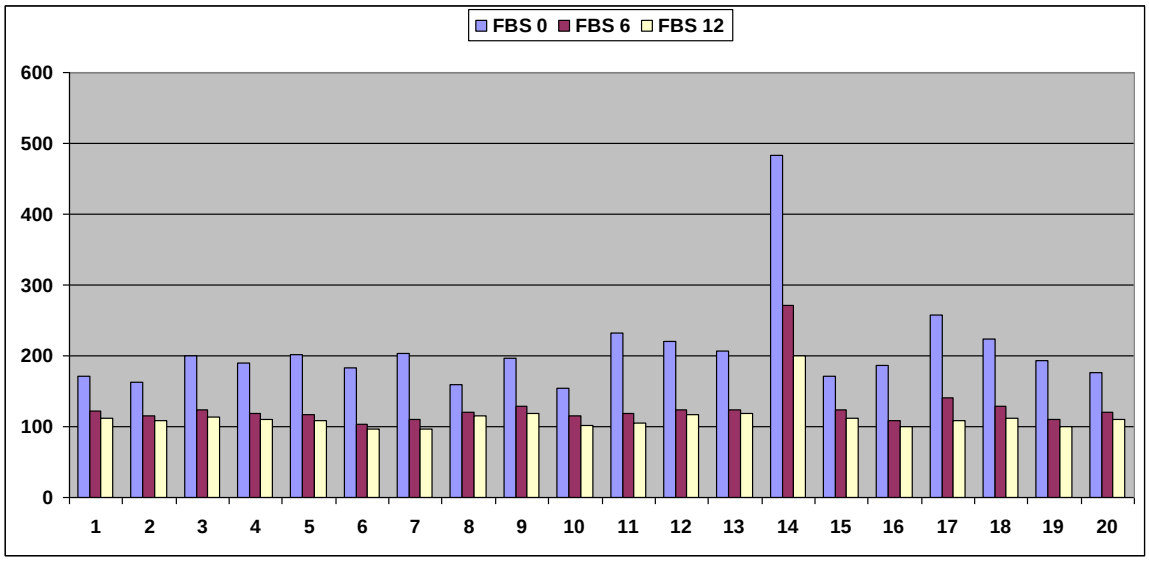

Fig. (3): Diagram illustrating change in FBS 0, 6 & 12 months

P value index indicate difference between 3 groups :

- PI indicate difference between Basal and 6jnonths HBAlc. Mean Difference: 1.329 ±0.097
- P2 indicate difference between Basal and 12 months HBAlc. Mean Difference: 1.721 ± 0.118
- P3 indicate difference between 6 months and 12 months HBAlc Mean Difference: 0.392 ± 0.068

