

## ONLINE FIRST

# Obesity, Type 2 Diabetes Mellitus, and Other Comorbidities

## A Prospective Cohort Study of Laparoscopic Sleeve Gastrectomy vs Medical Treatment

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**Objective:** To compare the effect of sleeve gastrectomy vs medical therapy on type 2 diabetes mellitus and other obesity-related comorbidities (obstructive sleep apnea syndrome, hypertension, and dyslipidemia) in prospectively enrolled and matched obese patients with type 2 diabetes.

**Design:** A prospective cohort study. Morbidly obese patients with type 2 diabetes who either underwent sleeve gastrectomy or conventional therapy were followed up and assessed for their diabetic state and other comorbidities every 3 months for 18 months.

**Setting:** Centre for the Surgical-Medical Treatment of Morbid Obesity, Policlinico "Umberto I," University of Rome "Sapienza," Italy.

**Patients:** A total of 30 morbidly obese patients with type 2 diabetes who underwent sleeve gastrectomy (group A) and a total of 30 morbidly obese patients with type 2 diabetes who underwent conventional therapy (group B).

**Results:** In group A, the preoperative mean (SD) body mass index, fasting plasma glucose level, and hemoglobin A<sub>1c</sub> level were 41.3 (6.0), 166.6 (68.1) mg/dL, and

7.9% (2.1%), respectively, and, at 18 months, these values were 28.3 (5.4), 96.2 (29.4) mg/dL, and 6.0% (1.5%), respectively. For 80% of patients, diabetes was resolved. With regard to other comorbidities, the prevalence of obstructive sleep apnea syndrome dropped from 50% to 10%, and patients reduced significantly their use of medication for hypertension and dyslipidemia. In group B, the preoperative mean (SD) body mass index, fasting plasma glucose level, and hemoglobin A<sub>1c</sub> level were 39.0 (5.5), 183.7 (63.5) mg/dL, and 8.1% (1.7%), respectively, and, at 18 months, these values were 39.8 (5.0), 150 (48) mg/dL, and 7.1% (1.3%), respectively. All patients remained diabetic and continued or increased their level of hypoglycemic therapy. With regard to other comorbidities, we observed an increase in the use of medication for hypertension and dyslipidemia, and the prevalence of obstructive sleep apnea syndrome did not change.

**Conclusions:** This study confirms the efficacy of sleeve gastrectomy in the treatment of morbidly obese type 2 diabetic patients when compared with conventional medical treatment.

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**O**WING TO ITS ASSOCIATION with an array of vascular, metabolic, and psychosocial complications, obesity is one of the major health challenges throughout the world. The association between obesity and diabetes is well established because 90% of patients with type 2 diabetes mellitus (T2DM) show excess body weight.<sup>1</sup>

### See Invited Critique at end of article

Obesity with T2DM is highly relevant not only in terms of quality-of-life impair-

ment 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.<sup>2</sup>

Because weight loss has an effect on improving T2DM and other comorbid conditions,<sup>3</sup> 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.<sup>4</sup>

A meta-analysis of the world bariatric surgery literature summarized diabetes outcomes for 3188 patients in 103 treatment arms,<sup>5</sup> 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.

With regard to laparoscopic sleeve gastrectomy (LSG), in a recent review that analyzed 27 studies and 673 patients, it is 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<sub>1c</sub> (HbA<sub>1c</sub>) 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.<sup>6</sup>

To our knowledge, there have been very few studies that have compared bariatric surgery with medical treatment, and studies comparing intensive medical treatment with LSG are lacking. The purpose of the present study was to compare the effects of LSG and medical therapy on T2DM in prospectively enrolled and matched obese patients and to evaluate the use of medications to treat hypertension and dyslipidemia, comorbid conditions frequently associated with obesity and diabetes.

