Six months results of laparoscopic sleeve gastrectomy in treatment of obesity and its metabolic complications

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Abstract

Background: Laparoscopic sleeve gastrectomy (LSG) has become a popular bariatric surgical procedure, with proven results in achieving weight loss, however data regarding its effectiveness on metabolic syndrome (MetS) components are scarce. The aims of the present study were to assess the outcomes of LSG on weight loss and obesity associated metabolic complications at six months following intervention.

Patients and methods: This was a retrospective study on 124 consecutive obese patients (29.8% men), who had undergone LSG between 01/01/2008 and 12/31/2010, in a highly specialized clinic. The dynamic of anthropometric and biochemical data between baseline and six months following LSG were evaluated. We also determined the change in MetS...
prevalence and used logistic regression to estimate predictors of MetS remission

Results: 6 months after LSG, the body mass index (BMI) decreased from 46.84±8.62 to 33.81±7.04 kg/m² (p<0.001). Mean excess BMI loss (EBL) was 65.24±25.16 %. The best results on weight loss were observed in young patients, not affected by MetS, with lower initial BMI. Lipids profile suffered a significant improvement (HDL cholesterol increased, while LDL, total cholesterol, triglycerides decreased, p<0.05 for each). HOMA-IR values decreased by 73.2 %, from 5.24±4.49 to 1.30±1.22 (p<0.001). MetS prevalence was reduced from 74.3% to 18.4% (p<0.001). In multivariate analysis, % EBL remained the only significant predictor of MetS remission, the risk for lack of a MetS remission being practically 3 times higher in patients with EBL < 50%, compared to those with EBL > 50% (OR: 2.97, CI: 1.1 – 10.23, p<0.05).

Conclusions: As early as 6 months after LSG we recorded a significant weight loss and improvement in insulin resistance and lipids metabolism, as well as an impressive reduction in metabolic syndrome prevalence.

Key words: gastric sleeve, metabolic syndrome, HOMA-IR, weight loss

Introduction

Obesity continues to be a global health care problem, due to its increasing prevalence and associated comorbidities. (1). Obese patients, especially those with abdominal obesity, are at increased risk for developing diabetes, hypertension, dyslipidemia, nonalcoholic fatty liver, osteoarthritis and other chronic diseases. (2) The clustering of hyperglycemia/insulin resistance, increased waist circumference, hypertension and dyslipidemia has been termed the metabolic syndrome and identifies people with increased risk for atherosclerotic cardiovascular disease and type 2 DM, and, as a result, with increased mortality (3).

Bariatric surgery, a highly effective treatment for morbid obesity and its related conditions, induces a long-lasting profound weight loss (4), as well as considerable and persistent improvement in metabolic syndrome prevalence (5). However, there are significantly more data regarding the resolution of obesity associated metabolic disturbances following malabsorptive procedures than following purely restrictive operations (6). Another important issue is that people with metabolic syndrome have the highest morbidity and mortality after malabsorptive bariatric surgery (7,8) and may benefit from less invasive approaches.

Laparoscopic sleeve gastrectomy (LSG) is a restrictive bariatric procedure which involves subtotal gastric resection of the fundus and the body, to create a tubular gastric conduit constructed along the lesser curve of the stomach. It was originally conceived as a first stage procedure, for achieving
and 50 mg/dL in women, or on treatment; blood pressure of at least 130/85 mmHg or on treatment; and serum glucose level of at least 110 mg/dL.

Excess BMI loss (EBL) was calculated by assuming a normalized body weight at a BMI of 25 kg/m² and determined by dividing the post-op BMI change by the pre-op BMI minus 25. Visceral adiposity index (VAI), a novel sex-specific index highly correlated with visceral adiposity measured by magnetic resonance imaging (the gold standard method) was defined using Amato formula (14):

\[
\text{Male VAI} = \left( \frac{\text{WC}}{39.68 + (1.88 \times \text{BMI})} \right) \times \frac{\text{TG}}{1.03} \times \frac{1.31}{\text{HDL}}
\]

\[
\text{Female VAI} = \left( \frac{\text{WC}}{36.58 + (1.89 \times \text{BMI})} \right) \times \frac{\text{TG}}{0.81} \times \frac{1.52}{\text{HDL}}
\]

