16 Laparoscopic Sleeve Gastrectomy: Management of Complications

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Abbreviations

BMI	Body mass index
CT	Computerized tomography
EWL	Excess weight loss
GEJ	Gastroesophageal junction
GERD	Gastroesophageal reflux disease
LSG	Laparoscopic sleeve gastrectomy
Post-LSG GL	Postoperative laparoscopic sleeve gastrectomy gastric leak
RYGB	Roux-en-Y gastric bypass
SEMS	Self-expandable metallic stent
SG	Sleeve gastrectomy
SIRS	Systemic inflammatory response syndrome

Introduction

Laparoscopic sleeve gastrectomy (LSG) has become an important modality in the treatment of morbid obesity. The mechanisms of weight loss include caloric restriction and hormonal alterations. Reduction of ghrelin level occurs secondary to resection of the gastric fundus. LSG was originally performed as the restrictive component of the duodenal switch procedure and also as a bridge procedure to laparoscopic Roux-en-Y gastric bypass. In 1993, Almogy et al. [1, 2] performed open sleeve gastrectomy (SG) in super-obese male patients (BMI > 55) who were older than 55 years. In 1999, Gagner and Patterson performed the first LSG as part of a duodenal switch procedure at Mount Sinai Hospital in New York [3]. Recently, LSG has gained more popularity as an independent bariatric procedure after reports showing effective, safe, and timesaving procedure. It currently accounts for more than 5 % of all bariatric operations performed worldwide [4]. A recent report from the bariatric outcomes longitudinal database (BOLD) demonstrated that between June 2007 and May 2009, LSG was the third most common bariatric procedure performed in the United States [5] (Video 1).

Several important studies have been published showing the mean excess weight loss that ranges between 52 and 61 % with follow-up of at least 5 years [6]. Brethauer et al. [7] reported a systematic review of 36 studies of sleeve gastrectomy (SG) as both a staging and primary bariatric procedure. The mean preoperative BMI from the 1,749 patients undergoing SG as a primary procedure was 46.6 kg/m^2 (range, 37.2–54.5). The mean percent excess weight loss (EWL) was 60.4 % (range, 36.0–85.0 %), and the overall complication rate of all reports ranged from 0 to 21.7 % (mean, 6.2 %). Although the LSG has been shown to effect significant weight loss with a low complication rate, LSG has a specific significant morbidity pattern including gastric staple-line leak, gastric fistula, bleeding, and obstruction or stricture. The lesser common surgical adverse effects of the procedure are rise in the incidence of gastroesophageal reflux and nutrient deficiencies (Table 1).

Gastric Leak (GL)

Leaks are the most concerning and potentially life-threatening complication after LSG.

Definition of Terms and Classification of Gastric Leak

A leak is the egress of gastrointestinal contents through a suture or staple line into a cavity. Thus, luminal content can exit through the gastrointestinal wall freely into the peritoneal cavity or can collect next to an anastomosis or

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Table 1. Complications of laparoscopic sleeve gastrectomy

Early complications
• Gastric leak
• Gastric fistula
• Bleeding
• Obstruction/stricture
Late complications
• GERD
• Nutrient deficiencies

suture or staple line [8]. Gastric leak has also been described in terms of:

1. Time to diagnosis

Poujoulet et al. classified these leaks based on the period in which they appear:

Early: leaks that appear between the first and third day after surgery

Intermediate: leaks that appear between the fourth and seventh day after surgery

Late: those that appear more than eight days after surgery [8]

Regimbeau et al. [9] also classified gastric leak, post-LSG as either *early onset* (postoperative day 1–7) or *delayed onset* (after postoperative day 8)

2. Site of leakage

Identification of the gastric leak site is based on anatomic thirds (upper, middle, or distal third of the remaining stomach)

3. Clinical aspect

The clinical presentation has been described in terms of systemic signs of inflammation and sepsis (tachycardia >100/min, hyperthermia >38 °C), peritonitis (diffuse abdominal tenderness), pulmonary symptoms (cough and expectoration), and intra-abdominal abscess (localized abdominal tenderness). A clear treatment algorithm should be established based on the patient's status: stable or unstable and controlled or uncontrolled leak. Patients who are manifesting signs of sepsis or instability should be managed operatively. Laparoscopy or laparotomy should include drainage and washout of the infected collection

Incidence of Postoperative Laparoscopic Sleeve Gastrectomy Gastric Leak (Post-LSG GL)

Gastric leaks represent one of the most dangerous complications of bariatric surgery. In the literature, the incidence of GL after LSG ranges from 0 to 7 % [9–11] (Table 2). Most leaks appear in the proximal third of the stomach, close to the gastroesophageal junction or near the angle of His. Burgos et al. [12] reported 85.7 % of leaks in the proximal third and only 14.3 % in the distal third. A.A. Saber et al. [11] analyzed 29 publications using a MEDLINE search and reported on 4,888 patient records. The mean BMI ranged from 34 to 65.4 kg/m^2, and all 29 studies documented a leak rate, which ranged from 0 to 7 %. The mean leak rate for all 29 studies was 2.4 %, which accounted for 115 leaks in 4,888 cases of sleeve gastrectomy. There did appear to be a higher leak rate in patients with a BMI > 50 kg/m^2.

Table 2. Incidence of gastric leak after LSG

Authors	Year	Patients (n)	Proportion of gastric leaks (%)
Johnston et al.	2003	100	1
Hann et al.	2005	130	0.7
Hamoui et al.	2006	118	0.8
Cottam et al.	2006	126	2
Roa et al.	2006	62	2
Lalor et al.	2007	148	1
Nocca et al.	2007	163	6
Weiner et al.	2007	120	3
Lee et al.	2007	216	1
Serra et al.	2007	993	0.6
Mui et al.	2008	70	1
Rubin et al.	2008	120	0
Skrekas et al.	2008	93	4.3
Lalor PF et al.	2008	148	0.7
Moy et al.	2008	135	1.4
Kasalicky et al.	2008	61	0
Arias et al.	2009	130	0.7
Burgos et al.	2009	214	3.2
Casella et al.	2009	200	3
Stroh C et al.	2009	144	7
Sanchez et al.	2009	540	2
Frezza et al.	2009	53	3.7
Menenakos et al.	2009	261	4
Armstrong et al.	2010	185	0
Ser et al.	2010	118	3.39
Csendes et al.	2010	343	4.66
Dapri et al.	2010	75	5
Lacy et al.	2010	294	4
Ser et al.	2010	118	3
Srinivasa et al.	2010	253	2
Bellanger et al.	2011	529	0

Six studies specifically addressed super-obese patients with a mean BMI > 50 kg/m^2. In the super obese, the mean leak rate was 2.9 % or 23 leaks of 771 patients compared with the leak rate of only 2.2 % (92/4,117) for those with mean BMI < 50 kg/m^2 (not significant $P > 0.05$).

Causes of Post-LSG GL

It is possible that these types of proximal leaks (i.e., those at the gastroesophageal junction or near the angle of His) have multiple different etiologies. One plausible theory is that the final staple line is placed across the gastroesophageal junction or distal esophagus causing poor staple-line configuration. Another more likely is the vascular theory. As Basso et al. explains [13], the cardias (distal esophagus and esophagogastric junction) are supplied in the right and anterior side by branches of the left gastric artery and left inferior phrenic artery. The posterior left side is vascularized mainly by fundic

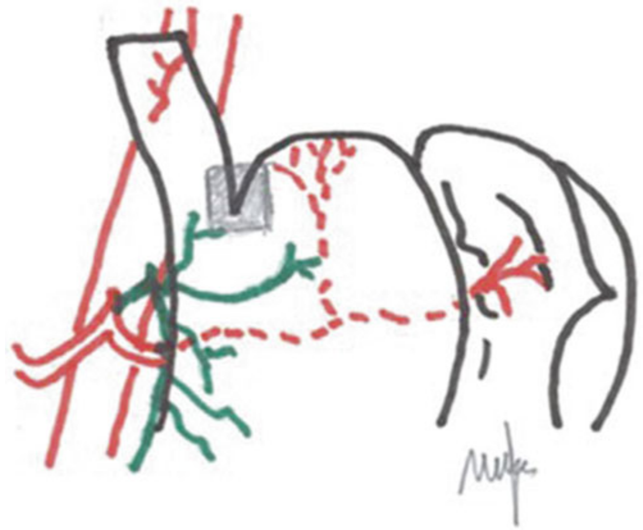

FIG. 1. Critical area of vascularization (LGA: Lt gastric artery). Reproduced with permission from *OBES SURG 2012*;22:182-187. Technical controversies in laparoscopic sleeve gastrectomy.

branches of the splenic artery and, if present, by the posterior gastric artery. The arterial supply of the esophagus is segmental. Complete dissection of the fundus requires division of the short gastric vessels, of the posterior gastric artery, and of the phrenic branches when present. A "critical area" of vascularization may occur laterally, just at the esophagogastric junction at the angle of His (Fig. 1) (Video 2).

