

Laparoscopic sleeve gastrectomy for morbid obesity

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Abstract

The incidence of obesity is steadily rising, and it has been estimated that 40% of the US population will be obese by the year 2025 if the current trend continues. In recent years there has been renewed interest in the surgical treatment of morbid obesity in concomitance with the epidemic of obesity. Bariatric surgery proved effective in providing weight loss of large magnitude, correction of comorbidities and excellent short-term and long-term outcomes, decreasing overall mortality and providing a marked survival advantage. The Laparoscopic Sleeve Gastrectomy (LSG) has increased in popularity and is currently very "trendy" among laparoscopic surgeons involved in bariatric surgery. As LSG proved to be effective in achieving considerable weight loss in the short-term, it has been proposed by some as a sole bariatric procedure. This editorial focuses on the particular advantages of LSG in the treatment of morbid obesity.

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Key words: Obesity; Bariatric surgery; Sleeve gastrectomy; Ghrelin; Weight loss

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INTRODUCTION

The incidence of obesity is steadily rising, and it has been estimated that 40% of the US population will be obese by the year 2025 if the current trend continues^[1]. An alarming indicator of the health crisis related to the epidemic of obesity is that 15% of children and adolescents are obese (body mass index BMI > 95th percentile on the Centers for Disease Controls and Prevention standard charts), and over 20% are at risk (BMI > 85 percentile)^[2]. In recent years there has been renewed interest in the surgical treatment of morbid obesity in concomitance with the epidemic of obesity, and application of the laparoscopic techniques to the field of bariatric surgery as well. Bariatric surgery proved effective in providing weight loss of large magnitude, correction of comorbidities and excellent short-term and long-term outcomes^[3-5], decreasing overall mortality and providing a marked survival advantage^[6,7]. The number of laparoscopic Roux-en-Y Gastric Bypass (LRYGBP) procedures have continued to increase in the last few years. This has contributed to the profound enthusiasm of the surgical community for bariatric surgery. In this context, new bariatric procedures can be rapidly accepted by the surgical community, as has already happened in the case of laparoscopic adjustable gastric banding (LAGB). The latter is a paradigm of the "surgical enthusiasm" for a bariatric procedure. LAGB has rapidly reached wide diffusion, giving the label of bariatric surgeon to any laparoscopic surgeon able to place a band around the stomach of an obese patient. However, with time this procedure proved not to be the panacea that one would have thought it to be after its introduction. Due to a high rate of long-term failure, the literature indicates fewer LAGB procedures and more Roux-en-Y gastric bypass (RYGBP) procedures are being performed, and surgeons are choosing laparoscopic RYGBP^[8-10]. The Laparoscopic Sleeve Gastrectomy (LSG) is being performed more frequently and is currently very "trendy" among laparoscopic surgeons involved in bariatric surgery. LSG is not a new operation as it is the restrictive part of a more complex malabsorptive bariatric procedure; i.e., the biliopancreatic diversion with duodenal switch (BPD-DS)^[11,12]. Gagner and coworkers adapted the BPD-DS to the laparoscopic approach^[13], and then introduced the concept of the staged approach to very obese patients

with the LSG being the first step^[14]. As LSG proved to be effective in the short-term in achieving considerable weight loss, it has been proposed by some to be used solely as a bariatric procedure.

SURGICAL TECHNIQUE

LSG involves a longitudinal resection of the stomach on the greater curvature from the antrum starting opposite of the nerve of Latarjet up to the angle of His. The first step of the procedure is the division of the vascular supply of the greater curvature of the stomach, which is achieved with the section of the gastro-colic and gastro-splenic ligaments close to the stomach. The greater curvature must be completely freed up to the left crus of the diaphragm to completely resect the gastric fundus that harbours the ghrelin secreting cells of the stomach. The second step of the procedure is the longitudinal gastrectomy that "sleeves" the stomach to reduce it to a narrow tube. A naso-gastric tube is used to obtain a precise calibration and to avoid stenosis of the gastric plasty. There is no consensus as to where to start the gastrectomy, and which calibre of the naso-gastric tube to use. Gagner recommended starting the gastrectomy 10 cm proximal to the pylorus^[14]. Baltazar recommended starting 4 cm from the pylorus in the case of DS, and only 2 cm from it if the LSG is intended as the sole bariatric procedure^[15]. Different calibres of naso-gastric tubes have been reported by different authors from 32 Fr^[15] to 60 Fr^[14]. The rationale for starting closer to the pylorus and using a small calibre bougie to fashion the gastric tube is to increase the restrictive character of the procedure. The final volume of the gastric tube has been reported to be as small as 60 mL^[15] and as large as 200 mL^[13,14]. The staple line can then be reinforced with sutures or Seamguard to reduce the rate of staple line leak or bleeding^[16] (Figure 1).