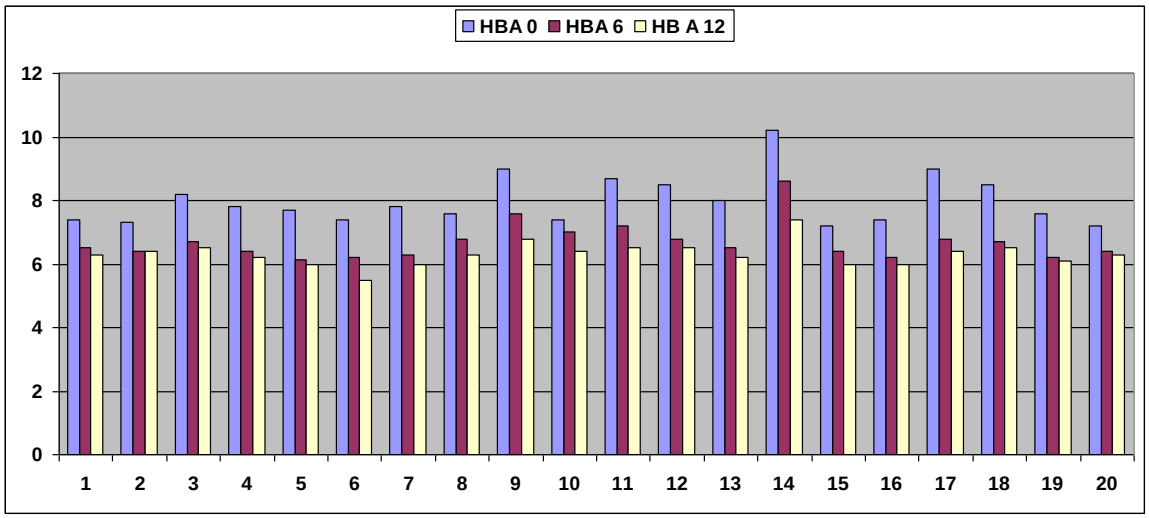

Fig. (4): Diagram illustrating change in HBA_{1C} 0, 6 & 12

DISCUSSION

Morbid obesity is a problematic growing disease throughout the world and is followed by increasing incidence of type 2 diabetes that accounts for 90-95% of all cases of diabetes. Weight loss is a major objective, although difficult to achieve with medical treatments. Many recent studies demonstrated that bariatric surgery has the potency to achieve marked and sustained weight loss, and is also associated with a significant improvement in control of type 2 diabetes. The principal aim of this study is to evaluate the efficiency laparoscopic sleeve gastrectomy (SG) in improving type 2 Diabetes Mellitus.

SG was conceived as the restrictive part of a more complex procedure that combines malabsorptive and restrictive concepts: the biliopancreatic diversion with duodenal switch (BPD-DS), first described by Hess and Hess, l and simultaneously by Marceau, in 1988.

The SG, as part of the BPD-DS, consists of creating a maximal gastric reservoir or tube of 150 to 200 mL but, as an isolated procedure, the gastric pouch size usually varies from 60 to 120 mL, depending on the size of the bougie we introduce into the stomach to perform the SG.

The removal of the gastric fundus appears to play a major role in resolving diabetes among patients who receive gastrectomy. This action reduces the amount of ghrelin while increasing levels of glucagon-like peptide-1 and peptide YY. LSG was most beneficial in resolving obesity and diabetes among morbidly obese patients with diabetes. However, there was less of an effect of LSG on hypertension and hyperlipidemia.

Obesity with T2DM is highly relevant not only in terms of quality-of-life impairment but also in terms of monetary costs incurred over time. The American Diabetes Association estimates that, in 2020, the annual cost of caring for persons with diabetes will approach $ 192 billion[(6)].

Because weight loss has an effect on improving T2DM and other comorbid conditions, weight loss must become part of the treatment plan whenever possible. However, despite the available medical therapies, including diet modifications and exercise, successful treatment of obesity is hard to achieve and maintain. When medical intervention is either ineffective or impractical, bariatric surgery must be considered as a possible treatment option for obese patients with T2DM. [(7)]

The mechanism of T2DM resolution after LSG is intriguing. After the discovery of incretins, especially glucagon-like peptide-1 (GLP-1), it has been postulated that a chronic increase in the production of GLP-1 might result in an increase in β-cell mass. [(8)]

Recent studies have shown that LSG increases the production of GLP-1 and peptide YY (PYY) and can accelerate gastric emptying. [(9)]

In addition, LSG resulted in significantly decreased levels of ghrelin because of the resection of the ghrelin-producing gastric fundus which results in mitigation of appetite and weight reduction. **(10)**

In this study a total of 20 patients (7 men and 13 women) were included. Baseline Mean BMI was 54.95 ± 7.86 kg/m2, baseline mean FBS 208.6±69.58 & baseline mean HBA1 c 8 ± 0.78 .

There was a significant change in the results 6 and 12 months post LSG , as the BMI mean shows a decrease by 7.58 kg/m2 ,me mean decrease in blood glucose was 81.5 mg/dL and hemoglobin A_{ic} ($HbAi_c$) levels shows improvement by 1.3.

After 12 months, the decrease in BMI mean was 13.35kg/m2, FBS was 95.4 mg/ dL, while hemoglobin A_{1c} (HbA_{1c}) was decreased by 1.68.