They describe a resection line avoiding the critical area by leaving 1–2 cm of gastric remnant just at the gastroesophageal junction to avoid the area described (Fig. 2).

Nocca et al. described particular caution at this same region in those patients who had previously undergone adjustable gastric band and were undergoing conversion to sleeve gastrectomy. The concern was due to the increased fragility of gastric tissue from the fibrosis after contact with the silicone band [14]. Bellanger et al. [15] describes two basic principles for minimizing leaks. The first and most important is to avoid creating a stenosis at the level of the angular incisures, and the second (as previously described) is to avoid resection too close to the esophagus in the area of the cardia. The mid-sleeve stenosis (at the incisura) can be from a truly stenotic lumen (Fig. 3) or, more commonly, twisting or kinking of the sleeve at the incisura that causes a functional obstruction (Figs. 4 and 5). This relative downstream obstruction in the setting of a proximal leak can lead to a persistent fistula that does not resolve with conservative management. Yehoshua et al. [16] showed that high intraluminal pressure and low compliance of the gastric tube may be the main cause of leak and fistulas in this area.

Patient factors described in the literature, with a greater incidence of leak, include older age, BMI > 60 kg/m^2, malnutrition, and a history of laparoscopic gastric banding. Some authors distinguish between mechanical and ischemic causes

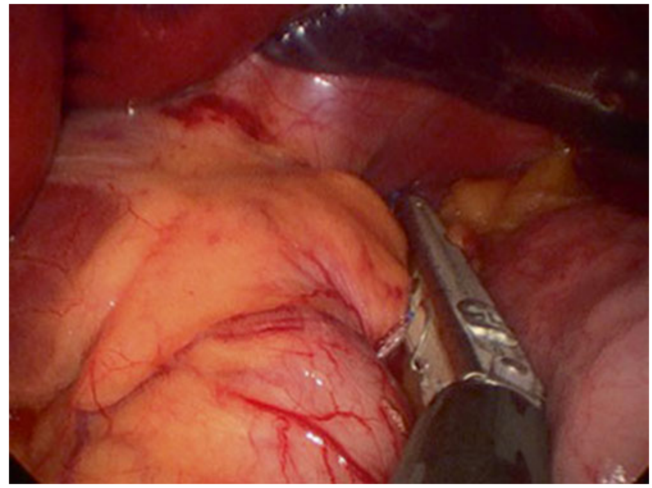

FIG. 2. Proximal staple line away from the gastroesophageal junction. Reproduced with permission from *OBES SURG 2012*;22:182-187. Technical Controversies in Laparoscopic Sleeve Gastrectomy.

of post-LSG GL. Baker et al. [17] suggest that fistulas on the staple line may have multiple causes, but these can be divided into two categories: mechanical-tissular causes and ischemic causes. In both situations, intraluminal pressure exceeds tissular and suture line resistance, thus causing the fistula. Classic ischemic fistulas tend to appear between 5 and 6 days after surgery, when the wall healing process is between the inflammation phase and fibrotic phase. When the cause is mechanical tissular, fistulas are usually discovered before this period, that is, within the first 2 days after surgery.

Incomplete Staple-Line Formation [17, 18]

Staple size must be selected appropriately for the tissue on which it is to be used. This is necessary to allow for proper staple formation while in turn achieving optimal staple-line strength and tissue compression. Undersizing staple cartridge increases the risk for inadequate staple formation or can lead to excessive tissue compression. This can exceed the tissue's tensile strength, leading to tearing and perforation. Incomplete staple-line formation occurs when a blue cartridge is used on thick gastric tissue. Greater staple height loads, such as green load cartridges (Ethicon), should be used on thick stomach as they are designed to be stronger (wider diameter) and form longer leg lengths (open, 5.5 mm; closed, 2.0 mm) when compared with blue load cartridges (open, 3.85 mm; closed, 1.5 mm)

Full thickness over sewing past affixed staple line may increase the risk of tearing at the point of suture penetration in the distended gastric pouch (Fig. 6). This effect is not likely to be significant in low pressure areas.

Finally, care must be taken while firing the stapler near the angle of His. Migration of the stapler with incorporation

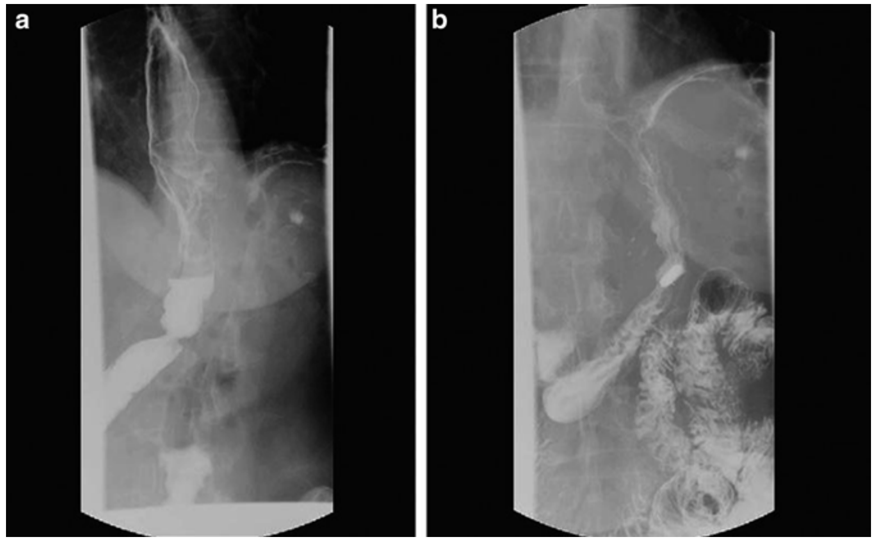

Fig. 3. Upper GI contrast study showing extravasation of contrast from the upper stomach into the left subphrenic space (**a**). Stenosis of the midportion of the sleeve is present where the barium tablet is lodged (**b**) (*arrow*). Reprinted with permission from Obes Surg 2012; vol 20, issue 9. Gastric Leak After Laparoscopic Sleeve Gastrectomy.

Fig. 4. Representation of the spiral sleeve. The functional stenosis is caused by twisting of the sleeve. Reproduced with permission from *SURG ENDOSCOPY 2012*;26:738–746. Management options for symptomatic stenosis after laparoscopic vertical sleeve gastrectomy in the morbidly obese.

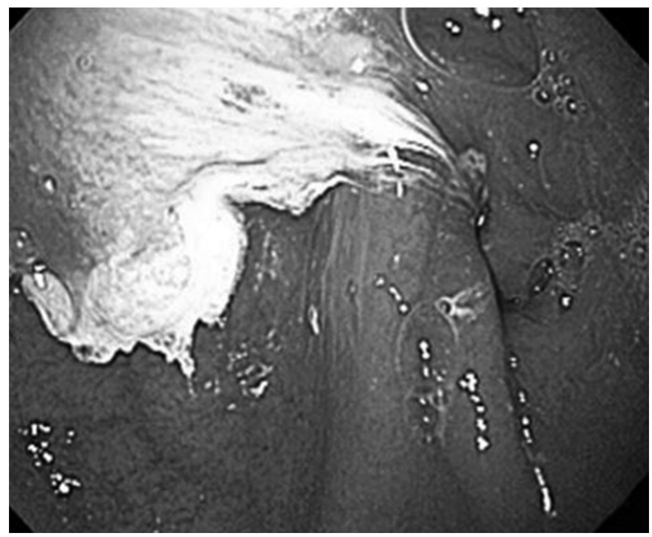

Fig. 5. Endoscopic view demonstrating the functional stenosis. Reproduced with permission from *SURG ENDOSCOPY 2012*; 26:738-746. Management options for symptomatic stenosis after laparoscopic vertical sleeve gastrectomy in the morbidly obese.

of the esophagus can weaken the staple line because of the weaker nature of esophageal tissue. Bunching of fundus or a thick fundus can also lead to leaks if inadequate staple formation or tissue shearing occurs. The ultimate goal in staple formation is to produce mechanically sound staple lines, which can withstand pertinent pressure forces until the tissue response endows significant strength overtime.

This formation must achieve adequate staple formation and yet avoid tearing the tissue.

Diagnosis for Post-LSG GL

A high index of suspicion and early identification of leaks after LSG are critical to achieving an acceptable outcome after this complication. Unexplained tachycardia, fevers, abdominal pain, or persistent hiccups after the procedure should alert surgeons to investigate for a leak (Table 3).