**Surgical intervention**

The surgical technique of LSG is described further on and it was previously described (15): The operation was performed under general anesthesia with the surgeon standing between the patient’s abducted legs. Pneumoperitoneum was obtained through a Veress needle introduced into the left abdominal quadrant. Six trocars were used (3 reusable of 15 mm and one of 5 mm):

- the first trocar, a 10 mm canula used for the camera, was placed near the umbilicus;
- the second 10 mm trocar (camera), 6-7 cm subxiphoid 4 cm to the left of the median line, with the patient in supine position;
- the two 15-mm trocars were placed in the left and right anterior axillary line 4-5 cm under the costal margin.
- a 5 mm trocar is introduced at the lateral border of the left rectus
- a 11-mm Ternamian trocar (Karl Storz, Germany) was placed subxyphoid to retract the liver.

The first trocar was blindly introduced and the rest under direct vision of the extra-long 42 cm 45°lateral view endoscope. The exact site of this trocar depended on liver size. A 10 mm Cuschieri liver retractor (Karl Storz, Germany) was inserted through the subxyphoid trocar was used to retract the left liver cranially and to the right side. The patient, with the patient in supine position; 4 cm to the left of the median line, with the patient in supine position; the patient in supine position;

A 10 mm LigaSure device (EndoGIA®, US Surgical, Norwalk, CT, USA) was used for the division of the gastric greater curvature vascular supply. Once the lesser sac has been entered, at the level of incisura angularis, the dissection is continued to the pylorus and, in a cephalad direction, toward the angle of His. The retro-gastric ligaments were always divided. At the level of the spleen, the short gastric vessels are carefully coagulated separately. The dissection reaches the root of the left pillar of the hiatus, and all the attachment to the left crus are released to allow free movements of the fundus without any fixation.

Gastric transection started 2 cm from the pylorus using ENDO-GIA 3.5/60-mm or 48/60 linear staplers (Covidien, US). For the horizontal partial division of the antrum an ENDO-GIA 4.8/60-mm stapler was inserted through the right sided 15 mm trocar. This step facilitates the proper insertion towards the pyloric channel of a 36 Fr trans oral bougie, which we used for the gastric tube calibration. Then, 5-7 ENDO-GIA 3.5/60-mm staplers were fired up to the angle of His, close to the endogastric tube.

To avoid strictures of the gastric sleeve, the stapled line was oriented far from 2-3 cm far from incisura angularis. In order to prevent the helicoidal twist of the stomach, the narrow gastric tube was tailored with the equal contribution of the anterior and posterior gastric wall. Diluted methylene blue dye was used to detect any leaks. The resected stomach was easily removed through the left 15-mm trocar opening without using a collection bag. A silicone drain was left along the sleeve suture-line through one of the left ports for 3 days. Mean operative time was 90.4 ± 35.8 min. On postoperative day 1 small sips of clear liquids were taken orally by the patients. On postoperative day 2, the patients were subjected to Gastrografin x-ray study for leaks and empting, and then, clear liquids were permitted orally. On postoperative day 3, the patients were discharged. The drain was removed in the POD 2.

**Statistic analysis**

The SPSS software (SPSS Inc. Chicago IL), version 17.0, was used to perform all statistical analysis. Data are reported as mean ± SD, range. Between groups comparisons were carried out using independent samples t test or ANOVA, or chi-squared test for proportions. Changes from baseline were analyzed using paired samples t test. Correlations were performed using Pearson analysis and logistic regression was used to identify the most relevant predictive factors for inadequate weight loss and lack of MetS remission. P < 0.05 was considered statistically significant.

