Weight loss after sleeve gastrectomy in patients with diabetes: preliminary study in one year of activity

L. ROMANO¹, S. NECOZIONE², G. CIANCA¹, M. SCHIETROMA¹, F. CARLEI¹, A. GIULIANI¹

¹Department of General Surgery, San Salvatore Hospital; Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy
²Epidemiology Unit, Department of Life, Health and Environmental Sciences, University of L'Aquila, L'Aquila, Italy

Abstract. – OBJECTIVE: The objective of our study is to investigate whether diabetes mellitus could adversely affect post-laparoscopic sleeve gastrectomy (LSG) weight loss.

PATIENTS AND METHODS: A retrospectively recorded database of patients who underwent LSG from September 2018 to September 2019 in our Hospital in L'Aquila was analyzed. The post-operative weight loss was evaluated in terms of body mass index (BMI) variation, percentage of excess weight loss (%EWL) and percentage of total weight loss (%TWL). The association between these parameters and diabetes was analyzed at 3 and 6 months of follow-up.

RESULTS: The two groups (patients with and without diabetes) were considered comparable in terms of anthropometric and preoperative parameters. At 3 and 6 months of follow-up, the decrease in BMI resulted to be directly associated with the time and the group. The mean BMI at 3 and 6 months was higher in patients with diabetes. Changes in % EWL and % TWL were similar in both groups.

CONCLUSIONS: It is rational to expect a lower weight loss in obese diabetic patients after LSG. This should not be considered as a contra-indication to bariatric surgery that, being a metabolic surgery, has as main goal the resolution or improvement of co-morbidities.

Key Words: Sleeve gastrectomy, Diabetes mellitus, Weight loss.

Introduction

Obesity is a significant disease worldwide. In the US, it affects 34% of the adult population. In Europe, the WHO statistics reported in 2015 an overall obesity rate among adults of 21.5% in males and 24.5% in females. Obesity is closely related to many comorbid conditions: hypertension, hyperlipidemia, obstructive sleep apnea, metabolic syndrome, insulin resistance and type 2 diabetes mellitus (T2DM). This last-mentioned pathology has a particular relevance, since hyperglycemia by itself increases the risk of damages to the cardiovascular system, kidneys and other organs.

Studies demonstrated that patients with a body mass index (BMI) >35 kg/m² have a notable increased risk of developing T2DM compared with those with a lower BMI. The prevalence of T2DM in patients with obesity class II and class III is reported to be from 16 to 18% and 18 to 44%, respectively. Weight-loss programs involving diet, exercise and conservative therapies are the first strategies proposed for these patients. When conservative measures fail, bariatric surgery may become an indication. In 2011, the American Diabetes Association (ADA) recognized it as an effective treatment for obesity and for its related comorbidities. In detail, bariatric surgery reduces food intake or its absorption. Weight loss improves insulin sensitivity and β-cell function. To date, the term ‘metabolic surgery’ is becoming popular: some studies suggested that gastric bypass and sleeve gastrectomy might improve glycated hemoglobin (HbA1c) and blood glucose levels regardless of weight loss.

Nowadays, Roux-en-Y gastric bypass (RYGB) and laparoscopic sleeve gastrectomy (LSG) are the main surgical options. RYGB has been invariably considered as the standard of care in case of diabetics obese patients, but the global trend of...
the last years showed an increase in LSG\textsuperscript{12}. There is not enough evidence to demonstrate that RYGB is superior to LSG in the resolution of T2DM in morbid obese patients\textsuperscript{11,13}.

Although LSG is generally associated with good long-term weight loss, approximately 5\% to 10\% of patients do not lose sufficient weight\textsuperscript{14}. Among all the possible factors that could be responsible of this failure, a role has been recognized in some comorbidities, in particular T2DM. This factor has been studied in literature, but it has just been related to RYGB: it seems that diabetic patients tend to achieve a lower weight loss after this kind of surgery, in spite of an important metabolic improvement\textsuperscript{15-18}. To our knowledge, there is not much scientific literature regarding the role of T2DM in the outcomes after LSG, so the aim of our study is to investigate whether this disease could adversely affect post-LSG weight loss.

**Patients and Methods**

A retrospectively recorded database of patients who underwent LSG from September 2018 to September 2019 at the Department of General Surgery of the San Salvatore Hospital in L’Aquila (Italy) was analyzed.

All patients included in the dataset met the 1991 National Institutes of Health criteria Consensus Development Conference Guidelines for bariatric surgery (BMI ≥ 40 kg/m\textsuperscript{2}, or ≥ 35 kg/m\textsuperscript{2} with two or more obesity-related conditions)\textsuperscript{19}. The database analyzed patients with diabetes mellitus (DM group) and without diabetes (non-DM group) who had undergone primary laparoscopic sleeve gastric resection. The collected information included demographic data, co-morbid conditions at the time of surgery, preoperative weight and BMI, postoperative weight loss. The post-operative weight loss was evaluated in terms of BMI variation, percentage of excess weight loss (% EWL) and percentage of total weight loss (% TWL). The association between these parameters and T2DM was analyzed at 3 and 6 months of follow-up.