The signs and symptoms of the patients who develop a leak are similar to patients with other types of abdominal infections. However the clinical presentation of gastric leak ranges from the patient being completely asymptomatic

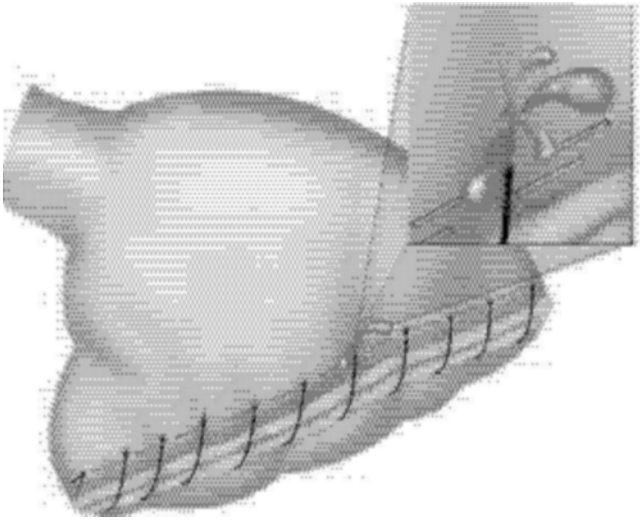

Fig. 6. Oversewing causing leaks when the pouch is distended and suture bowstrings and tissue tear.

Table 3. Potential signs of post-LSG GL

A high index of suspicion
1. SIRS
– Unexplained tachycardia (>100/min)
– Fever (>38 °C)
2. Abdominal pain
– Diffuse abdominal tenderness (diffuse peritonitis)
– Intra-abdominal abscess (localized peritonitis)
3. Pulmonary symptoms (subphrenic abscess or complex bronchogastric fistula)
– Cough
– Expectoration
– Persistent hiccups

(identified by fluoroscopic study) to the presentation of peritonitis, septic shock, multiorgan failure, and death. Burgos et al. report a series of 7 leaks in 214 patients (3.3 %), of which 5 patients presented abdominal pain, fever, tachycardia, tachypnea, and increased laboratory signs of infection. They observed that tachycardia is an initial sign of early leak [12]. Casella et al. reported leaks in 3 % of 200 patients. In general, the symptomatology was abdominal pain, vomiting, and fever; only one patient was asymptomatic [19]. According to Tan et al. [20] and de Aretxabala et al. [21], early-onset GL presents with severe, sudden abdominal pain (together with fever, nausea, and vomiting), whereas delayed-onset GL is usually of a more insidious nature (with gradually increasing abdominal discomfort and fever). Patients with early-onset GL show signs of sepsis caused by gastrointestinal contents in the peritoneal cavity, and they require at least a surgical lavage and the placement of drains. For patients with delayed-onset GL, fluid frequently collects near to the stomach and does not spread to the rest of the cavity. Four clinical presentations have approximately the same frequency: systemic signs of inflammation, peritonitis, abscess, and pulmonary symptoms. Pulmonary symptoms can be caused by a subphrenic abscess (in both early- and delayed-onset GL) or complex bronchogastric fistula (delayed-onset GL). Medical and surgical teams must be aware of initial, atypical presentations or those occurring during follow-up: [1] bronchogastric fistulas (revealed by chronic cough and managed with a pulmonary lobectomy [2], acute hematemesis revealing a left gastric artery aneurysm associated with fistula and self-expandable metallic stent (SEMS), and [3] a typical Wernicke–Korsakoff syndrome linked to vitamin deficiency in patients who are, in fact, subjected to long-term fasting.

Investigation

If the surgeon becomes concerned about a leak and a drain was left in place at the time of surgery, the drain fluid can be sent for an amylase level. If the fluid amylase level is much higher than normal serum levels (in the 1,000s), this suggests that saliva is entering the drain. Regardless of the drain amylase level, early imaging is warranted if clinical suspicion of a leak exists. An upper gastrointestinal contrast study is frequently used postoperatively to assess the presence of a gastric leak as well as demonstrate patency of the sleeve gastrectomy. In general, a water-soluble contrast material is used (Gastrografin). While standing, the patient swallows 20 mL of Gastrografin and radiographs are taken. The characteristics of a tubularized stomach (i.e., dimensions, emptying, and the presence or absence of leak or stricture) are then evaluated (Figs. 7 and 8). In case of doubt, or in order to increase sensitivity, abdominal computerized tomography (CT) scan can be performed. CT scan can provide additional information in regard to fluid collections or abscess in the left upper quadrant (Figs. 9 and 10) or the presence of subdiaphragmatic air (Fig. 11).

Abdominal CT scan should be performed with intravenous and oral contrast material. It is useful to identify the postoperative normal anatomy and the presence of complications after sleeve gastrectomy. Findings suggestive of GL are extravasation of contrast agent through the wall of the gastric sleeve, accumulation adjacent to the sleeve, free intra-abdominal liquid, free intra-abdominal gas, and residual contrast agent in the drainage tube.

Management of Post-LSG GL (Fig. 12)

Interventional options include surgery (laparoscopy or laparotomy with abdominal washout, abdominal drainage close to the staple line, and feeding jejunostomy), endoscopic procedures (self-expandable metallic stents (SEMS), clips, biological glue, pigtail drains, and T-tube gastrostomy drain), and radiological procedures (percutaneous drainage).

The management of the leak depends on the patient's clinical condition. The surgeon managing this complication

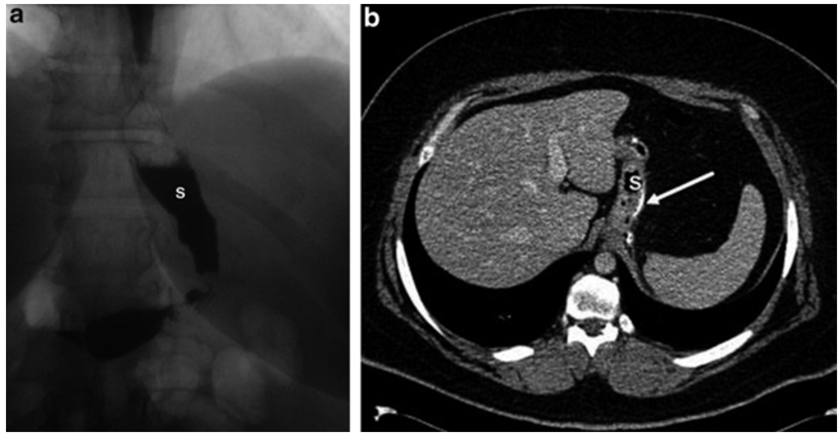

Fig. 7. Normal images after LSG. (**a**) Contrast study: *S* gastric sleeve; (**b**) CT image: *S* gastric sleeve; *arrow* shows gastric staple line.

Fig. 8. An upper gastrointestinal contrast radiograph showing proximal gastric leak. A cavity is observed adjacent to the stomach (*white arrow*). Reproduced with permission from *OBES SURG 2011*; 21:1232-1250. Gastric Leak After Sleeve Gastrectomy: Analysis of Its Management.

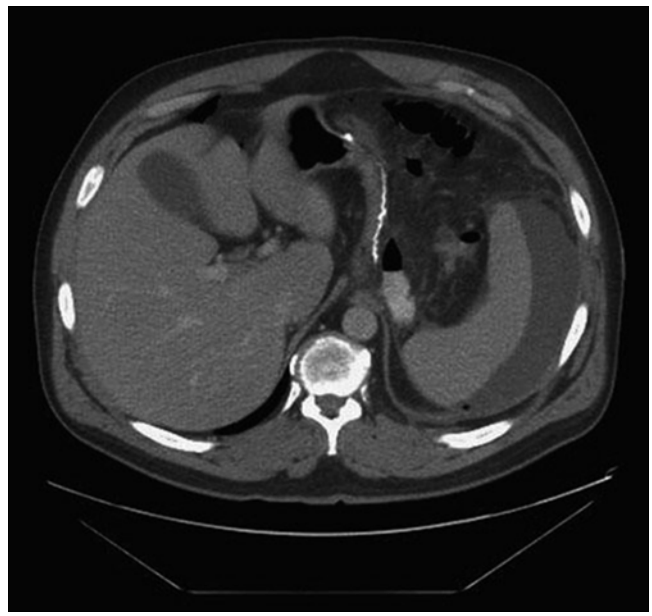

Fig. 9. Abdominal CT scan showing the staple line of the sleeve gastrectomy with contrast extravasation proximally into an extraluminal collection immediately adjacent to the gastric sleeve staple line. Reproduced with permission from *OBES SURG 2010*;20:1289-1292. The Use of Endoscopic Stent in Management of Leaks After Sleeve Gastrectomy.

must have a clear treatment strategy or algorithm based on the patient's status, the duration of the leak, and the resources available.

