The impact of laparoscopic sleeve gastrectomy on obesity-associated comorbidities

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Abstract. Background: Morbid obesity is often associated with numerous comorbidities. Diseases like hypertension, type 2 diabetes mellitus, alveolar hypoventilation, sleep apnea, increase mortality in patients with morbidobesity. Surgery has become the treatment of choice, with long-lasting effect, of morbid obesity and its comorbidities.Aim: Assess the immediate and remote results of using LSG by analyzing the evolution of obesity-associated comorbidities: type 2 diabetes, hypertension, respiratory dysfunction, sleep apnea, metabolic syndrome, and their relation to weight loss Results: In our study, there was a statistically significant resolution of diabetes of 91.5% (p=0.002). A significant decrease in the percentage of patients with high blood pressure and a statistically significant drug dose reduction correlated with weight loss, a significant decrease in total cholesterol and HDL-cholesterol ratio. The maximum effect on lipid metabolism is recorded in the first 6-12 months after surgery, with a gradual decrease 2 years postoperatively (p=0.2). Conclusion: LSG leads to a dramatic improvement of several comorbidities of obesity: type 2 diabetes mellitus, obstructive sleep apnea, hypertension, hyperlipidemia.

Key Words: obesity, bariatric surgery, weight loss, type 2 diabetes, hypertension, sleeve gastrectomy.

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Introduction

In recent decades, there has been an alarming rise in obesity in the general population, associated with increased rates of comorbidities with an important economic impact on the health system (Weiner et al 2013).

Morbid obesity is not only an independent cardiovascular risk factor, but it is often associated with numerous comorbidities. Diseases like hypertension, type 2 diabetes mellitus, alveolar hypoventilation, sleep apnea, coagulation changes with risk of developing deep vein thrombosis and pulmonary embolism may increase mortality in patients with morbid obesity (Chang et al 2016; Sjostrom et al 2012).

Surgery has become the treatment of choice, with long-lasting effect, of morbid obesity and its comorbidities including type 2 diabetes mellitus, hypertension, metabolic syndrome (Booth et al 2014; Kral & Naslund 2007). Malabsorptive bariatric procedures such as laparoscopic Roux-en-Y gastric bypass (LRYGB) or laparoscopic biliopancreatic diversion (LBPD) seem to have a higher rate of comorbidity resolution than the purely restrictive techniques like laparoscopic adjustable gastric banding (LAGB) and greater effectiveness in excess weight loss (Cummings et al 2004; Vest et al 2012).

Laparoscopic sleeve gastrectomy (LSG) was initially introduced as a step of LBPD in super-obese patients. In recent years, the procedure has become increasingly popular as a primary bariatric procedure in the treatment of obesity (Benaiges et al 2015; Burgerhart et al 2014; Gumbs et al 2007). Initially classified as a purely restrictive procedure, it was later demonstrated that it involves more complex mechanisms of action, determining changes in certain gastrointestinal hormones such as ghrelin, glucagon-like peptide 1 (GLP-1), peptide YY (PYY) with important role in regulating carbohydrate metabolism and weight (Bohdjalian et al 2010; Tymitz et al 2011).

The aim of this study is to assess the immediate and remote results of using LSG by analyzing the evolution of obesity-associated comorbidities: type 2 diabetes, hypertension, respiratory dysfunction, sleep apnea, metabolic syndrome, and their relation to weight loss.

Material and method

Patient selection criteria were age between 18 and 60 years, a body mass index (BMI) greater than 40 without comorbidities or a BMI between 35 and 39 with major obesity-associated comorbidities. Exclusion criteria were severe diseases with major risk of surgical and anesthetic complications, psychiatric disorders, hiatal hernia. All patients had to sign the informed consent form to participate in the study, which was approved by the Ethics Committee of the Municipal Clinical Hospital.

Preoperative evaluation was performed by a multidisciplinary team: surgeon, anesthesiologist, cardiologist, gastroenterologist, radiologist, endocrinologist, nutritionist, and psychologist. The following parameters were recorded while conducting the preoperative assessment: weight, height, blood pressure, drug type and doses for treatment of associated diseases. Laboratory tests included a complete blood count, a liver function test, C-reactive protein (CRP) levels, the lipid profile, blood sugar and glycated hemoglobin (HbA1c) tests in patients with type 2 diabetes or in patients with newly diagnosed diabetes. Abdominal ultrasound, gastrointestinal endoscopy, echocardiography, EKG, ventilatory function tests were performed as routine preoperative screening tests.