70% of the patients showed remission of diabetes by HBAlc level below 6.5, improved in 25% of the patients between(6.5 -7), and was still above 7 in 5% of patients.

All patients discontinued insulin by the 6th month postoperatively.

Forteen patients discontinued all antidiabetic medications by the 10th month postoperatively.

Six patients achieved reasonable diabetic control by oral hypoglycemic medications, 4 patients reduced the requirement of oral drugs and 2 patients continued on same doses with better results.

A longer follow up period is needed of course to follow the group of patient whose diabetes didn't resolve. Another 12 months of follow up might carry better results for the non-resolvers.

Wahal et al.(11) performed a study on 10 patients with BMI 30-35 kg/m2 and T2DM underwent LSG. The primary endpoints included impact on diabetic medication, fasting plasma glucose and glycated hemoglobin at 3 months. The mean pre operative BMI was 33.6 ±1.5 kg/m2. Six patients were on oral hypoglycemic agents (OHA) and four were on insulin as well as OHA. At 3-months follow-up, all 6 patients on OHA were off any anti-diabetic medication. Insulin could be stopped in all four patients.

Remission of diabetes, defined as glycated hemoglobin (HbA_{lC}) < 6.5% and Fasting Plasma Glucose (FPG) <126mg/dl with complete stoppage of diabetic medication, was seen in 4 patients. The changes in the meal stimulated plasma insulin at 30 minutes con-elated well with an associated increased meal stimulated plasma GLP1. Median fasting leptin levels reduced from 34.17 ng/ml to 11.03 ng/ml. Mean gastric emptying time decreased from 34 to 22.2 min. **(11)**

A meta-analysis of the world bariatric surgery literature summarized diabetes outcomes for 3188 patients in 103 treatment arms**.** Finding complete T2DM resolution, defined as a normal fasting plasma glucose level and cessation of diabetes medications, in 78.1% of patients during a 2-year follow-up. Specifically, remission occurred in 95.1% of patients after a biliopancreatic diversion with duodenal switch, in 80.3% of patients after a Roux-en-Y gastric bypass, in 79.7% of patients after gastroplasty, and in 56.7% patients after laparoscopic adjustable gastric banding **(12)**.

With regard to laparoscopic sleeve gastrectomy (LSG), in another review that analyzed 27 studies and 673 patients, it was reported that diabetes resolved in 66.2% of the patients, improved in 26.9% of the patients, and was unchanged in 13.1% of patients. The mean decrease in blood glucose and hemoglobin A_{lc} (HbA_{1c}) levels after an LSG were 88.2 mg/dL (to convert to millimoles per liter, multiply by 0.0555) and 1.7% (to convert to a proportion of total Hb, multiply by 0.01), respectively**.** **(13)**

In a study **Lee et al.(14)** compares treatment strategies of medical/lifestyle therapy vs LSG among such patients.

LSG has proved highly effective in alleviating type 2 diabetes and its complications compared with traditional medical treatment, this prospective cohort study involving 60 morbidly obese patients with type 2 diabetes: 30 who underwent sleeve gastrectomy and 30 who received conventional medical therapy.

Of the 30 patients in the surgical group, 24 (80%) had their diabetes resolved by 18 months after surgery and reduced their mean body mass index (BM1) from 41.3 kg/m^2 before surgery to 28.3 kg/m^2 18 months later *(P*<001). Conversely, mean BMI in the traditional treatment group increased from 39 kg/m^2 at study entry to 39.8 kg/m^2 18 months later *(P* > .05), and all patients in the group remained diabetic. **(14)**

In another reteospective study that compared obese subjects undergoing bariatric surgery with obese patients allocated to a matched, conventionally treated control group with an average follow-up of 12 months.