If the leak presents as a well-defined abscess several days or weeks after surgery and the patient is clinically stable, percutaneous image-guided drainage (Fig. 13) or pigtail drainage (Fig. 14), antibiotics, and nutritional support with parenteral nutrition or a nasojejunal tube is appropriate. If drainage is adequate, endoluminal therapies can be used to facilitate closure of the leak. This process often includes placement of endoscopic clips, fibrin glue (Fig. 15), or bioabsorbable fistula plugs and endoluminal stenting across the leak. Stenting has been shown to be effective in small series of selected cases, but results can be variable depending on the size and duration of the leak. Although placement of self-expanding, covered, or partially covered stents (Polyflex or WallFlex stents, Boston Scientific, Natick, MA) may be beneficial, the current stent technology is not ideal for this anatomy. The difficulty is in the two different lumen diameters and the curvature of the gastric lumen (Fig. 16). Before attempts at stenting, the extraluminal collection must be adequately addressed in all cases, and surgical placement of drains with washout of the infected field is often warranted to promote closure of the leak. Because successful outcomes after stenting often occur in carefully selected patients, evidence is currently insufficient to make any broad claims that stenting accelerates or promotes closure

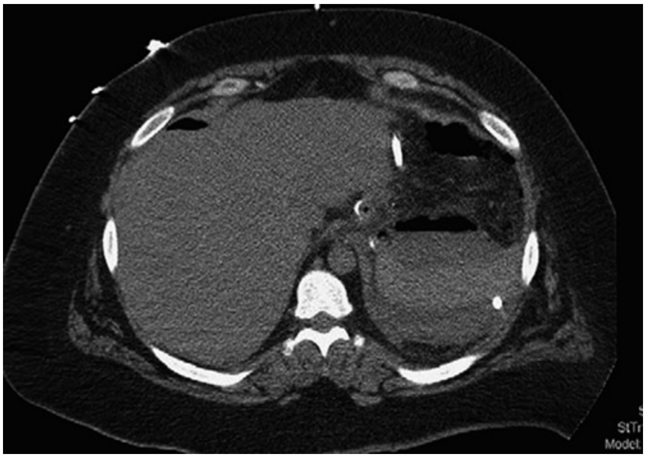

FIG. 10. CT scan showing a left upper quadrant abscess after post-LSG GL.

FIG. 11. CT scan showing a contained leak after laparoscopic sleeve gastrectomy. Arrow is abscess with free air, blood, and debris.

of leaks for all patients. Nevertheless, stenting may be a useful therapeutic adjunct in some patients and is associated with acceptable risk.

One advantage of stent placement in these patients is that it may allow patients to resume oral intake while the leak heals.

Patients who are manifesting signs of sepsis or are unstable should be managed operatively with laparoscopy or laparotomy (Fig. 17). Drainage and washout of the infected collection and wide drainage of the area is the primary goal of the operation. Primary closure of the defect can be performed if discovered early. Direct primary closure of the defect with or without sealants should be reserved for cases that were diagnosed early (within 24–48 h) and have good tissue viability. Closed suction or sump drains should be placed and the omentum can be sewn over the defect to help contain the contamination. If the patient is stable during the case, a feeding jejunostomy should be placed for long-term enteral access.

In contrast to a Roux-en-Y gastric bypass (RYGB), LSG leaks are more difficult to manage and tend to be more chronic in nature. Proximal leaks (Fig. 18) may be differentiated from distal ones due to the quality of material that may be seen in the drain. Proximal leaks often have saliva and gastric acid, while distal leaks may additionally drain bile. In proximal leaks the use of drains (surgical or percutaneous) plus alimentary support should be initiated. Complementary to the adequate drainage, the use of endoscopic procedures like fibrin sealant in combination with somatostatin and placement of endoluminal stents have promising results. There are less reports on the management of distal leaks; however, the same principles as previously described should be applied (Fig. 19). Rosenthal et al. [22] presented a case report with a distal and proximal disruption of the staple line. A T-tube gastrostomy with a large proximal and distal limb was placed into the most distal area of disruption. After thorough oversewing and drainage of the proximal site and T tube (distal), a feeding jejunostomy was placed. Four weeks postoperatively, the T tube was removed after the patient had a negative Gastrografin study and tolerated oral fluids with a clamped T tube. Persistent leaks (both proximal and distal) may require conversion to a low pressure system such as RYGB.

Another important factor when treating proximal or distal leaks is to rule out distal obstruction, in particular at the incisura. If present, an EGD and endoscopic deployment of a covered stent across the leak site and obstruction will both cover the leak and more importantly decrease the pressure in the gastric lumen (Figs. 20 and 21).

“Treatment success” was defined as absence of contrast agent leakage in CT and endoscopic evaluations after permanent, covered SEMS, T-tube, or pigtail drains had been removed.

In contrast, “treatment failure” was defined as the need for radical surgery for persistent GL (total gastrectomy or Roux-en-Y gastroenterostomy at the site of GL).

Several principles should be followed when an esophageal stent is considered for management of a gastric leak after sleeve gastrectomy. First, an endoscopy must be performed to evaluate the site of the leak, the size of the leak, and the viability of the conduit. Gastric leaks at the proximal and mid-aspect of the gastric sleeve are the only leaks that are amenable to endoscopic treatment with stent. A leak at the distal staple line of the gastric sleeve, near the gastric antrum, will not be amenable to endoscopic stenting as the stent may be too small in diameter and would not provide appropriate sealing of the defect and potentially lead to a higher degree of migration. The selection of the size of the stent is based on evaluation of the gastric sleeve diameter at the time of endoscopy. Another strategy to minimize stent

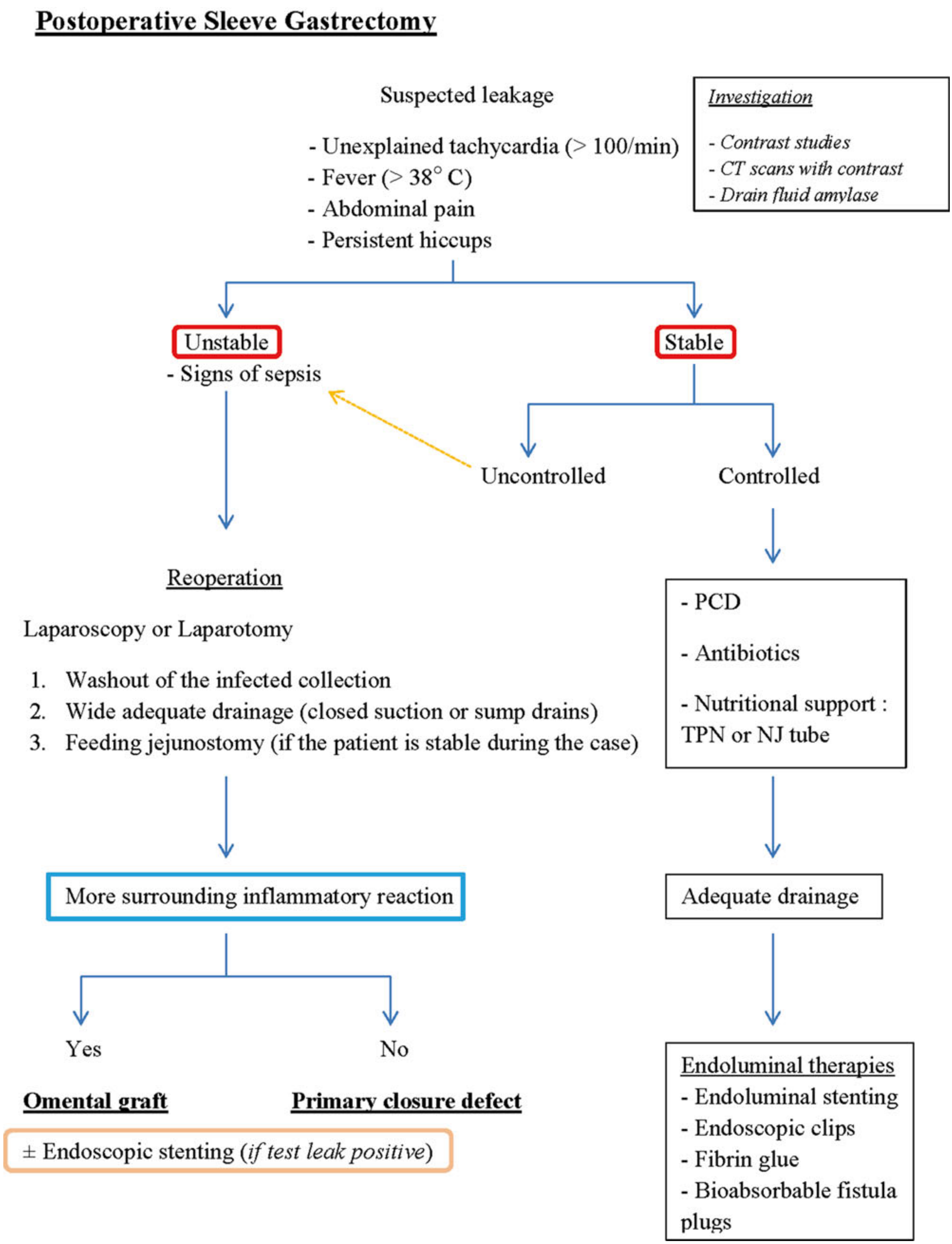

FIG. 12. Algorithm for managing post-LSG GL.