## METHODS

A total of 30 morbidly obese patients with T2DM, diagnosed according to American Diabetes Association guidelines, underwent LSG (group A), and a total of 30 morbidly obese diabetic patients who matched the patients in group A were enrolled and underwent intensive conventional therapy (group B). Patients were sequentially enrolled from January 2009 to April 2010 at the Centre for the Surgical-Medical Treatment of Morbid Obesity (Policlinico "Umberto I," University of Rome "Sapienza," Italy). All patients eligible for bariatric surgery were offered surgical (ie, laparoscopic gastric banding, a laparoscopic gastric bypass, LSG, and laparoscopic biliopancreatic diversion with duodenal switch) or medical treatment. All patients gave their informed consent, and each patient selected between the 2 types of treatment. The type of surgery was chosen by the patient, although diabetic patients were advised to undergo LSG.<sup>7-9</sup> Patients selecting procedures other than LSG were not included in our study.

Patients were included in our study according to National Institutes of Health criteria for bariatric surgery indications. All the contraindications to bariatric surgery according to these criteria represented exclusion criteria for our study.<sup>10</sup> The 2 groups were matched for body mass index (BMI; calculated as weight in kilograms divided by height in meters squared), sex, HbA<sub>1c</sub> level, C-peptide level, type of therapy, and duration of diabetes.

Patients were followed up and assessed for their diabetic state with routine laboratory tests and anthropometric measurements every 3 months. No dropout was registered. Remission of T2DM was defined as a fasting glucose level of less than 100 mg/dL, an HbA<sub>1c</sub> level of less than 6.0% without the use of hypoglycemic drugs, and a glucose level of less than 140 mg/dL using the 120-minute oral glucose tolerance test for glycemia. In each group, the presence of hypertension and dyslipidemia

**Table 1. Demographics Characteristics and Baseline Values of Morbidly Obese Patients With T2DM Who Either Underwent Sleeve Gastrectomy (Group A) or Conventional Therapy (Group B)**

Characteristic or Measure	Group A (n = 30)	Group B (n = 30)	P Value
Age, mean (SD), y	53.0 (8.1)	56.0 (8.2)	≥.05
BMI, mean (SD)	41.3 (6.0)	39.0 (5.5)	≥.05
FPG, mean (SD), mg/dL	166 (68.1)	183 (63.5)	≥.05
HbA <sub>1c</sub> , mean (SD), %	7.9 (2.1)	8.1 (1.7)	≥.05
T2DM duration, mean (SD), y	6.2 (6.2)	7.8 (6.1)	≥.05
T2DM duration of >10 y, No. of patients	11	10	≥.05
Medication use, No. of patients			
OHA	23	22	≥.05
Insulin	6	6	
C-peptide, mean (SD), ng/mL	3.9 (1.9)	4.5 (4.7)	≥.05
OSAS, No. (%) of patients	15 (50)	7 (23)	.03
Hypertension, No. (%) of patients	25 (83)	25 (83)	≥.05
Dyslipidemia, No. (%) of patients	28 (90)	26 (86)	≥.05

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); FPG, fasting plasma glucose; HbA<sub>1c</sub>, hemoglobin A<sub>1c</sub>; OHA, oral hypoglycemic agents; OSAS, obstructive sleep apnea syndrome; T2DM, type 2 diabetes mellitus.

SI conversion factors: To convert fasting plasma glucose to millimoles per liter, multiply by 0.0555; to convert HbA<sub>1c</sub> to a proportion of total Hb, multiply by 0.01; and to convert C-peptide to nanomoles per liter, multiply by 0.331.