PHYSIOLOGY OF LSG

One of the mechanisms involved in weight loss observed after the LSG is the dramatic reduction of the capacity of the stomach. The concept of restriction has been widely used in bariatric surgery in vertical banded gastroplasty (VBG) and LAGB. The distension of the small gastric pouch in the LAGB procedure or VBG is supposed to account for the feeling of early fullness, enhanced satiety and decreased hunger experienced by a patient after the ingestion of small quantities of food. The fact that the use of small calibre nasal-gastric tubes, as small as 30 Fr for LSG as proposed by Baltazar, provides faster and increased weight loss is in favour of the role of mechanical restriction as an important determinant in terms of weight loss that can be obtained with LSG^[15].

The hormonal modifications induced by LSG differ from those found after a purely restrictive procedure as LASGB. Ghrelin, a peptide hormone mainly produced in the fundus of the stomach, is supposed to be involved in the mechanisms regulating hunger and has been a focus of interest in a growing number of recently published papers^[17]. Ghrelin is secreted by the endocrine cells of the stomach (X/A-like cells), which reside in the oxyntic

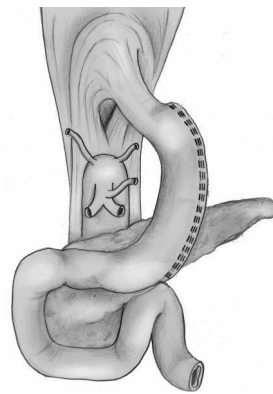


Figure 1 Laparoscopic sleeve gastrectomy.

glands of the gastric fundus^[18-20]. Gastric ghrelin producing cells are in contact with the basolateral membrane adjacent to the blood-stream and most of them do not come in contact with gastric content^[18-21]. The gastric fundus contains 10 to 20 times more ghrelin per 1 × g of tissue than the duodenum^[18-22] with diminishing concentrations being found in the jejunum and ileum^[18,19,23]. Ghrelin has been also found in different additional tissues in very low concentrations such as the lungs, kidney, pancreatic islets, gonads, adrenal cortex, placenta and others^[24]. Ghrelin regulates the secretion of growth hormone release and is a potent orexigenic (appetite-stimulating) peptide. This last effect of ghrelin is mediated by the activation of ghrelin receptors in the hypothalamus/pituitary area^[25].

There is some evidence that body weight is the major determinant in the long-term regulation of the plasma concentration of ghrelin^[26,27]. Accordingly, it has been shown that plasma concentration of ghrelin is increased in the case of negative energy balance situations such as low-calorie diets^[26,28], chronic exercise^[28,29], cancer anorexia^[28], and anorexia nervosa^[29], and are decreased in positive balance situations such as weight regain after overfeeding, or during the weight recovery phase of anorexia nervosa^[30] or in obese patients^[31]. However as no putative mechanisms have been elucidated so far to explicate the changes in the plasma levels of ghrelin in the long term, further studies are necessary to define this issue.

On the other hand, plasma concentration of ghrelin is acutely regulated by the intake of food with a meal to meal variation^[31,32]. Plasma ghrelin concentration rises just before the onset of meal and declines thereafter suggesting that ghrelin could play a role in the signal of meal initiation^[18,23,33,34], acting as the counterpart of the several meal-related satiation factors such as cholecystokinin, peptide -YY, glucagons-like peptide 1. Although the mechanisms responsible for the postprandial suppression of ghrelin are not known there is evidence that neither gastric nutrients nor gastric distension affect the plasma level of ghrelin^[35]. Different studies investigated the plasma levels of ghrelin after different bariatric procedures, such as LASGB, LRYGBP and BPD^[17]. Unfortunately, the results of these studies are difficult to compare because the patients studied were in different states of energy balance, the techniques of sampling were different, and either the fasting or postprandial ghrelin levels were reported^[17]. Nevertheless, there is overall evidence that LASGB is

associated with significantly increased total plasma levels of ghrelin as opposed to LRYGBP, which is followed by a decrease of ghrelin^[36-41].