Fig. 13. Percutaneous drainage to drain a collection adjacent to the remnant stomach. Reproduced with permission from *OBES SURG 2011*;21:1232-1250. Gastric Leak After Sleeve Gastrectomy: Analysis of Its Management.

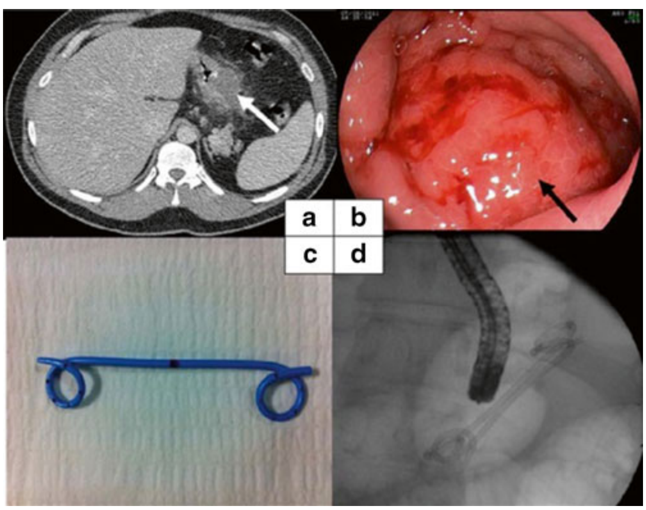

Fig. 14. Delayed-onset gastric leak. (**a**) A fluid collection bulging in the stomach (*white arrow*). (**b**) Fluid collection bulging in the stomach (*black arrow*). (**c**) A pigtail drain. (**d**) Abdominal X-ray showing two pigtail drains after the endoscopic procedure. Reproduced with permission from *OBES SURG 2012*:22;712-720. Is There a Place for Pigtail Drains in the Management of Gastric Leaks After Laparoscopic Sleeve Gastrectomy?.

migration is to use a longer stent whereby the distal aspect of the stent is rested along the wall of the gastric antrum which preclude the stent from luminal migration (Table 4).

Serra and colleagues [23] reported on the use of coated self-expanding stents for management of leaks after sleeve gastrectomy in three patients with control of leaks in 66 % of cases. Casella et al. [25] reported the use of endoscopic stent for leak at the gastroesophageal junction after sleeve gastrectomy in five patients with complete healing occurring in all patients, suggesting that the staple-line leak can be safely and successfully managed without reoperation in patients with hemodynamic stability (rate of success of 100 %). Eubanks et al. [24] reported a success rate of 84 %. Tan et al. reported a success rate for closure of only 50 % due to stent-related complications. Other studies have suggested routine stent removal no later than 6 weeks in order to avoid tissue hyperplasia and difficult extraction. Tolerance to stents is variable (nausea, vomiting, drooling, and retrosternal discomfort) but tends to disappear after the first few days. Covered SEMS also present significant morbidity–mortality, with migration being one of the main concerns (Fig. 22). The high migration rate has been explained by the "abnormal" placement of the stent along the last portion of the esophagus and the gastric pouch. The type of stent used may also lead to higher rates of migration. Fully covered stents will have the greatest degree of migration while less covered stents will have a greater degree of tissue ingrowth.

Gastric Fistula

A chronic fistula (Fig. 23) after LSG is a challenging problem. If a leak or gastrocutaneous fistula persists for months despite adequate surgical drainage, endoluminal therapy, and nutritional support, the patient's gastrointestinal anatomy should be evaluated for a distal obstruction or stricture. Reoperation may be the only solution. Several surgical options have been reported. Therapy may include resection of fistula and proximal stomach with the creation of a Roux-en-Y esophagojejunostomy, bringing a Roux limb up and creating a gastrojejunal anastomosis directly on the leak site, placing a jejunal patch over the leak site, or placing a T tube into the leak site. Evidence is insufficient to support one approach over another, and the type of salvage procedure should be determined by the patient's anatomy and the surgeon's judgment and experience.

Bleeding Complications

The incidence of staple-line hemorrhage has been reported to be 0–8.7 % [27]. Common sites of bleeding include the sleeve staple line, the short gastric vessels, the spleen, and the omental vessels that have been divided during the dissection of the greater curvature. When bleeding is identified, conservative management including stopping anticoagulation and appropriate fluid or blood resuscitation is usually sufficient in most of cases [28, 29]. Bleeding complications requiring reoperation occur less than 2 % of the time after LSG [30]. Laparoscopic stapling devices have become pivotal tools in the field of laparoscopic

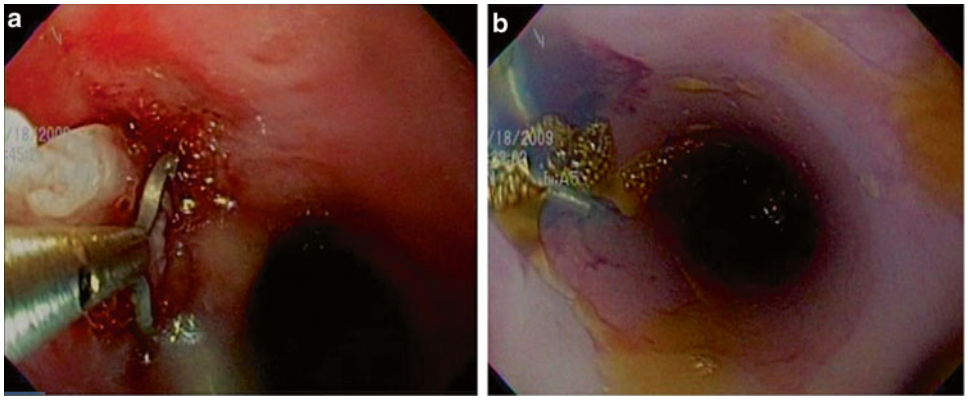

FIG. 15. Endoscopic placement of (**a**) fibrin glue and (**b**) clips across a small leak at the gastroesophageal junction after sleeve gastrectomy followed by placement of a stent across the leak.

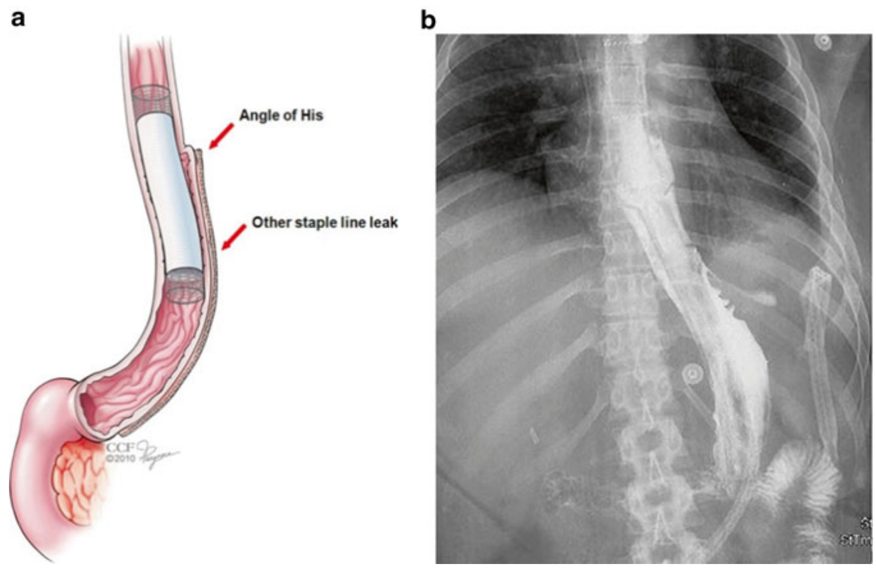

FIG. 16. (**a**, **b**). Schematic illustration of gastric anatomy after sleeve gastrectomy with stent in situ and shows a small persistent leak of contrast refluxing up around the stent (*arrow*).