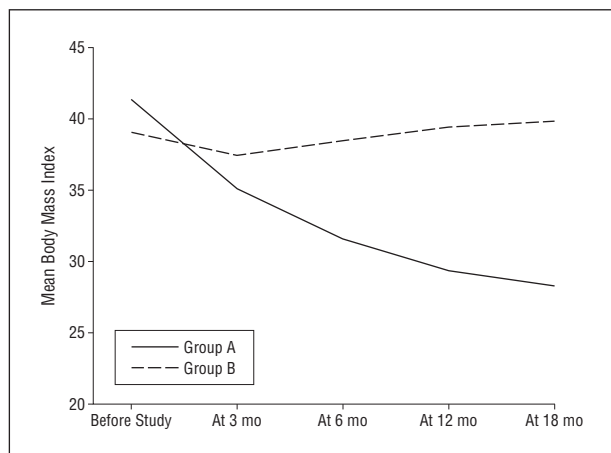
(according to Adult Treatment Panel III criteria) and obstructive sleep apnea syndrome (OSAS; determined by use of polysomnography) were assessed at recruitment and after 18 months. Use of medications was evaluated as the number of unique therapeutic classes of antihypertensive and hypolipemic drugs that the patient took at recruitment and after 18 months.

### GROUP A

Group A consisted of 30 patients (21 women and 9 men) with a mean (SD) BMI of 41.3 (6.0) (range, 35.2-53.4), a mean (SD) age of 53.0 (8.1) years, and a mean (SD) duration of T2DM of 6.2 (6.2) years; 23 patients were taking oral hypoglycemic agents, and 6 patients were receiving insulin treatment. Nineteen patients had diabetes for more than 10 years, and 11 patients were diabetic for less than 10 years. Hypertension was present in 25 patients, dyslipidemia was present in almost all patients (ie, 28 of 30 patients), and 6 patients received hypolipemic therapy. Severe OSAS that was being treated with continuous positive airway pressure therapy was present in 15 patients.

### GROUP B

Group B consisted of 30 patients (20 women and 10 men) with a mean (SD) BMI of 39.0 (5.5) (range, 35-48), a mean (SD) age of 56.0 (8.2) years, and a mean (SD) duration of T2DM of 7.8 (6.1) years; 22 patients were taking oral hypoglycemic agents, and 6 patients were receiving insulin treatment. Twenty patients had diabetes for more than 10 years, and 10 patients were diabetic for less than 10 years. Hypertension was present in 25 patients, dyslipidemia was present in almost all patients (ie, 26 of 30 patients), and 12 patients received hypolipemic therapy. Severe OSAS that was being treated with continuous positive airway pressure was present in 7 patients (**Table 1**). The present study has been approved by our institutional ethical committee.



**Figure 1.** Trends in body mass index (calculated as weight in kilograms divided by height in meters squared) among 30 morbidly obese patients with type 2 diabetes who underwent sleeve gastrectomy (group A) and 30 morbidly obese patients with type 2 diabetes who underwent conventional therapy (group B), assessed every 3 months for 18 months.

### SURGICAL TECHNIQUE

Sleeve gastrectomy was performed according to the technique previously described. By using 5 trocars, LSG was performed using a linear stapler, calibrated with a 48-Fr transoral bougie. The resection started at 6 cm from the pylorus up to the angle of His, in order to obtain a 60-mL capacity gastric pouch.<sup>11</sup>

### CONVENTIONAL THERAPY PROGRAM

The program consists of the best available medical practice for the treatment, education, and follow-up of morbidly obese diabetic patients. Patients had office consultation every 3 months throughout the 18 months of the study. Medical staff included experienced diabetologists, a dietitian, and a nurse. Every patient in group B received a program based not only on pharmaceutical agents but also on lifestyle modifications recommending a 1200-cal diet and regular physical activity (ie, at least 200 min/wk of moderate-intensity aerobic activity).