As LASGB preserves the whole stomach, the gastric fundus, which is the major ghrelin producing tissue, is not excluded from contact with food. Ghrelin levels are increased with diet induced weight loss. Interestingly RYGBP has been shown to be associated with low levels of circulating ghrelin that persist at 1 and 3 years follow-up^[42,43]. On the contrary, LASGB, VBG^[44], and antireflux surgical procedures^[37,45-48] are not associated with a decline of the circulating levels of ghrelin^[42]. The most important difference between these procedures and LRYGBP is the contact of food with the gastric fundus of the stomach. The mechanism hypothesized to explain why ghrelin is down-regulated after LRYGBP is the override stimulation theory as described by Cummings. The empty stomach that is acutely associated with increased levels of circulating ghrelin would result in a continuous stimulatory signal that ultimately suppresses ghrelin production^[23-26]. However, whether weight loss after LRYGBP is directly related to the changes in plasma levels of ghrelin is still a matter of debate^[49].

Holdstock *et al.*^[50] found increased levels of ghrelin 12 mo after GBP and argued that weight loss is not directly related to plasma concentration of ghrelin. Faraj *et al.*^[51] proposed that the plasma levels of ghrelin are related to the state of energy balance. During the period of weight loss after GBP, ghrelin is secreted by sources other than the stomach because of the negative energy balance resulting in plasma levels higher than controls. Once patients have completed their weight loss phase and have reached a state of energy balance, plasma levels of ghrelin are comparable to those of controls despite massive weight loss. The disparate results reported in the literature on the mechanism involved in weight loss after LRYGBP imply that the relationship between the mechanical effects of surgery and neuroendocrine response is complex and far from being clearly elucidated.

Lager *et al.*^[52] reported significantly reduced levels of ghrelin in 10 obese patients undergoing LSG at 1 and 6 mo after surgery. Interestingly, these patients were prospectively compared with 10 patients undergoing a LASGB procedure that resulted in significantly increased levels of ghrelin at 1 and 6 mo. This was paralleled by a superior weight loss in the group of patients undergoing LSG, which might be related to the low levels of circulating ghrelin with no compensatory hunger. In the case of BPD, the circulating levels of ghrelin are differently affected, depending on the type of gastrectomy that is associated with the BPD. In the case of BDP, according to Scopinaro, the gastric fundus is preserved and ghrelin levels are not reduced as reported by Adami *et al.*^[47]. On the contrary, when the BPD is associated with the pylorus preserving sleeve gastrectomy and duodenal switch (BPD-DS), the circulating levels of ghrelin are markedly suppressed^[53].

Ghrelin seems to play a key role in the complex energy balance loop and it is logical to hypothesize that its changes are involved in the neurophysiologic mechanisms responsible for the changes in appetite observed after bariatric surgery. At the moment, the short term results of LSG are more similar

to those observed after LRGBP than other purely restrictive procedures. Whether the observed change in circulating ghrelin level is a predictor of the long-term success of a given bariatric procedure, such as LSG, is not yet clear.

PRO AND CONS OF LSG

The seducing potential of LSG relies in the fact that this operation is a straightforward procedure that can be generally completed laparoscopically, even in the case of an extremely obese patient. It does not involve any digestive anastomosis, no mesenteric defects are created eliminating the risk of internal hernia^[54], no foreign material is used as in the case of gastric banding, the whole digestive tract remains accessible to endoscopy, it is not associated with Dumping syndrome, the risk of peptic ulcer is low and the absorption of nutrients, vitamins, minerals and drugs is not altered.

However, some points need to be underlined at least for those who are too enthusiastic about LSG. First, although LSG is generally an easy procedure, it may become a true nightmare in the very obese patient, especially in men with a huge left liver lobe, and the long staple line may leak postoperatively. Secondly, in face of the eventual regain of lost weight or insufficient weight loss, the surgeon must be ready to do a second procedure that must be part of his technical armamentarium. The last problem is represented by the choice of the second procedure, which is traditionally the BPD-DS in the case of patients with a BMI > 50. Other teams propose the LRYGBP but it is still not clear whether the latter can provide further weight loss in the case of patients with an initial BMI > 50. The Scopinaro procedure or the VVLRGBP are other alternatives, and the stomach might be re-sleeved in case of gastric tube dilation.

RESULTS OF LSG

Only a few studies on sleeve gastrectomy for morbid obesity have been published so far. By performing a search in PubMed MEDLINE (National Library of Medicine) for English-language articles published until March 2007 using the key words *laparoscopic*, *sleeve gastrectomy*, and considering only series reporting at least 30 patients, a total of 6 papers reporting a total of 328 cases was obtained^[15,55-59]. Table 1 summarizes relevant data collected from these articles.