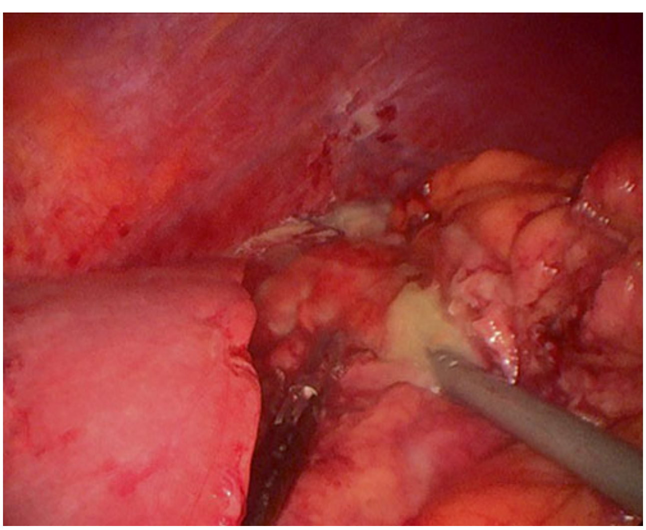

FIG. 17. Reintervention. Abscess drainage. Reproduced with permission from *OBES SURG 2010*;20:1306-1311. Gastric Leak After Laparoscopic Sleeve Gastrectomy.

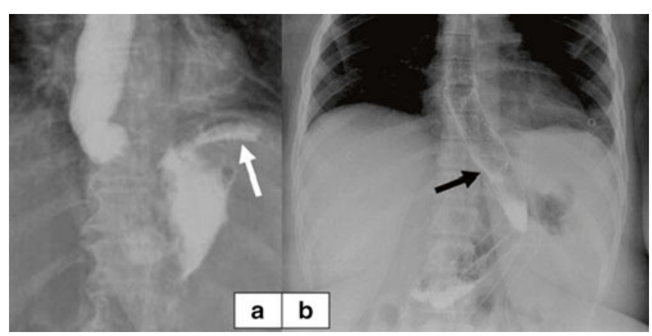

FIG. 18. (**a**) Gastrografin esophagography with gastric leak on the upper third of the staple line (*white arrow*). (**b**) Abdominal X-ray showing two covered SEMS inserted in order to bypass the gastric leak (*black arrow*). Reproduced with permission from *OBES SURG 2012*:22;712-720. Is There a Place for Pigtail Drains in the Management of Gastric Leaks After Laparoscopic Sleeve Gastrectomy?.

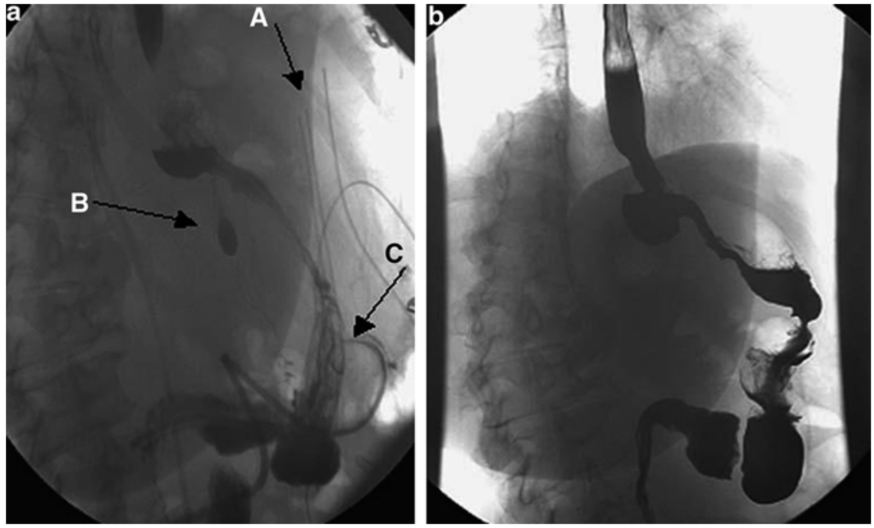

Fig. 19. (**a**) First postoperative day. Gastrografin swallow showing drains (A), proximal leak (B), and T-tube gastrostomy drain distal leak (C). (**b**) Gastrografin swallow 6 months after surgery.

Fig. 20. Upper gastrointestinal contrast study showing a stent deployed for treatment of a proximal staple-line leak and a partial obstruction at the mid-aspect of the gastric sleeve. Note that there is a bending of the stent at its midpoint due to the stricture in the gastric sleeve. The stent protects the leak and allows contrast to pass through the stricture into the duodenum. Reproduced with permission from *OBES SURG 2010*;20:1289-1292. The Use of Endoscopic Stent in Management of Leaks After Sleeve Gastrectomy.

Fig. 21. Upper gastrointestinal contrast study on day 7 after stent deployment showing good contrast flow from esophagus through the stent into the gastric antrum. No evidence of proximal leak was observed. A percutaneous drain was placed to drain a subphrenic collection. Reproduced with permission from *OBES SURG 2010*;20:1289-1292. The Use of Endoscopic Stent in Management of Leaks After Sleeve Gastrectomy.

bariatric surgery. However, they are also associated with complications such as leak, bleeding, fistula, and technical failure, even though these complications are uncommon. In theory, reinforcing the staple line should increase its strength and help decrease the incidence of complications associated with staple lines. Furthermore, there seems to be no reason to believe that reinforcement would lead to harmful effects. Although the importance of staple-line reinforcement in bariatric operations has been described in the literature, it remains controversial in LSG. The majority of papers that report on staple-line reinforcement in bariatric procedures are related to its use in laparoscopic gastric bypass.

The options for reinforcement include oversewing the staple line, application of fibrin glue sealants, and incorporation of buttressing materials. Staple-line buttressing has been

TABLE 4 Endoscopic stent for gastric leak after laparoscopic sleeve gastrectomy

Author	Year	Number of patients	Number of covered SEMS	Success rate (%)	Migration rate (%)
Serra et al.[23]	2007	3	7	66	14
Eubanks et al. [24]	2008	19	34	84	58
Casella et al. [19]	2009	5	11	100	9
Tan et al. [20]	2010	14	8	50	25
Pequignot et al. [10]	2011	25	50	84	8
Chand et al. [26]	2010	6	6	66	17

FIG. 22. Migration to the antrum of endoluminal stent (*white arrow*). Reproduced with permission from *OBES SURG 2011*;21:1232-1250. Gastric Leak After Sleeve Gastrectomy: Analysis of Its Management.

FIG. 23. Endoscopic image of gastrocutaneous fistula.

developed to improve staple-line strength by increasing the tissue thickness, resulting in decreased bleeding and risk of leak. In the bariatric literature their use remains controversial. Few published papers exist that compare the incidence of staple-line leakage or hemorrhage to that of nonreinforced staple lines in LSG procedures.

Choi et al. [31] performed a meta-analysis of eight articles (two RCTs and six cohort studies; Table 5). There were 1,335 patients in the eight studies (507 patients in the control groups and 828 patients in the intervention groups). Although there was no significant effect of overall reinforcement of the staple line in this meta-analysis, reinforcement with a buttress seemed to decrease staple-line hemorrhage (Fig. 24). On the other hand, reinforcing the staple line with oversewing may increase the risk of staple-line hemorrhage, although this result had no statistical significance.

In a subgroup analysis of this meta-analysis, reinforcing the staple line with a buttress may decrease the risk of staple-line hemorrhage and overall complications, but it is not clear whether it decreases the risk of staple-line leak after LSG. It was also unclear if the effect of reinforcing the staple line with oversewing showed any advantage when compared to the control group in regard to leak, hemorrhage, and overall complications. In addition, it could lead to strictures of the gastric sleeve and cause tears of the suture line (Fig. 7). In practice, according to Gagner's report [27], 65.1 % of 106 surgeons who participated in the Second International Consensus Summit for Sleeve Gastrectomy in 2009 answered that they reinforced the staple line of the gastric tube. Of these, 50.9 % reinforced the staple line with oversewing, 42.1 % used a buttress, and 7 % did both.