Surgeries were performed with the patient placed in the reverse Trendelenburg position using 5 trocars (three 12 mm trocars, one 10 mm trocar, and one 5 mm trocar). After dissection of the greater curvature of the stomach, the resection starts at 6 cm proximal to the pylorus, followed by calibration of the Faucher probe between 32 and 36 Fr with linear staplers up to the gastroesophageal junction. The mechanical suture was reinforced with a continuous suture. Suture tightness was tested by administering 100-150 ml of methylene blue solution intraoperatively. Patients were assessed at the 1st, 3rd, and 6th postoperative month and then every year. Patients were re-evaluated by measuring the following parameters: weight, blood pressure, complete blood count, HbA1c in patients with type 2 diabetes, CRP levels, and by performing echocardiography, EKG, ventilatory function tests in patients with altered preoperative values, and abdominal ultrasound. There have been changes in drug type and dose during each follow-up examination. Excess BMI loss (EBMIL) was calculated at each follow-up time point.

Remission of high blood pressure was taken into consideration in patients with systolic pressures below 130 mm Hg without medication. Type 2 diabetes remission was observed in patients with an HbA1c level of ≤ 6% and a blood sugar level of ≤ 120 mg/dl.

Statistical analysis was performed using MedCalc Statistical Software program version 16.8.4 (MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org; 2016). The Kolmogorov-Smirnov test was used to check the normal distribution of continuous variables. The Mann-Whitney test was employed to assess the difference between groups. The correlation between two continuous variables was checked using Spearman's rank correlation coefficient. A p value of <0.05 was considered statistically significant.

Results

Among patients who underwent LSG between 2010 and 2014 at the Municipal Clinical Hospital in Cluj-Napoca, 95 were selected for this study, of which 60 women and 35 men with a mean age of 41.8 ± 11.2 years. Average preoperative weight was 144 ± 24 kg (101-240) with an average BMI of 48.5 ± 7.2 (36-68). All patients (100%) were evaluated at 6 months postoperatively, 82 (86%) at one year and 62 (65%) at two years. EBMIL was 52.61% at 6 months postoperatively, 71.47% at one year, and 69.94% at 2 years. There was a significant increase in EBMIL between the 3 measurements (p<0.001). There was a negative correlation between EBMIL and preoperative BMI at 6 months (r -0.656, p<0.0001) and 12 months (r -0.530, p<0.0001). There was a moderate negative correlation between age and EBMIL at 6 months (r -0.310; p=0.002) and a negative correlation between age and EBMIL at 12 months (r -0.231; p=0.03) and 24 months (r -0.282; p=0.02).

Preoperative hypertension (HTA) was present in 48 patients (50%), of which 37 (79%) with chronic antihypertensive treatment. At 6 months, hypertension was present in 35 patients (36.8%), with a statistically significant decrease (p<0.001). Medication was modified in 11 (11.6%) patients. At 1-year follow-up, of patients diagnosed with hypertension, 21 (25.5%) had hypertension, resulting in a statistically significant decrease (p<0.001). Dose reduction was used in 9 patients (11%) and 61 (74.45) patients had normal blood pressure without medication, the decrease being statistically significant (p<0.001). At 2-year follow-up, of patients diagnosed with hypertension, 18 (29%) had hypertension, dose reduction was used in 8 (12.9%) patients, and 44 (71%) had normal blood pressure without medication. There was no correlation between 6-month EBMIL and resolution of hypertension (p=0.6) or dose reduction (p=0.3). The resolution of hypertension was correlated with 12-month EBMIL, which was lower in patients with hypertension than in those without hypertension (65.2 ± 12.8 vs. 73.6 ± 11.9) (p=0.008). At 24-month follow-up, there was also a correlation between the resolution of hypertension and 24-month EBMIL, which was lower in patients with hypertension than in those without hypertension (60.8 ± 19.5 vs. 73.6 ± 14.6) (p=0.008).