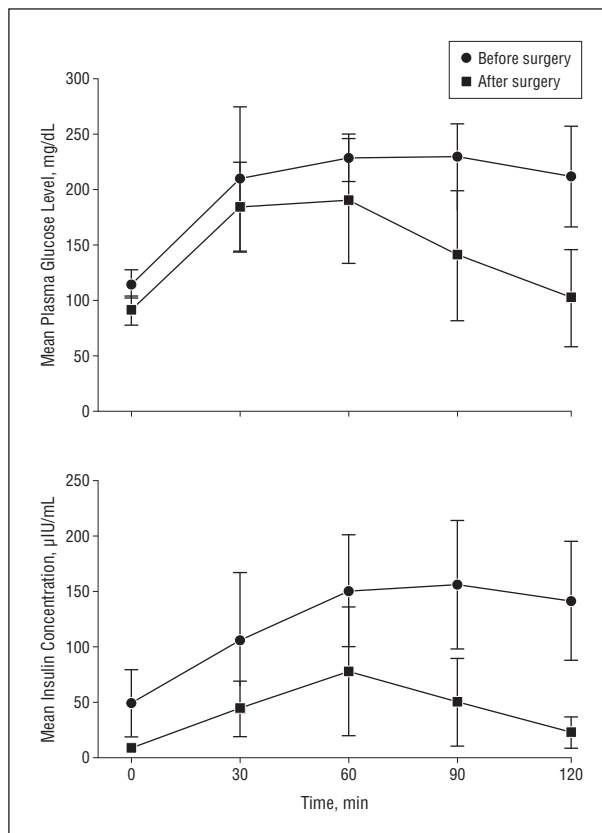
### STATISTICAL ANALYSIS

The *t* test and the  $\chi^2$  test were used to evaluate the statistical significance of the differences. Means were calculated with standard deviation using SPSS software (SPSS Inc). Statistical significance was set at  $P < .05$ . A multivariable linear regression model was used to control for confounding factors and to test the interactions.

## RESULTS

### GROUP A

The postoperative mean (SD) BMI was 35.1 (3.8), 31.6 (3.9), 29.4 (4.9), and 28.3 (5.4) at 3, 6, 12, and 18 months, respectively (**Figure 1**). The postoperative mean (SD) fasting plasma glucose level was 109 (37), 101 (31), 99 (30), and 97 (29) mg/dL at 3, 6, 12, and 18 months, respectively. The postoperative mean (SD) HbA<sub>1c</sub> level was 6.5% (1.7%), 6.3% (1.2%), 6.1% (1.0%), and 6.0% (1.5%) at 3, 6, 12, and 18 months, respectively. The preoperative mean (SD) C-peptide level was 3.9 (1.9) ng/mL (to



**Figure 2.** Mean plasma glucose levels and mean insulin concentrations during the oral glucose tolerance test (OGTT) before and 6 months after laparoscopic sleeve gastrectomy. The comparison of the OGTT results before and after surgery showed the reduction in glucose level after surgery and the reduction in the amount of insulin required (to convert the insulin concentration to picomoles per liter, multiply by 6.945).

convert to nanomoles per liter, multiply by 0.331); for 20 patients with a duration of T2DM of less than 10 years, the mean (SD) C-peptide level was 4.0 (1.1) ng/mL, and for 10 patients with a duration of T2DM of more than 10 years, the mean (SD) C-peptide level was 2.8 (0.7) ng/mL.

All patients with a fasting plasma glucose level of less than 126 mg/dL in the absence of hypoglycemic treatment underwent an oral glucose tolerance test 6 months after surgery. The mean (SD) glucose level at 120 minutes was 101 (43) mg/dL after an LSG. The comparison of the oral glucose tolerance test results before and after surgery showed the reduction in the peak glucose level after surgery and the reduction in the amount of insulin required (**Figure 2**).

Remission of diabetes, as already defined according to the criteria adopted by Buse et al,<sup>12</sup> was achieved for 24 of 30 patients (80%), for all 20 patients (100%) with a T2DM duration of less than 10 years, and for 4 of 10 of patients with a T2DM duration more than 10 years (40%).