**Operative Approach**

Sleeve gastric resection operations were laparoscopically performed in all 43 patients. The surgical technique involved a conventional 4 ports approach. The greater curvature of the stomach was detached from the omentum using the laparoscopic ultrasonic scalpel; the dissection was started at 6 cm from the pylorus, along a 36-French orogastric bougie, using ECHELON FLEX\textsuperscript{TM} ENDOPATH\textsuperscript{®} Stapler (Ethicon, Cincinnati, OH, USA). The last dissection was made leaving at least 1.5 cm from His corner\textsuperscript{1}. Indocyanine green, fluorescent angiography was used to evaluate the vascularization of the stomach, along the stapled line\textsuperscript{20}. Then, a methylene blue-leak test was performed through the bougie at the end of the operation.

**Statistical Analysis**

Anthropometrics variables were compared with χ\textsuperscript{2} test, Fisher’s exact test or Wilcoxon Rank sum, to evaluate if the groups’ baseline characteristics were comparable. The hypothesis of normality of the assessed variables was rejected with the Shapiro-Wilk test. A two-factor mixed-design ANOVA using the repeated statement with the general linear model procedure was performed on logarithmically transformed data to evaluate both the effects of time and those of the group (DM or non-DM) on the changes in post-operative weight loss. Statistical analysis was performed with SAS statistical software (version 9.4, 2012; SAS Institute Inc, Cary, NC, USA).

**Results**

During the period identified for the study, 43 patients underwent primary LSG. Of these patients, 17 (39.5\%) had T2DM. The two groups (DM and non-DM) were considered comparable in terms of age, sex, preoperative weight, preoperative BMI and prevalence of co-morbidities (excluding DM). The main comorbidities considered were hypertension, sleep apnea, gastroesophageal reflux and degenerative joint disease. General characteristics of the study population are reported in Table I. Of the 17 patients of DM group, 3 of them (17.6\%) referred to take more than one drug for this specific disease (insulin or oral hypoglycemic agents).

**Weight Loss (Tables II and III)**

At 3 and 6 months of follow-up, the decrease in BMI resulted to be directly associated with the time (p<.0001) and the group (DM or non-DM) (p=0.041) (Figure 1), with a statistically significance interaction time*group (p=0.014). The mean BMI at 3 months was higher in DM group than in non-DM group (37.0 kg/m\textsuperscript{2} vs. 34.2 kg/m\textsuperscript{2}) and this difference has also been observed at
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6 months follow-up (34.1 kg/m² vs. 30.1 kg/m²). Changes in % EWL and % TWL were similar in both groups. These changes were significantly related to time, but no differences seemed to be among the two analyzed groups (Figures 2 and 3). In conclusion, the presence of T2DM affects the changes over time of the BMI, but no difference was noted for the other parameters.

Despite a lower BMI reduction in the DM group, 47.1% of these patients referred resolution or improvement of T2DM at 6 months follow-up (evaluated as suspension or reduction of the drug). Moreover, at the same follow-up, patients who did not report improvement of the disease had a lower mean % EWL than those with improvement or remission of DM (38.4% vs. 46.4%, respectively).

Table I. General characteristics of the study population.

<table>
<thead>
<tr>
<th>Variable</th>
<th>DM N = 17</th>
<th>non-DM N = 26</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender F/M</td>
<td>12/5</td>
<td>20/6</td>
<td>0.728*</td>
</tr>
<tr>
<td>AGE (years), mean</td>
<td>47.1</td>
<td>45.6</td>
<td>0.623*</td>
</tr>
<tr>
<td>Preoperative weight (kg), mean</td>
<td>113.3</td>
<td>111.1</td>
<td>0.709*</td>
</tr>
<tr>
<td>Preoperative bmi (kg/m²), mean</td>
<td>41.9</td>
<td>41.0</td>
<td>0.526*</td>
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Comorbidities

<table>
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<tr>
<th>Comorbidities</th>
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<th>non-DM</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Hypertension</td>
<td>8/17</td>
<td>8/26</td>
<td>0.280*</td>
</tr>
<tr>
<td>Sleep apnea</td>
<td>7/17</td>
<td>7/26</td>
<td>0.329*</td>
</tr>
<tr>
<td>Gastroesophageal reflux disease</td>
<td>2/17</td>
<td>1/26</td>
<td>0.552*</td>
</tr>
<tr>
<td>Degenerative joint disease</td>
<td>7/17</td>
<td>16/26</td>
<td>0.191*</td>
</tr>
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</table>

Variables are compared with Fisher’s exact test (a) or with Wilcoxon Rank sum test (b) or with χ² test (c). p < 0.05 is considered a statistically significant difference.