Type 2 diabetes was preoperatively diagnosed in 30 patients (31.5%), of which 10 (10.6%) were under treatment with oral antidiabetic drugs (OADs) and 2 patients were under insulin therapy. At 6-month follow-up, 78 (82.1%) patients with type 2 diabetes had normal blood sugar levels without OADs, and one patient was transferred from insulin therapy to oral antidiabetic drugs. There was a statistically significant reduction in the incidence of type 2 diabetes at 6-month follow-up (p=0.001). At 12-month follow-up, 75 (91.5%) of the patients diagnosed and followed-up throughout this period had normal blood sugar levels without OADs, 7 (8.5%) requiring treatment with OADs. There was a statistically significant reduction in the incidence of diabetes at 12-month follow-up (p=0.002). At 2-year follow-up, dose reduction was used in 3 (4.5%) of the patients diagnosed with type 2 diabetes, and 60 patients (96.8%) had normal blood sugar levels without medication. There was no statistically significant reduction in the incidence of diabetes at 24-month follow-up (p=0.08). Reduced BMI at 12-month follow-up was correlated with the resolution of diabetes, 12-month EBMIL was lower in patients with diabetes than in those without diabetes (61.8 ± 13.1 vs. 72.2 ± 12.3) (p=0.05). There was no statistically significant difference in EBMIL in patients with diabetes between 6-month and 24-month follow-up (p=0.6; p=0.1).

Hypercholesterolemia was preoperatively diagnosed in 53 patients (55.7%) and hypertriglyceridemia in 50 patients (52.6%). None of the patients with dyslipidemia had preoperative lipid-lowering treatment.

The HDL-cholesterol ratio was 4.7 ± 2.3 preoperatively, 2.7 ± 0.8 at 6-month follow-up, 2.5 ± 0.6 at 12-month follow-up, and 2.5 ± 0.6 at 24month follow-up. There was a statistically significant decrease in the HDL-cholesterol ratio between the preoperative measurement and 6-month follow-up (p<0.001), and between 6-month and12-month follow-up (p<0.001). There

was no statistically significant decrease in the HDL-cholesterol ratio between 12-month and 24-month follow up (p=0.2).
There was a statistically significant decrease in cholesterol levels of about 25.1 ± 23 in the first 6 months after surgery (194 ± 50.1 vs. 169.6 ± 36.8; p<0.001), 8.7 ± 20.2 between 6-month and12-month follow-up (171.4 ± 35.9 vs. 162.7 ± 29.5; p<0.001). There was no significant change in total cholesterol levels between 12-month and 24-month follow-up (p=0.4).
Ventilatory function tests diagnosed 51 patients (53.7%) with ventilatory defect, of which mild obstructive ventilatory defect in 2 (2.1%) patients, moderate defect in 8 (8.4%) patients, and severe defect in 1 (1.1%) patient. Restrictive ventilatory defect was present in 39 patients, of which 23 (24.2%) had mild defect, 15 (15.8%) moderate, and 1 (1.1%) had severe defect. Sleep apnea was diagnosed in 4 patients (4.2%). An improvement in ventilation was observed in 38 patients (40%) at 6-month follow-up, in 32 patients (23.2%) at 1-year follow-up, and in 7 patients (11.3%) at 2-year follow-up. There was no correlation between weight loss and the improvement in ventilation (p=0.5) in the study group.
Mean CRP levels were 7.8 ± 2.4. CRP levels were not recorded in 9 (9.4%) patients with chronic inflammatory diseases or acute infection during postoperative follow-up. At 6-month follow-up, mean CRP levels were 4 ± 1.8, at 1-year follow-up 2 ± 1.6, at 2-year follow-up 0.7 ± 0.4. There was a statistically significant negative correlation between EBMIL and CRP at 6-month follow-up (r=-0.351; p=0.001), 12-month follow-up (r -0.284; p=0.01) and 2-year follow-up (r=-0.148; p=0.2).