Prior to surgery, 23 patients were taking oral hypoglycemic agents, and 6 patients were receiving insulin therapy as monotherapy or combined with an oral hypoglycemic agent. In total, 87% of patients received hypoglycemic therapy, and 13% of patients received only diet therapy. After surgery, the 20 patients with a T2DM duration of less than 10 years discontinued hypoglyce-

**Table 2. Values at Baseline and 18 Months After Surgery of Morbidly Obese Patients With T2DM Who Either Underwent Sleeve Gastrectomy (Group A) or Conventional Therapy (Group B)**

Value	Mean (SD)		P Value
	Before Surgery	18 mo After Surgery	
<b>Group A</b>			
BMI	41.3 (6.0)	28.3 (5.4)	<.001
HbA <sub>1c</sub> , %	7.9 (2.1)	6.0 (1.5)	.018
FPG, mg/dL	166 (68)	97 (29)	.005
HDL, mg/dL	48.3 (13.5)	61.0 (16.4)	.014
Triglycerides, mg/dL	169 (64)	97 (48)	.001
<b>Group B</b>			
BMI	39.0 (5.5)	39.8 (5.0)	≥.05
HbA <sub>1c</sub> , %	8.1 (1.7)	7.1 (1.3)	.02
FPG, mg/dL	183 (63)	150 (48)	.03
HDL, mg/dL	46.6 (9.8)	48.0 (10.9)	≥.05
Triglycerides, mg/dL	199 (130)	173 (103)	≥.05

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); FPG, fasting plasma glucose; HbA<sub>1c</sub>, hemoglobin A<sub>1c</sub>; HDL, high-density lipoprotein; T2DM, type 2 diabetes mellitus.

SI conversion factors: To convert HbA<sub>1c</sub> to a proportion of total Hb, multiply by 0.01; to convert fasting plasma glucose to millimoles per liter, multiply by 0.0555; to convert HDL cholesterol to millimoles per liter, multiply by 0.0259; and to convert triglycerides to millimoles per liter, multiply by 0.0113.

mic therapy. Patients who continued antidiabetic therapy (8 patients) had a T2DM duration of more than 10 years (3 patients continued taking oral hypoglycemic agents, and 5 patients continued receiving insulin therapy along with oral hypoglycemic agents).

For the 5 patients who continued insulin therapy, after surgery, the insulin dosage decreased from a mean of 89 IU insulin daily to a mean of 26 IU of insulin daily, and a reduction in the use of oral hypoglycemic agents at 6 months was observed; all 5 patients remained stable 18 months after surgery. In all other patients with a T2DM duration of less than 10 years, antidiabetic therapy was discontinued within 1 month of surgery.

With regard to dyslipidemia, there was no significant difference between preoperative and postoperative values in total cholesterol and low-density lipoprotein cholesterol. A significant increase in high-density lipoprotein cholesterol and a significant reduction in triglycerides plasma levels occurred 18 months after surgery (**Table 2**).

The prevalence of hypertension, before and after surgery, did not differ significantly; however, a significant reduction in the requirement of antihypertensive drugs was observed (**Table 3**) because the patients had a better therapeutic response. The prevalence of OSAS was significantly reduced after surgery, from 50% (15 of 30 patients) to 10% (3 of 30 patients) ( $P = .03$ ).

#### GROUP B

The mean follow-up period was 18 months. The mean (SD) BMI was 37.4 (4.5), 38.5 (5.7), 39.4 (5.5), and 39.8 (5.0), respectively, at 3, 6, 12, and 18 months (Figure 1). The mean (SD) fasting plasma glucose level was 137 (59),