**Results**

Of our 124 patients, 37 (29.8%) were men and 87 (71.2%) were women. The mean age was 42.32 ± 10.58 years (ranging from 22 to 62) and mean BMI was 46.93 ± 8.56 kg/m² (45.77 ± 7.6 kg/m² in women, 49.01 ± 9.49 kg/m² in men, p < 0.05). In the subgroup analysis considering the initial BMI, there were significant differences between patients in the lowest BMI group and those in the intermediate and highest BMI group (Table 2). Younger patients (< 35 years) had a higher %EBL than the older groups, despite having no difference in the

**Table 1**

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean% EBL</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Lowest BMI</td>
<td>70.9%</td>
<td>NS</td>
</tr>
<tr>
<td>Intermediate</td>
<td>67.34±7.18</td>
<td>NS</td>
</tr>
<tr>
<td>Highest BMI</td>
<td>60.52±19.41</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Table 2**

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean% EBL</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Younger</td>
<td>74.2%</td>
<td>NS</td>
</tr>
<tr>
<td>Older</td>
<td>67.34±7.18</td>
<td>NS</td>
</tr>
</tbody>
</table>
The presence of metabolic syndrome resulted in lower %EBL in affected patients (62.47±25.7 vs 73.53±21.82, p<0.05) (Table 2).

In univariate analysis, %EBL negatively correlated with age (r=-.267, p<0.01) and several preoperative parameters: BMI (r=-.577, p<0.001), VAI (r=-.241, p<0.05), systolic BP (r = -.271, p<0.01), fasting glucose (r = -.181, p<0.05), triglycerides (r=-.264, p<0.01) and uric acid (r=-.217, p<0.05). We tried to investigate which of this factors could predict suboptimal weight loss (defined as %EBL<50). In a multivariate model, using age, systolic BP , V AI, BMI, fasting glucose, triglycerides and uric acid as covariates, only high BMI was a significant predictor of an unsuccessful outcome (OR=0.91, CI: 0.85 – 0.99, p<0.05).

**Metabolic benefits beyond weight loss**

**Lipids and VAI changes**

We looked at lipids profiles in patients not treated with lipid lowering therapies, before and 6 months after LSG (N=93 patients). HDL increased significantly in these patients (from 45.31±11.83 to 48.4 ± 11.74 mg/dl, p<0.01), while the rest of the measured lipids decreased (total cholesterol from 212.09±38.19 to 194.98 ± 38.81 mg/dl, p<0.01; LDL cholesterol from 135.02 ± 34.53 to 124.47 ± 34.96 mg/dl, p<0.01; triglycerides from 155.3 ± 63.76 to 106.09 ± 53.89 mg/dl, p<0.01). We tried to investigate which of this factors could predict suboptimal weight loss (defined as %EBL<50). In a multivariate model, using age, systolic BP, VAI, BMI, fasting glucose, triglycerides and uric acid as covariates, only high BMI was a significant predictor of an unsuccessful outcome (OR=0.91, CI: 0.85 – 0.99, p<0.05).

Mean VAI values decreased with 34.5%, 6 months after LSG, from 6.13 ± 3.7 to 4.01±2.88, p<0.01.

**Insulin resistance**

From our 124 patients, 95 were not diabetics, so insulin resistance was assessed using HOMA-IR. There was a significant decrease both in fasting glucose (from 101.64±21.16 mg/dl to 84.17±8.74 mg/dl) and in fasting insulin level (from 20.38±14.83 μui/ml to 6.21±5.71 μui/ml). Mean HOMA-IR values decreased by 75.2 %, from 5.24 ± 4.49 to 1.30 ± 1.22 (p<0.001) – Fig. 1

**Metabolic syndrome remission**

Laparoscopic sleeve gastrectomy resulted in a decrease in Metabolic Syndrome prevalence from 74.2% to 18.4% (p<0.05). All components of metabolic syndrome were significantly ameliorated after bariatric surgery, both in mean value (Table 1) and in prevalence - Fig. 2.