Discussions

One of the most important parameters in assessing a bariatric technique is weight loss. Data on weight loss after LSG vary regardless of the method used. This variability is probably due to the heterogeneous groups of patients and the different duration of postoperative follow-up. There have been attempts to identify certain factors that can influence weight loss after surgery: baseline BMI, age, gender, immediate preoperative weight loss, etc. (Perrone et al 2016). Among these factors, there is a significant correlation between preoperative BMI and weight loss percentage, therefore patients with a greater BMI have a lower weight loss percentage (Livhits et al 2012). A disadvantage of LSG, similar to other bariatric procedures, is the tendency of some patients to hit a weight-loss plateau or to gain weight two years after surgery. This trend is more pronounced in purely restrictive techniques than in malabsorptive procedures. Data published for LSG indicate that this trend is present in approximately 20% of patients, with 10% of patients turning to revision bariatric surgery as a consequence (Homan et al 2015; Weiner et al 2011).
In our group of patients there was a negative correlation between EBMIL and age and between EBMIL and preoperative BMI at all follow-up intervals. EBMIL increased significantly at 6-month, 1-year and 2-year follow-up, and two of the patients followed-up for 2 years (3.22%) resorted to revision bariatric surgery.
The chronic inflammatory state that accompanies morbid obesity is well known, justified by the higher levels of cytokines in these patients. C-reactive protein, leptin, adiponectin, interleukin 6 are among the proinflammatory cytokines present in significant amounts in obese patients. By emphasizing the process of atherosclerosis, these cytokines are cardiovascular risk factors, being important to measure their levels in assessing this risk (Brethauer et al 2011). Patients in this study showed increased preoperative CRP levels (7.8 ± 2.4), with a statistically significant decrease at 6, 12, 24-month follow-up. At 6-month and 12-month follow-up, the reduced CRP levels were correlated with EBMIL.
Besides its impact on weight loss, the first effect of bariatric surgery observed and studied was that on diabetes. It had been a relatively short period of time since the first published studies to the recognition as metabolic surgery, mainly due to the effects of bariatric surgery on type 2 diabetes (Pories et al 1995; Sjöström 2013). A recently published systematic review shows a 60-70% rate of resolution of type 2 diabetes, but the follow-up was only conducted for a relatively short period of time of 1 year (Gill et al 2010). In the case of LSG, the mechanisms that lead to the resolution or improvement of type 2 diabetes seem to be related to changes in gastrointestinal hormones postoperatively (ghrelin, glucagon-like peptide 1, peptide YY) (Karamanakos et al 2008).
In our study, there was a statistically significant resolution of diabetes at 6 months of 82.1% (p=0.001). At 12-month follow-up, there was a statistically significant resolution of diabetes of 91.5% (p=0.002). At 2-year follow-up, 3 (4.5%) of the patients diagnosed with type 2 diabetes had drug dose reduction and 60 (96.8%) had normal blood sugar levels without OADs, without reaching statistical significance (p=0.08). Resolution of diabetes in our patients is comparable with literature data, the fairly high percentage of patients who achieved resolution of type 2 diabetes being probably due to a better adherence to postoperative nutritional recommendations.
The relationship between obesity and hypertension is well known, although the mechanisms underlying this association are not fully elucidated. The meta-analysis published by Buchwald et al. Shows that, for other bariatric techniques than LSG, there was a postoperative resolution of hypertension of 47.45%, 61.65%, 68.17% (Buchwald & Oien, 2013). Similar results were also obtained by the Swedish Obese Subjects (SOS) trial. A systematic review of the effect of LSG on hypertension published in recent years, demonstrated a complete resolution of hypertension in 58% of patients and hypertension improvement in 17% of patients (Sarkhosh et al 2012).
Our results show a significant decrease in the percentage of patients with high blood pressure and a statistically significant drug dose reduction correlated with weight loss at 1-year (p=0.008) and 2-year follow-up (p=0.008).
The effect of bariatric surgery on lipid metabolism is well known, published studies demonstrating lower LDL and triglyceride levels and higher HDL levels in association with the reduced cardiovascular risk (Buchwald et al 2010). The Swedish Obese Subjects (SOS) trial obtained the same results postoperatively, but with less powerful impact on TG and cholesterol over 10 years after surgery (Sjostrom et al 2012).
In our study, there was a significant decrease in total cholesterol and HDL-cholesterol ratio at 6-month (p<0.001) and 12-month follow-up (p<0.001). It can be observed that the maximum effect on lipid metabolism is recorded in the first 6-12 months after surgery, with a gradual decrease 2 years postoperatively (p=0.2).

Conclusion

LSG leads to dramatic improvement of several comorbidities of obesity, including type 2 diabetes mellitus, obstructive sleep apnea, hypertension, hyperlipidemia. Due to the relative simplicity of the technique, short learning curve, less morbidity and no significant difference in the comorbidity resolution LSG proves to be a serious alternative to other malabsorbtive techniques.
It is necessary to further analyze the effects of LSG on obesity-associated comorbidities for longer postoperative follow-up intervals in order to assess the long-term effectiveness of the technique.

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