**Table 3. Multivariable Linear Regression Analysis of the 2 Groups of Morbidly Obese Patients With T2DM**

Variable	Difference in Group A	Difference in Group B	P Value
EWL, % of patients	71	-2.8	<.001 <sup>a</sup>
BMI	-13.5	0.17	<.001 <sup>b</sup>
Total cholesterol, mg/dL	-6.0	-14.4	≥.05 <sup>c</sup>
HDL cholesterol, mg/dL	10.8	1.3	<.01 <sup>d</sup>
LDL cholesterol, mg/dL	-3.6	-7.0	≥.05 <sup>c</sup>
Triglycerides, mg/dL	-63.5	-30.3	.011 <sup>c</sup>
Basal glucose levels in patients with diabetes for >10 y, mg/dL	-116.2	-36.1	.05 <sup>a</sup>
Basal glucose levels in patients with diabetes for <10 y, mg/dL	-45.0	-30.4	≥.05 <sup>a</sup>
HbA <sub>1c</sub> levels in patients with diabetes for >10 y, %	-2.9	-0.31	<.001 <sup>a</sup>
HbA <sub>1c</sub> levels in patients with diabetes for <10 y, %	-1.23	-1.24	≥.05 <sup>a</sup>

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); EWL, excess weight loss; HbA<sub>1c</sub>, hemoglobin A<sub>1c</sub>; HDL, high-density lipoprotein; LDL, low-density lipoprotein; T2DM, type 2 diabetes mellitus.

SI conversion factors: To convert HDL and LDL cholesterol to millimoles per liter, multiply by 0.0259; to convert triglycerides to millimoles per liter, multiply by 0.0113; to convert glucose to millimoles per liter, multiply by 0.0555; and to convert HbA<sub>1c</sub> to a proportion of total Hb, multiply by 0.01.

<sup>a</sup>Adjusted for age, sex, and BMI.

<sup>b</sup>Adjusted for age and sex.

<sup>c</sup>Adjusted for age, sex, BMI, and T2DM duration.

<sup>d</sup>Adjusted for age, sex, BMI, T2DM duration, and total cholesterol level.

130 (33), 158 (52), and 150 (48) mg/dL, respectively, at 3, 6, 12, and 18 months. The mean (SD) HbA<sub>1c</sub> level was 6.8% (1.5%), 6.5% (1.1%), 7.5% (1.5%), and 7.1% (1.3%), respectively, at 3, 6, 12, and 18 months (Table 2).

At recruitment, 22 of 30 patients (73.3%) received oral hypoglycemic agents, and 6 of 30 patients (20%) received insulin. After 18 months, 28 patients received oral hypoglycemic agents, and in 8 of these 28 patients, insulin was also administered. The insulin requirement increased from 53 to 71 IU daily during the 18-month follow-up period.

#### GROUP A VS GROUP B

Comparing results in both groups, we found significant differences regarding excess weight loss, the decreases in BMI and triglycerides, and the increase of high-density lipoprotein cholesterol. The decreases in the levels of fasting plasma glucose and HbA<sub>1c</sub> were significantly different only in patients with a T2DM duration of more than 10 years (Table 3).

#### COMORBIDITIES

During the follow-up, no significant differences in the levels of total, low-density lipoprotein, and high-density lipoprotein cholesterol and of triglycerides were observed. The prevalence of hypertension did not change. Seven patients were affected by OSAS and treated with continuous positive airway pressure both at baseline and 18 months after treatment.



## DOSAGE OF ANTIHYPERTENSIVE AND LIPID LOWERING DRUGS

At recruitment, use of antihypertensive and hypolipemic drugs in the 2 groups of patients did not differ significantly. At 18 months, medication use decreased in the surgical group (group A) from a mean number of 1.5 to 0.83 pills for antihypertensive drugs and from a mean number of 0.4 to 0.2 pills for hypolipemic drugs ( $P < .05$ ), whereas it increased, although not significantly, in the medically treated group (group B) from a mean number of 1.53 to 1.78 pills for antihypertensive drugs and from a mean number of 0.53 to 0.83 pills for hypolipemic drugs.

### COMMENT

The efficacy of bariatric surgery on obesity and related comorbidities is well established, and the effect on T2DM has been documented in several studies. The Swedish Obese Subjects Study<sup>13</sup> is a prospective controlled 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 10 years. The author of that study<sup>13</sup> 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.<sup>13</sup>

At present, medical and surgical therapies have been confronted in randomized fashion in one study only. Dixon et al<sup>14</sup> 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)<sup>15</sup> 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.