TABLE 5 Characteristics and outcomes of the included trials

Trials	Country and year	Type of study	Reinforcement			Type of reinforcement	Control		
			Leak	Hemorrhage	Overall		Leak	Hemorrhage	Overall
Consten et al.	USA, 2004	Cohort	0/10	0/10	0/10	Buttressing	0/10	2/10	3/10
Silecchia et al.	Italy, 2009	Cohort	–	–	4/29	Oversewing	–	10/56	
Sanchez-Santos et al.	Spain, 2009	Cohort	10/381	2/381	14/381	Combined	8/159	2/159	14/159
Ser et al.	Taiwan, 2010	Cohort	0/78	2/78	8/78	Oversewing	4/40	0/40	6/40
Dapri et al.	Belgium, 2010	RCT	1/25	–	3/25	Oversewing	1/25	–5/25	
2/25	–	6/25	Buttressing	1/25	–	5/25			
Daskalakis et al.	Germany, 2011	Cohort	3/144	4/144	9/144	Buttressing	7/86	6/86	14/86
Stamou et al.	Greece, 2011	Cohort	2/96	0/96	2/96	Buttressing	4/91	3/91	12/91
Musella et al.	Italy, 20111	RCT	1/40	4/40	9/40	Oversewing	2/40	2/40	4/40

OBES SURG 2012;22:1206-1213. Reinforcing the Staple Line During Laparoscopic Sleeve Gastrectomy: Does It Have Advantages? A Meta-analysis. Reprinted with permission

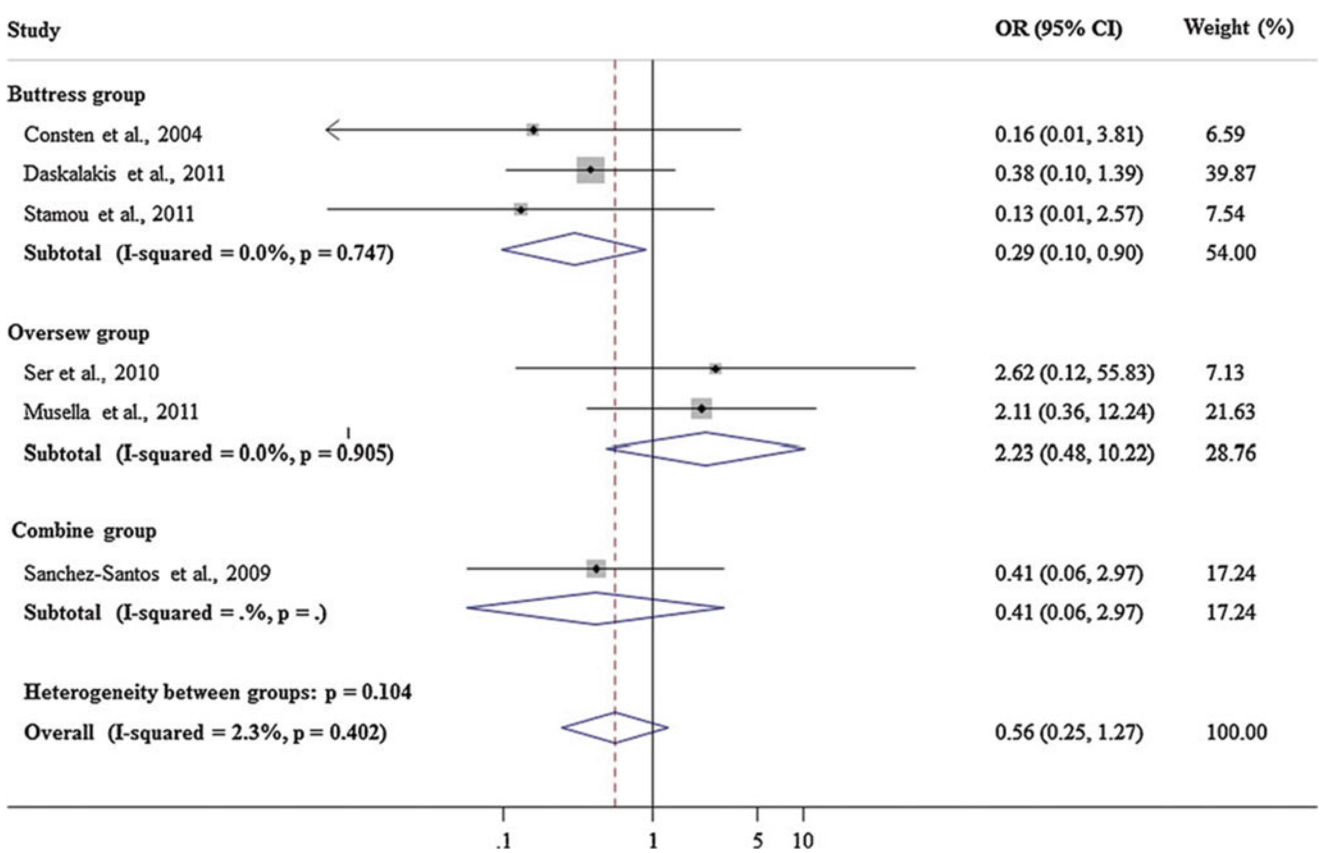

FIG. 24. The forest plot shows the OR of staple-line hemorrhage after LSG of the reinforcing staple-line group and the control group with fixed-effect-model meta-analysis (OR, odds ratio). Reproduced with permission from *OBES SURG 2012*;22:1206-1213. Reinforcing the Staple Line During Laparoscopic Sleeve Gastrectomy: Does It Have Advantages? A Meta-analysis.

Obstruction and Strictures

Sleeve stenosis can occur due to unintentional narrow tubularization of the stomach. It currently is reported to occur in 0.26–4 % of LSG operations [7, 32, 33]. This may underestimate the true incidence of stenosis in current practice because early published series of LSG tended to use larger bougies with the intention of two-stage weight loss. In a recent review of 36 studies evaluating LSG as a primary and staged procedure, Brethauer et al. [7] demonstrated that the rate of postoperative strictures requiring endoscopic or operative intervention was 0.6 % in studies with more than 100

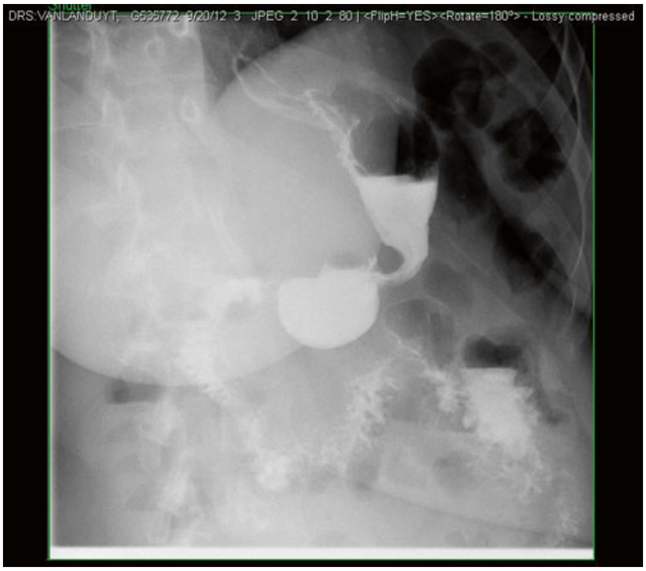

FIG. 25. Gastric stricture at incisura angularis after sleeve gastrectomy (*arrow*).

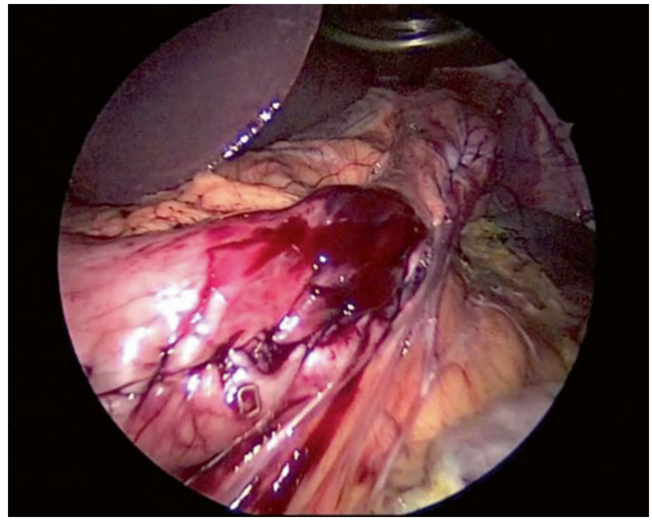

FIG. 26. Hematoma after sleeve gastrectomy.

patients. The most common site of luminal narrowing is at the incisura (Fig. 25).

Some authors have reported that the stenosis rate does not correlate with bougie size used. For example, Cottom et al. [34] reported using 46- to 50-Fr bougies with a stenosis rate of 3.9 %, whereas Lalor et al. [35] reported using either a 44- or 52-Fr bougie with a stenosis rate of only 0.7 %. This suggests another technical cause independent of bougie size contributing to the stenosis rate. Notably, Cottom et al. [34] stated that by changing their overall technique from imbricating the staple line to covering it with fibrin glue caused their stenosis rate to disappear.