Mean initial BMI ranged from 37.2 kg/m²^[57,58] to 65.4 kg/m²^[56] with a case of a patient with an extreme BMI at 91 kg/m²^[56]. These data suggest that very high and even extreme BMI does not represent a contraindication to LSG. In fact, the two staged approach is becoming the rule in the case of super-super obese patients (BMI > 60 kg/m²) in which more complex procedures such as RYGBP or biliopancreatic diversion are very difficult to perform. The rationale of the staged approach to super and super-super obese patients is to achieve a substantial weight loss with the consequent amelioration of obesity-related comorbidities with a simple procedure such as LSG, thus allowing the second procedure in patients with lower operative risks. Of the 328 cases, data on gender

Table 1 Studies of Sleeve Laparoscopic Sleeve Gastrectomy including at least 30 patients

| Study type | Sample size | Sex | Age(yr) | Mean follow up (mo) | Death (%) | Complications | Mean operative time (min) | Initial BMI | EWL (%) | Reference |
|---|-------------|------|--------------|---------------------|-----------|---|---------------------------|---|---|-----------|
| Retrospective | 31 | NA | NA | 3-27 | 3.2 | n.1 bleeding (requiring laparoscopic reoperation) | | Gr 1: > 61 Gr 2: > 40 Gr 3: 25-30 Gr 4: NA | NA | 15 |
| Retrospective | 60 | 8 M | 30 (16-62) | 12 | 1.6 | 1 leak 1 delayed bleeding 1 atelectasis 1 postoperative vomiting | 70 (45-100) | 37.2 (30-56.1) | NA | 57 |
| Retrospective | 126 | 59 M | 49.5 (20-74) | 12 | 0.8 | 5 strictures 2 leaks 2 pulmonary embolus 5 respiratory insufficiencies 4 renal failures | 143 (90-120) | 65.4 (45-91) | 45 (for the 54 pts who underwent the phase II operation LRYGBP) | 56 |
| Prospective | 41 | 13 M | 44.6 ± 9.7 | 22.2 | 0 | 1 leak 1 transient renal failure bleeding | 111 ± 31 | 57.3 ± 6.5 | NA (but average BMI after 1 yr was 40.8 ± 8.5) | 55 |
| Randomized prospective (LSG vs gastric banding) | 40 | 9 M | 40 (22-65) | 36 | 0 | 1 bleeding 1 gastric ischemia | NA | 39 (30-53) | 66 | 58 |
| Retrospective | 30 | 7 M | 40 (17-69) | 6 | 0 | 3 dehydrations 1 leak | 80 (65-130) | 41.4 (33-59) | 52.8 | 59 |

NA: Non Applicable; M: Men; EWL: Excess Weight Loss; min: Minutes; pts: Patients; ref: Reference.

were available for 297 cases, for a total of 96 males (32%) and 201 females (68%) undergoing the procedure. In fact, beside high BMI, male gender is another important risk factor for postoperative morbidity and mortality and is associated with technical difficulties at the time of surgery. Men, in fact, often have an android body habitus whereby excess body fat is localized in the peritoneal cavity and the left lobe of the liver is often enlarged rendering the access to the stomach and hiatal region difficult^[55]. Thus, the relatively high percentage of male patients undergoing SG in the literature reflects the choice of the bariatric surgeon in favour of SG, which is less challenging than other procedures requiring larger dissections and intestinal anastomoses.

In 3 of the 6 studies analyzed (total of 130 patients)^[57-59], LSG was performed as the sole procedure; i.e. not followed by other types of bariatric operations. However, one of these patients^[57] underwent a laparoscopic gastric bypass one year after LSG because he failed to achieve a satisfactory weight loss. In the last 3 studies, enrolling a total of 198 patients^[15,55,56], LSG was intended as the first step of a combined approach to achieve an initial weight loss in "difficult" patients with the second step being a LRYGBP or DS. Among the 198 patients undergoing the LSG as the first step of the combined approach strategy, 51 patients finally underwent the second procedure: 36 had a LRYGBP and 15 a DS. Interestingly, in the 3 studies in which LSG was performed as a first step procedure, only a part of the initially programmed second procedures were finally performed. It can be speculated that at least in some of the cases the weight loss achieved after LSG alone was satisfying^[55,56,59].

Mean operative time was clearly reported in 4 of the 6 studies^[55-57,59], ranging from 70 min^[57] to 143 min^[56]. As

expected, the operative time is longer in patients with high BMI.

Unfortunately complete data about excess weight loss are reported in 3 of the 6 studies^[57-59]. This is a main concern as the primary outcome of bariatric surgery is excess weight loss, and a given procedure cannot be evaluated correctly if the functional results are not reported. Mean excess weight loss ranged from 52.8% (follow up 6 mo)^[59] to 83.3% (follow up 12 mo).