The efficacy of LSG on remission of T2DM and/or improvement in symptoms has been shown in numerous literature reports (eg, Vidal et al<sup>16</sup>), but, to our knowledge, it has never been compared with intensive medical therapy. The strength of our study is 2-fold. First, in both groups of patients, the clinical features of T2DM ( $\beta$ -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 Lee et al,<sup>17</sup> 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  $\beta$ -cell function prior to the bariatric procedure appears to be one of the most important determinants for remission and/or improvement of diabetes.

In patients with a T2DM duration of less than 10 years, the remission rate was 100%, as we already reported in a recent paper,<sup>18</sup> 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<sub>1c</sub> ( $P < .001$ ) 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.

Moreover, the reductions in the levels of HbA<sub>1c</sub> and fasting plasma glucose in the medically treated group were obtained with a major increase in the dosage of antidiabetic drugs (oral hypoglycemic agents and insulin) 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<sub>1c</sub> level was significantly lower than the preoperative mean (SD) HbA<sub>1c</sub> level of patients who remained diabetic (6.6% [0.7%] vs 10.1% [1.9%]). The preoperative HbA<sub>1c</sub> 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. Eighteen 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.

Many authors have carefully summarized the prevailing theories of the mechanisms involved in the surgical resolution of T2DM in morbidly obese patients. These mechanisms primarily incorporate the action of weight loss, the role of hormones, intestinal malabsorption, and the role of gastrointestinal rearrangement.

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  $\beta$ -cell mass.<sup>19</sup> Recent studies have shown that LSG increases the production of GLP-1 and peptide YY (PYY)<sup>20</sup> and can accelerate gastric emptying.<sup>21,22</sup> In addition, LSG resulted in significantly decreased levels of ghrelin because of the resection of the ghrelin-producing gastric fundus,<sup>23</sup> which results in mitigation of appetite and weight reduction. In a recent report, we have shown that LSG, per se, can induce significant ghrelin, GLP-1, and PYY changes, further stressing

the physiological role of this procedure and highlighting the role of the stomach in the regulation of glucose metabolism. The removal of the gastric fundus and its products (ghrelin, acid secretion, and unknown anti-incretins) seems to play a major role in the physiology of T2DM remission. 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 confirm that bariatric surgery may represent an important source of information: different types of gastrointestinal rearrangements in different surgical procedures contribute differently to improved insulin secretion and improved sensitivity in diabetes.

In conclusion, our study confirms the efficacy of LSG in the remission and/or improvement of symptoms of T2DM and other obesity-related comorbidities. These effects compare favorably with those obtained in patients after intensive medical therapy. Furthermore, a significant reduction in the requirement of antihypertensive and hypolipemic drugs with a better clinical response and a significant reduction in the prevalence of OSAS were observed in the surgical group, whereas this effect was not reported in the medical group. Finally, LSG improves the lipid profile, in particular, leading to a significant increase in high-density lipoprotein cholesterol levels and a decrease in plasma triglyceride levels. All together, these data may have relevance to the cardiovascular risk and, consequently, to the reduction of mortality in these patients.

Midterm and long-term results are needed to confirm the positive effect (remission and/or improvement) of LSG on diabetes and, overall, on the chronic complications of the disease. Most importantly, the long-term results will allow us to compare the costs and benefits of bariatric surgery vs conventional medical treatments. The global risks from the long-term microvascular and macrovascular complications (retinopathy, nephropathy, and cardiovascular diseases) for obese patients with poorly or not completely controlled diabetes should be compared with the laparoscopic surgery risks in terms of surgical complications and mortality compounded by the long-term complications due to the occurrence of diabetes.