Table II. Descriptive analysis of the DM group (patients with diabetes).

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
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<td>BMI 6 months</td>
<td>17</td>
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<td>5.31</td>
<td>33.20</td>
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<tr>
<td>%TWL 6 months</td>
<td>17</td>
<td>18.54</td>
<td>8.42</td>
<td>18.18</td>
<td>7.02</td>
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<tr>
<td>%EWL 6 months</td>
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<td>25.87</td>
<td>14.93</td>
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<td>49.83</td>
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<table>
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<th>Variable</th>
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<th>SD</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
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</thead>
<tbody>
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<td>26</td>
<td>41.00</td>
<td>3.50</td>
<td>40.33</td>
<td>35.70</td>
<td>48.30</td>
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<td>BMI 6 months</td>
<td>26</td>
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<td>33.47</td>
<td>28.00</td>
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<tr>
<td>%TWL 6 months</td>
<td>25</td>
<td>16.53</td>
<td>6.88</td>
<td>17.00</td>
<td>2.74</td>
<td>29.17</td>
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<td>%EWL 6 months</td>
<td>25</td>
<td>26.50</td>
<td>7.89</td>
<td>25.00</td>
<td>8.22</td>
<td>42.50</td>
</tr>
</tbody>
</table>

SD: Standard deviation; BMI: body mass index; TWL: total weight loss; EWL: excess weight loss.

Table III. Descriptive analysis of the non-DM group (patients without diabetes).

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
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<th>SD</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
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</thead>
<tbody>
<tr>
<td>Preoperative BMI</td>
<td>26</td>
<td>41.00</td>
<td>3.50</td>
<td>40.33</td>
<td>35.70</td>
<td>48.30</td>
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<tr>
<td>BMI 6 months</td>
<td>26</td>
<td>30.15</td>
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<td>29.77</td>
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<td>6.88</td>
<td>17.00</td>
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<tr>
<td>%EWL 6 months</td>
<td>25</td>
<td>26.50</td>
<td>7.89</td>
<td>25.00</td>
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<td>42.50</td>
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<table>
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<th>SD</th>
<th>Median</th>
<th>Minimum</th>
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<tbody>
<tr>
<td>Preoperative BMI</td>
<td>26</td>
<td>41.00</td>
<td>3.50</td>
<td>40.33</td>
<td>35.70</td>
<td>48.30</td>
</tr>
<tr>
<td>BMI 6 months</td>
<td>26</td>
<td>30.15</td>
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<tr>
<td>%TWL 6 months</td>
<td>25</td>
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<tr>
<td>%EWL 6 months</td>
<td>25</td>
<td>26.50</td>
<td>7.89</td>
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<td>42.50</td>
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</tbody>
</table>

SD: Standard deviation; BMI: body mass index; TWL: total weight loss; EWL: excess weight loss.
Obesity and T2DM are in the Western world two of the most common diseases, and T2DM is actually the main comorbidity related to obesity. When compared to the results obtained with dietary and medical management, bariatric surgery seems to have an important role as a therapeutic strategy for both of these diseases. Buchwald et al reported in their work that, after bariatric surgery, over 75% of analyzed patients achieved complete resolution of diabetes, and 85% of them had considerable improvement. RYGB is still considered the preferred bariatric operation for the treatment of T2DM in morbid obese patients. At present there is no evidence to demonstrate that in these terms RYGB is more effective than LSG, although this last procedure has still few long-term data.

The global trend of the last years shows a decrease in RYGB and a marked increase in LSG, which is nowadays the preferred procedure in many centers, as it has several advantages. It preserves the physiology of the upper-GI and the integrity of the pylorus, there is not any intestinal bypass, it less frequently induces nutritional deficiencies and it can be converted into RYGB if its effects are not satisfactory. Moreover, it allows the stomach to be endoscopically explored. These observations and findings explain our choice to mainly perform LSG as first-line intervention.

Many recent studies demonstrated that LSG seems to be as effective as RYGB on the improvement of T2DM in obese patients. In particular, a systematic review of Gill et al reported that up to 70% of patients had resolution of the disease after LSG. At 6 months follow-up, reported...
rates of improvement or remission of the disease are around 60-80%27-29. Another study30 found a rate of remission of 62.5% after LSG and of 52% after RYGB and in a recent randomized trial was observed 42% of remission after RYGB and 37% after LSG to 1-year follow up31. 5-year resolution rate of T2DM after LSG is estimated to be approximately 60%, but long-term outcomes are just reported in small case series32.