Three postoperative deaths were recorded for 328 patients (death rate of 0.9%) and a total of 34 major and minor complications were reported (morbidity 10.3%). Fifteen of these were considered minor complications: 5 transient renal failures not requiring dialysis, 5 patients requiring ventilatory support for > 24 h, 1 pulmonary atelectasis, 1 case of prolonged postoperative vomiting treated conservatively and spontaneously resolved, 3 dehydrations. By excluding minor complications, a total of 19 major complications occurred (major complication rate 5.8%). Major complications managed conservatively included 4 cases of staple-line leaks, 5 strictures of the gastric plasty, 2 cases of bleeding and 2 cases of pulmonary embolus^[55-57]. Six patients with major postoperative complications required re-operation. Re-operations were performed by laparoscopy in 4 cases of intraperitoneal bleeding^[12,49,51,52]. One case of staple-line leak^[59] and a case of gastric ischemia required re-operation by laparotomy^[58].

Bariatric surgery is associated with a mortality rate of 0.1-2.0 in large studies^[60-64]. In a recent meta-analysis by Buchwald *et al*^[65], postoperative mortality was 0.5% for RYGBP, 0.1% for gastric banding, and 1.1% for malabsorptive procedures. In one of the largest prospective studies^[66], the SOS trial, postoperative complications occurred in 13% of patients, including

bleeding in 0.5%, embolism or thrombosis in 0.8%, wound complications 1.8%, and pulmonary complications in 6.1%. In a recent review of the literature, Baker *et al*^[67] reported an average rate of leak after LRYGBP of 2.77% (range 0.3% to 8.3%).

The evolution of obesity related comorbidities after SG has not been clearly reported. However, SG should be effective in improving comorbidities, such as non alcoholic fatty liver disease/nonalcoholic steatohepatitis (NAFLD/NASH)^[68], as with any other procedure that induces weight loss because the improvement of comorbidities is directly dependent on weight loss. Overall these results suggest that LSG is safe and effective in the short term to achieve a substantial weight loss. There is no evidence so far that weight loss obtained with LSG can be maintained in the long term.

WEIGHT REGAIN AFTER LSG INDUCED INITIAL WEIGHT LOSS

In other words, can LSG be proposed as a sole bariatric procedure? When the LSG is done as the first step of a staged approach in very obese patients, the second procedure is generally done when the weight loss reaches a plateau, in the case of weigh regain or simply when the patient can undergo more safely the second step regardless of weight loss stabilization or regain. The possible mechanisms that account for the limited weight loss or weight regain include a technical problem, such as an incomplete resection of the fundus of the stomach where the ghrelin producing cells are located. This may occur in patients with hiatal hernia, which is often associated with excessive body weight^[69]. Gastric dilatation has been evoked as being responsible for poor weight loss after LSG with or without DS^[70]. An excessive large pouch may be the result of an excessively large pouch created at the initial operation due to a too large calibration tube, or because of inappropriate surgical technique such as missed posterior gastric folds. Excessive pressure against the pouch wall by large meals, repeated vomiting or distal obstruction may also account for pouch dilation^[71]. Other factors may be claimed as responsible for poor weight loss or weight regain after LSG, such as the spontaneous dilation of the gastric tube over time, the switch to a high caloric, soft, liquid diet, and, last but not least, LSG may have a limited potential for weight loss as do most restrictive procedures.

The question whether the LSG may work as a sole bariatric procedure in the long term cannot be answered yet. For this reason LSG should be proposed as the first step of a staged approach in patients for whom a BPD-DS or LRYGBP seems too hazardous because of very high BMI (super obesity-BMI > 50 or super-super obesity-BMI > 60), and/or associated diseases whether related or not to obesity. The decision to do a LSG may also be made during surgery in the case of intraoperative findings, such as liver cirrhosis, adhesions, too thick mesenterica contraindicating a more complex procedure. Then, the second step may be deferred until deemed necessary because of insufficient weight loss or weight regain. On the other hand, the LSG

should not be proposed to patients with a BMI < 50 until evidence is provided for its effectiveness in achieving weight loss in the long term compared to the results obtained with RYGBP, which remains the gold standard of bariatric procedures at the moment. Exceptions might warrant a pure restrictive procedure, such as for patients with inflammatory bowel disease for whom the intestinal bypass is not advised, and transplanted patients for whom the intestinal bypass may interfere with the absorption of immunosuppressive drugs.

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