Finally, by extending the present study to a longer follow-up, the cost-benefit ratio of LSG vs medical treatment in obese diabetic patients will be better clarified, and the indications for surgery in diabetic patients with a BMI of less than 35 or in patients with poorly controlled diabetes may find a more rational approach.

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**Author Contributions:** Dr Leonetti had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Leonetti, Capoccia, Coccia, Paradiso, Abbatini, Soricelli, and Basso. **Acquisition of data:** Leonetti, Capoccia, Coccia, Casella, Paradiso, Abbatini, Iossa, Soricelli, and Basso. **Analysis and interpretation of data:** Leonetti, Capoccia, Casella, Baglio, Paradiso, Abbatini, Iossa, and Basso. **Drafting of the manuscript:** Leonetti, Capoccia, Coccia, Casella, Paradiso, Abbatini, Iossa, Soricelli, and Basso. **Critical revision of the manuscript for important intellectual content:** Leonetti, Capoccia, Casella, Baglio, Paradiso, Abbatini, and Soricelli. **Statistical analysis:** Leonetti, Capoccia, Coccia, Casella, Baglio, Paradiso, Abbatini, Iossa, Soricelli, and Basso. **Obtained funding:** Coccia. **Administrative, technical, and material support:** Leonetti, Capoccia, Coccia, Casella, Paradiso, Abbatini, Iossa, Soricelli, and Basso. **Study supervision:** Leonetti, Capoccia, Casella, Paradiso, and Basso.

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## INVITED CRITIQUE

### ONLINE FIRST

# Bariatric Surgery as a Highly Effective Intervention for Diabetes

## News Flash or Preaching to the Choir?

Leonetti and colleagues<sup>1</sup> present a nice study comparing the effects of laparoscopic sleeve gastrectomy and conventional medical therapy on type 2 diabetes mellitus in a prospectively enrolled and matched cohort of diabetic obese patients. The investigators observed that sleeve gastrectomy was a highly effective intervention for diabetes, much more so than conventional medical therapy.<sup>1</sup> This is a nice contribution, but, by now, this kind of outcome should not come as a surprise to any bariatric surgeon or regular reader of the *Archives of Surgery*.<sup>2,3</sup>

Bariatric surgery is an effective tool for weight loss that resolves many obesity-related comorbidities, perhaps most notably type 2 diabetes. Several gastrointestinal operations that were originally designed to treat morbid obesity also cause a dramatic improvement in the symptoms of type 2 diabetes and, frequently, a durable cure.<sup>4</sup> These same operations can prevent the progression from impaired glucose tolerance to diabetes in severely obese individuals.<sup>5</sup> When compared with medical diabetes management for morbidly obese patients with type 2 diabetes, bariatric surgery is also cost-effective.<sup>6,7</sup> Despite these facts, and the fact that nearly 9 million patients are affected by severe obesity, less than 1% of eligible patients undergo bariatric surgery.

A recent national survey<sup>8</sup> found that only 1 in 10 adults with severe or morbid obesity say they have had bariatric surgery recommended by their primary care physician. Another national survey<sup>9</sup> revealed that most primary care physicians believe that lifestyle changes are the most effective and available method for patients to lose weight, much more so than bariatric surgery. The survey study by Balduf and Farrell<sup>10</sup> found that only 3.8% of primary care physicians are familiar with the consensus statement on "Gastrointestinal Surgery for Severe Obesity," which was published by the National Institute of Health in 1991.

These findings demonstrate to the bariatric community that there is a great opportunity to partner with primary care physicians and to educate the public on the significant benefits and safety of bariatric surgery. National guidelines for bariatric surgery need to be developed for people with type 2 diabetes and a body mass index of 35 or more (calculated as weight in kilograms

divided by height in meters squared). An obese diabetic patient should have access to bariatric surgery in appropriate clinical circumstances. This access should be uniform, consistent, and not subject to potential bias, differences in opinion, or a lack of understanding regarding contemporary bariatric surgery outcomes.

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