Weight loss after bariatric surgery is responsible for diabetes improvement33, but this improvement often occurs even before the beginning of weight loss, maybe owing to changes in gut hormones secretion30. In the control of T2DM, also LSG is believed to act through an hormonal mechanism and not only thanks to its restrictive effect4.

The hormones mainly involved in these processes seem to be ghrelin and GLP-133,34. Ghrelin is produced by the gastric fundus. It is mainly known for promoting appetite in humans, and it has also been reported to increase insulin resistance. The first metabolic consequence of gastric resection by LSG is a decrease in plasma ghrelin concentration, directly related to the number of ghrelin-secreting cells removed by the surgery (gastric theory)33,35. In this way the removal of the gastric fundus contributes to the reduction of the sense of hunger, but it also might contribute to improve insulin sensitivity. There is also evidence36 that ghrelin acts over the β-cell as well the body weight. Moreover, ghrelin reduction seems to accelerate the gastric emptying and the intestinal transit, upregulating gut hormones, such as GLP-1 from intestinal enteroendocrine cells in the bowel (hindgut theory)37,38. GLP-1 normalizes blood glucose levels by upregulating insulin synthesis and proinsulin gene expression, as well as increasing peripheral insulin sensitivity39. Most of the hormonal mechanisms involved, however, are still far from being completely understood39.

All these results underline the role of LSG as a metabolic surgery, not just as a way to lose weight. It is evident that the efficacy in terms of glycemic improvement is independent of weight loss. Indeed, our results highlighted how diabetes itself could adversely affect post-LSG weight loss.

According to several studies, an unsatisfactory weight loss was reported in 10%-30% of patients after bariatric surgery40; after LSG, approximately 5% to 10% of patients do not lose sufficient weight40. This could be related to patient’s characteristics, scarce adherence to nutritional guidelines or psychological factors, but also diabetes appears to be one of the responsible factors41. In literature, the correlation between T2DM and poor weight loss has been widely studied after RYGB42-44, but there is not much material investigating whether it could also adversely affect the results after LSG.

In our study we found that diabetic patients achieved a higher BMI at 3 and 6 months of follow-up than the patients of the other group (non-DM). No differences were found in terms of age, preoperative BMI or presence of comorbidities, that could otherwise explain the difference in BMI variation.

There is still no shared certainty about the causes of the inverse relationship between diabetes and weight loss. Some authors speculate that, being T2DM characterized by insulin resistance, these high circulating insulin levels promote lipogenesis, adipocyte differentiation and muscle synthesis, and this could induce a lower degree of weight loss. In support of this theory, some reports stated that the poor long-term metabolic control, rather than the presence of T2DM, could be related to scarce weight loss after bariatric surgery45. Moreover, the medications themselves used in case of hyperglycemia (insulin or oral hypoglycemic agents), increase the circulating levels of insulin and promote its anabolic effects4,11,46. Among factors that could be related to a poor weight loss in patients with diabetes there may be also a reduction of urinary glucose losses and an increase in caloric intake to counteract hypoglycaemia42. According to our research, these mechanisms, initially studied for gastric bypass, seem to be confirmed also for sleeve gastrectomy and they could therefore be independent of the type of surgery.

Despite a reduced variation in BMI, almost 50% of diabetic patients of our sample had resolution or improvement of this disease at 6-months follow-up, confirming the statistically significant influence of LSG on glucose homeostasis. This is an important consideration, because weight loss should not be considered the first purpose of LSG, having it been recognized manly as a metabolic procedure. In fact, the 2nd Diabetes Surgery Summit proposed to consider metabolic surgery as one option47, along with lifestyle and medical therapy, to treat T2DM among patients with a BMI <35 kg/m2.

A valid criticism of our study is that we characterized as “diabetic” all patients who referred a previous diagnosis of diabetes and who were taking drugs for this, without specifying the degree of insulin resistance. Moreover, being a prelimi-
nary study, the sample size is still limited, as is the follow-up period. However, our first aim was to evaluate if these could be valid observations to carry on, so more numerous, consistent and prolonged studies are desirable.

Conclusions

In our analysis, the groups of patients were comparable in terms of anthropometric parameters, and we found that post-surgical decrease in BMI resulted to be directly correlated with the presence of T2DM. We also found that, in accordance with other studies, the lower weight loss did not affect the partial or complete remission of T2DM, reported at 6 months follow-up after surgery.

In summary, it is reasonable to expect a lower weight loss in obese and diabetic patients after LSG and both the surgeon and the patient must be aware of it. However, this should not be considered as a contraindication to bariatric surgery, whose major goal still is resolution of co-morbidities and improvement in quality of life.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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The authors declare the absence of any financial or personal relationships with other people or organizations that could inappropriately influence their work.

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