The author of that study concludes that surgery has dramatic positive effects on most cardiovascular risk factors, an excellent effect on established type 2 diabetes, and prevents the development of new cases of this disease. Finally, bariatric surgery was associated with a significant reduction of mortality. [15]

At present, medical and surgical therapies have been confronted in randomized fashion in one study only. It was found that remission of T2DM occurred in 73% of patients in the surgical group but in only 13% of patients in the control group. Another trial (ie, a retrospective study, which compared the effect of bariatric surgery and nonsurgical weight-reduction intervention) showed that the use of the Roux-en-Y gastric bypass induced considerable and lasting improvement in the prevalence of metabolic syndrome, with decreased doses of medication.[16]

The efficacy of LSG on remission of T2DM and/or improvement in symptoms has been shown in numerous literature reports. [17]

The strength of this study is 2-fold. First, in both groups of patients, the clinical features of T2DM (p-cell reserve, diabetes duration, and degree of glucose control) were well characterized in all patients enrolled in the study. Second, the results in the surgical group (group A) were compared with those obtained in an intensive, medically treated group (group B).

With a T2DM remission rate of 80% at 18 months, the results of the present study confirm the efficacy of LSG in the treatment of these patients. In agreement with previous reports on the evolution of T2DM following bariatric surgery, in the present trial, a number of clinical features of diabetes were found to be important determinants of the likelihood of biochemical remission. Preoperative C-peptide levels were significantly higher in patients with diabetes remission than in patients who improved but remained diabetic after surgery. These data confirm the study of **Sacks et al.[18],** who reported a percentage of resolution as low as 50% at 1 year after LSG in patients who had low preoperative C-peptide levels (<3 ng/mL, which suggests that this level could be the predictor of unsuccessful treatment of diabetes). Pancreatic (3-cell function prior to the bariatric procedure appears to be one of the most important determinants for remission and/or improvement of diabetes[18].

In patients with a T2DM duration of less than 10 years, the remission rate was 100%, as we already reported in another paper [19] concluding that diabetes duration is an important prognostic factor for diabetes remission and/or improvement. Therefore, comparing surgical with medical treatment in patients with more than 10 years of diabetes duration, we found that the effect of LSG is significantly more effective with regard to reducing fasting plasma glucose (*P*=.05) and HbA_{1c} (*P*<.001) levels. In these patients, although LSG was effective against diabetes in 40% of cases, it also allows for better metabolic control when medical therapy is unsuccessful [19].

Moreover, the reductions in the levels of HbA_1c and fasting plasma glucose in the medically treated group were obtained during the follow-up period. In the surgical group, however, medication use decreased significantly within the third month.

In addition, for patients whose symptoms of diabetes had resolved, the preoperative mean (SD) HbA_{1c} level was significantly lower than the preoperative mean (SD) HbA_{1c} level of patients who remained diabetic (6.6% [0.7%] vs 10.1% [1.9%]). The preoperative HbA_{1c} level, in accordance with other reports, seems to be a prognostic factor for diabetic **state.**

Medication use for obesity-related comorbidities decreased significantly following surgery. Twelve months after surgery, medication use for diabetes, hypertension, and dyslipidemia had decreased by 80%, 45%, and 45%, respectively, with consequent economic benefits. These factors are of relevance to a chronic, long-standing disease such as diabetes mellitus and should be taken into account during the decision-making process as an indication for bariatric surgery. [20]

Laparoscopic sleeve gastrectomy seems to be a restrictive procedure, but it also appears to induce significant hormonal changes of relevance in glucose homeostasis. These data confirms LSG contribute to improve and induce remission in Type 2 diabetes mellitus.

CONCLUSION

LSG is an effective primary bariatric procedure in the short term, as there is a significant change in the results 6 and 12 months post LSG , as the BMI mean after 6 months shows

a decrease by 7.58 kg/m2 ,the mean decrease in blood glucose was 81.5 mg/dL and hemoglobin A_{1c} (HbA_{1c}) levels shows improvement by 1.31 .

After 12 months, the decrease in BMI mean was 13.35kg/m^2, FBS was 95.4 mg/ dL, while hemoglobin A_{1c} (HbA_{1c}) was decreased by 1.68

70% of the patients showed remission of diabetes by HBA_{1c} level below 6.5, improved in 25% of the patients between(6.5 -7), and was still above 7 in 5% of patients.

However, concerns about the longevity of the operation remain. At the present time, more long-term results are necessary to determine the durability and incidence of late further physiological effects after LSG.

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