Of the 92 patients with metabolic syndrome, only 23 (25%) did not have a remission of their MetS at the 6 months follow-up (and were called MetS non-remitters). These non-remitters had a higher baseline BMI (50.55±9.29 versus 46.06±8.23 kg/m2, p<0.05) and a more unfavorable metabolic profile - higher triglycerides (227.75±134.21 versus 166.39±61.68 mg/dl, p<0.05) and lower HDL levels (38.75±6.51 versus 45.05±12.79 mg/dl, p<0.05). Baseline VAI was also higher in MetS non-responders (8.27±4.25 versus 5.7±3.31, p<0.01) and they lost significantly less of their excess weight (%EBL = 46.71 ±16.42 in non-responders versus 67.27±26.25 in responders, p<0.01). In multivariate analysis, % EBL remained the only significant predictor of MetS remission, a decrease in EBL<50%.

**Table 1. Baseline and 6 months data of study patients**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>6 months</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>46.84 ± 8.62</td>
<td>33.81 ± 7.04</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>126.5 ± 20.4</td>
<td>101.47 ± 17.37</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>0.91 ± 0.1</td>
<td>0.87 ± 0.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>136.12 ± 20.34</td>
<td>122.76 ± 14.71</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>82.15 ± 11.53</td>
<td>75.42 ± 10.53</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>212.09 ± 38.19</td>
<td>194.98 ± 38.81</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dl)</td>
<td>135.02 ± 34.53</td>
<td>124.47 ± 34.96</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dl)</td>
<td>45.31 ± 11.83</td>
<td>48.4 ± 11.74</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>155.3 ± 63.76</td>
<td>106.09 ± 53.89</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>VAI</td>
<td>6.13 ± 3.7</td>
<td>4.01 ± 2.88</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Uric acid (mg/dl)</td>
<td>6.18 ± 2.74</td>
<td>5.84 ± 1.35</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>MetS prevalence (%)</td>
<td>74.2</td>
<td>18.4</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

**Table 2. Weight loss in subgroup analysis**

<table>
<thead>
<tr>
<th>%EBL by initial BMI (kg/m²)</th>
<th>Mean value ± SD (range)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. &lt; 40</td>
<td>94.65 ± 29.74 (34.03 – 141.11)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>b. ≥40 – &lt; 50</td>
<td>60.75 ± 17.28 (31.19 – 106.28)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>c. ≥ 50</td>
<td>51.93 ± 14.83 (19.23 – 81.47)</td>
<td>&lt;0.001</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>% EBL by age (years)</th>
<th>Mean value ± SD (range)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. &lt; 35</td>
<td>75.53 ± 26.67 (31.19 – 139.84)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>b. ≥35 – &lt; 40</td>
<td>66.2 ± 22.08 (36.4 – 126.42)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>c. ≥ 40</td>
<td>57.38 ± 24.22 (19.23 – 141.1)</td>
<td>&lt;0.05</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>% EBL by MetS Presence</th>
<th>Mean value ± SD (range)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>73.53 ± 21.82 (44.59 – 123.48)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>YES</td>
<td>62.47 ± 25.70 (19.23 – 141.11)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
practically increasing 3 times the risk for lack of remission of Metabolic Syndrome (OR: 2.97, CI: 1.1– 10.23, p<0.05)

**Discussions**

In this study, we reported a significant weight loss 6 months after laparoscopic sleeve gastrectomy, with a mean EBL of 65%. This is in the range with the mean EBL of 60.4% (range 36.0 – 85.0, n=1749 patients) reported in a systematic review of the literature by Brethauer (16), in patients where LSG was intended as a definitive procedure, as it was the case in our patients. In a recent study, Angrisani found a mean EBL of 48.1% at 6 months, in a series of slightly heavier 121 patients, when LSG was performed as a staged or definitive procedure (17).

Excess weight loss correlated negatively with preoperative BMI, age, and several preoperative parameters associated with the presence of metabolic syndrome (systolic BP, fasting glucose triglycerides and uric acid). However, in multivariate analysis, initial BMI remained the only significant predictor of EBL.

The central metabolic disturbance linked to visceral obesity and metabolic syndrome is that of insulin resistance (IR) (18,19). Sleeve gastrectomy was shown to reduce insulin resistance but the mechanisms remain speculative. In our cohort we found a 75.2% decrease in HOMA IR, 6 months after LSG. These results are similar to those reported by Ianelli (20). In a very recent metaanalysis performed by Rao, the change in HOMA-IR at 3 months, 6 months and >16–18 months after LSG was found to be −12.14 ± 8.29, −43.00 ± 6.23, −38.51 ± 7.11 and −49.67 ± 13.63%, respectively (21). Some authors consider that caloric restrictions induced by LSG was responsible for the rapid improvement of glucose homeostasis (22), but this is contradicted by data reported by Rizzelo et al. They found a significant decrease in HOMA-IR as early as day 5 after surgery and definitely at 2 weeks in spite of no change in weight until this point; this was not found in control obese patients undergoing cholecystectomy, on the same diet protocol (23). These findings, along with the fact that LSG produces postprandial increases in insulin and GLP-1 equivalent to RYGB (24), suggest that other mechanisms may be responsible for the superior resolution rates of insulin resistance seen in sleeve gastrectomy patients, not expected from just a ‘restrictive’ procedure.

Insulin resistance is associated with atherogenic dyslipidemia (18) characterized by high plasma triglyceride (TG) levels, low HDL-C and an increase in small dense LDL-C levels. IR contributes to increase the levels of VLDL through the decreased insulin-mediated degradation of ApoB, the major lipoprotein of VLDL, that is further stabilized by the high levels of circulating free fatty acids. In addition, the TG of VLDL are transferred to HDL in exchange for cholesteryl esters and these TG-enriched HDL are rapidly cleared from the circulation by the hepatic lipase, leaving fewer HDL particles for the reverse transport of cholesterol from the vasculature.

It has been shown that bariatric surgery may improve lipid profile in obese patients, but the extent of this change varies based on the surgical procedure employed. In a retrospective analysis of 45 patients evaluated 1 year after LSG, Zhang observed improvement in HDL and triglycerides levels and no change in total and LDL cholesterol levels (25). Other authors also recorded modest improvements in total cholesterol levels (26,27). In our group of patients, we noticed a significant improvement in all lipids fractions, including a decrease in total cholesterol, LDL cholesterol and TG levels as well as an increase in HDL levels.

Visceral adiposity index (VAI) is a mathematical model that uses both anthropometric (BMI and WC) and biological (TG and HDL-cholesterol) common parameters (14). Data in the literature show that VAI score appears able to indirectly indicate both fat distribution and function and it may reflect
other non-classic cardiometabolic risk factors, such as altered production of adipokine s, increased lipolysis, and plasma-free fatty acids, which are not signified by BMI, WC, triglycerides, and HDL cholesterol separately. (14). Furthermore, it showed a strong independent association with both cardiovascular and cerebrovascular events and a better predictive power for incident diabetes events than its individual components (29). In our study, VAI score significantly decreased six months after bariatric surgery. To our knowledge, this is the first research reporting the impact of LSG on this parameter.

The positive effect of LSG on all metabolic syndrome components resulted in a significant decrease in its prevalence, from 74.2% to 18.4% (a 75.2% decrease). Data regarding the remission of metabolic syndrome in non-diabetic obese individuals are scarce, since the majority of studies looking at this aspect involved patients with type 2 DM. In a 12 months study on 91 severely obese T2DM patients, Vidal found a 62.2% rate of metabolic syndrome resolution after LSG. Very recently, Ianelli reported a 67% decrease in MetS prevalence, 6 months after LSG, but in a very limited number of patients (20), while in Hady's study the MetS rate was reduced by 53.08% after 1 year, in a group of patients heavier than ours. (29)

Our study showed that metabolic syndrome is largely a reversible phenomenon in obese patients undergoing LSG. When we tried to identify predictors of metabolic syndrome remission we observed that, even if the so called "non-remitters" were heavier and had a more unfavorable metabolic profile at baseline, the only significant factor remained the percentage of excess weight loss.

In conclusion, 6 months after LSG we recorded a significant weight loss and improvement in insulin resistance and lipids metabolism, as well as an impressive reduction in metabolic syndrome prevalence. Since LSG is a relatively new method and the mechanisms of weight loss are not completely elucidated, further studies are needed to prove the long time consistency of these results.

References