This type of stenosis most likely occurred due to overnarrowing of the sleeve at the incisura. Care must be taken to leave plenty of tissue anteriorly in this area, especially when the sleeve starts closer to the pylorus. Narrowing here can occur as the clinician begins to "cut the corner" even with a larger bougie in place due to over-retraction of the greater curvature during stapling. The process of retracting the greater curvature where tension is progressively applied can cause stretch on the stomach during division. Once the bougie is removed, the stomach will recoil, resulting in a narrowing. Although true strictures can occur, this problem after LSG is typically not a true mucosal or luminal stricture as much as it is an angulation or kinking of the stomach in this area. This functional obstruction presents as persistent dysphagia to solids and liquids, with nausea and vomiting. When creating the SG initially, this complication can be prevented through avoiding sharp angulation of the staple line and allowing for adequate lumen size as the stapler approaches the incisura.

A twisted or spiral sleeve is another cause of symptomatic stenosis. Progressive rotation of the staple line in an anterior to posterior plane can lead to a narrowing despite a fairly normal luminal diameter. This curve can make passage of enteric contents difficult, resulting in a functional stenosis. This often is demonstrated by easy passage of the endoscope or balloon dilator through the narrowed area. Much like a clown twisting a straight balloon, an anterior twist at the incisura can result in a functional stenosis (Fig. 4). An endoscope can pass through by pushing and twisting in the same direction, and a balloon dilator can be used to open the stenosis. However, the stenosis returns at withdrawal of the endoscope or deflation of the balloon dilator. A functional sleeve stenosis also can result from external sources such as a hematoma (Fig. 26) that causes the sleeve to scar in a kinked manner. Such complications should be promptly treated (Video 3).

The management algorithm (Fig. 27) of patients who have undergone LSG with persistent nausea, vomiting, or dysphagia. First, an UGI contrast study should be obtained. If this study demonstrates an abnormal finding or if the symptoms persist over time, an esophagogastroduodenoscopy should be performed with anticipation of performing a dilation. Repeat dilation can be performed as long as the patient demonstrates improvement in oral tolerance. Placement of a stent also can be considered, although a stent often is poorly tolerated by the patient due to pain and discomfort. Failure of progression to a normal diet warrants consideration of operative revision to an RYGB. Clinical significant short-segment stenoses may be treated successfully with endoscopic balloon dilation and stent. Long-segment stenoses are less likely to respond to

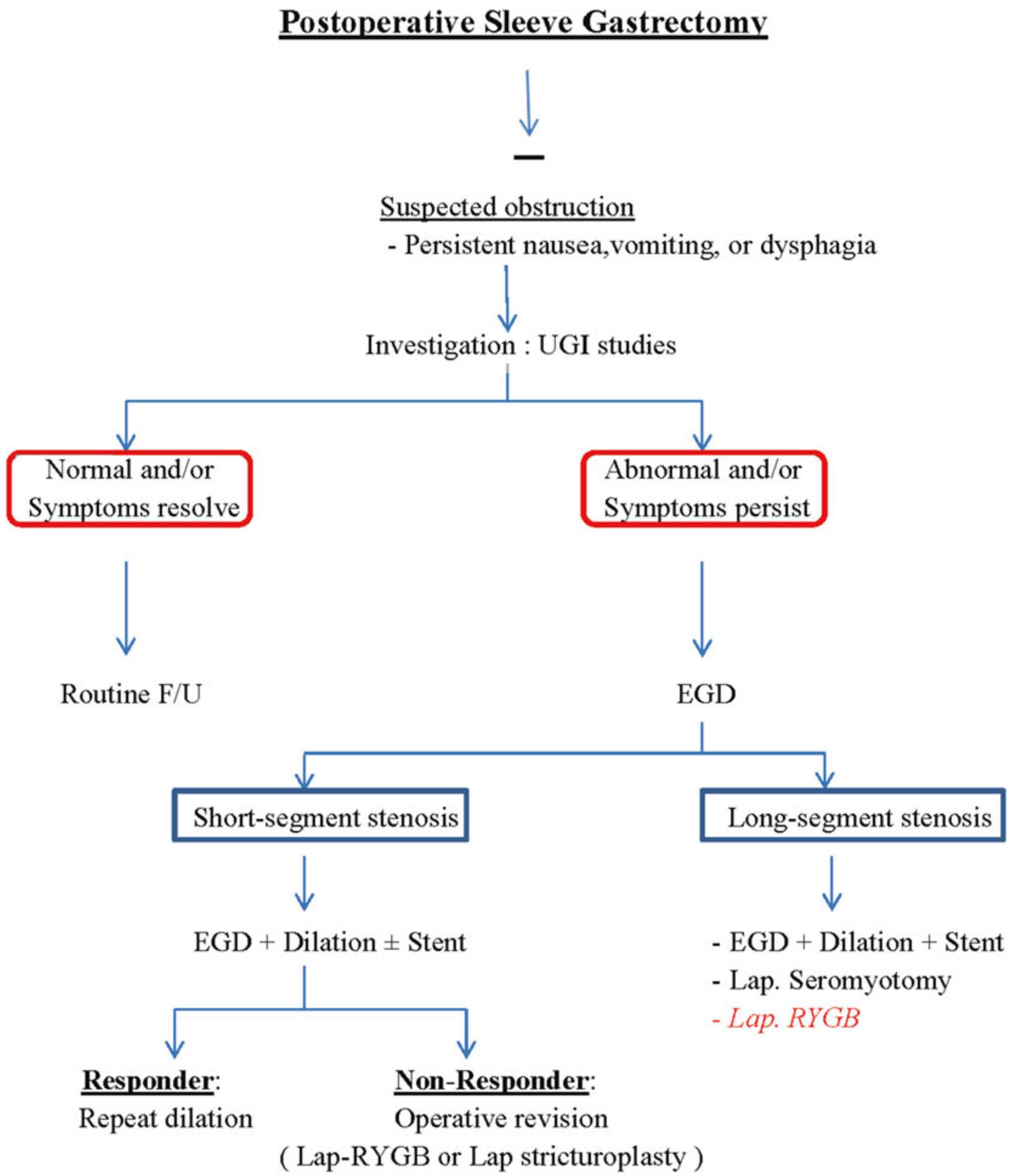

FIG. 27. Algorithm for managing post-LSG obstruction.

endoscopic techniques and may ultimately require conversion to Roux-en-Y gastric bypass.

Post-LSG GERD

GERD remains a concern after LSG and has a very wide clinical spectrum of manifestation. There is probably a continuum from mild reflux that may respond well to PPIs, through severe symptomatic reflux that may need a deployment of full treatment options (high-dose PPIs, propulsive medications, and behavioral and lifestyle changes) (Fig. 28). Severe symptoms may also include an inability to ingest oral food requiring hospitalization for assisted feeding and possible reoperation. Therefore, the true incidence of this complication after sleeve gastrectomy is unknown. The works that do report the incidence cite numbers from as low as 0.1 % for prolonged vomiting and 0.2 % for delayed gastric emptying [36] to as high as 13–30 % [37]. Symptomatic GERD has been reported to occur in 7.8–20 % of patients at 12–24 months after LSG in a selected series of more than 100 patients. At the Second and the Third International

Consensus Summits for Sleeve Gastrectomy, reflux disease was reported to occur in 6.5 % and 17 % of patients, respectively, after sleeve gastrectomy. Most studies reported an increase in reflux symptoms during the first year following sleeve gastrectomy, followed by a gradual decrease in symptoms up the third postoperative year.

Even Wernicke–Korsakoff syndrome has been reported after sleeve gastrectomy (SG) due to prolonged vomiting [38]. This wide variation in incidence may also lead to variations in diagnosing criteria. Most authors report prescribing PPIs for different periods of time to SG patients. Often early improvement of GERD symptoms occurs after LSG, but late onset of GERD symptoms has also been reported. In a report by Himpens and colleagues [38] with 6-year follow-up, the overall incidence of new-onset GERD (defined as symptoms requiring proton pump inhibitor use) was 26 %. The investigators attribute some of the new-onset GERD symptoms to the appearance of a neofundus (dilated pouch of fundus at the proximal sleeve) (Fig. 29) that occasionally requires reoperation. In patients in whom this dilated fundus was resected, GERD symptoms improved. Anatomical changes in the angle of His and GEJ area and retention of the fundus may play an important role in postoperative sleeve emptying. The more fundus left behind, the higher the propensity of the stomach to distend, especially in view of a functional obstruction. Larger retained fundus will produce more gastric acid, and this in turn may result in larger amount of acid available for refluxing into the esophagus (Fig. 30). It is clear that in cases where the fundus has been left behind, the anatomy of the gastroesophageal junction was disturbed to a lesser degree. The fundal dilatation probably represents the retention of the fundus at the operation while trying to avoid injury to the area of the esophagogastric junction or incomplete release of the posterior fundus.

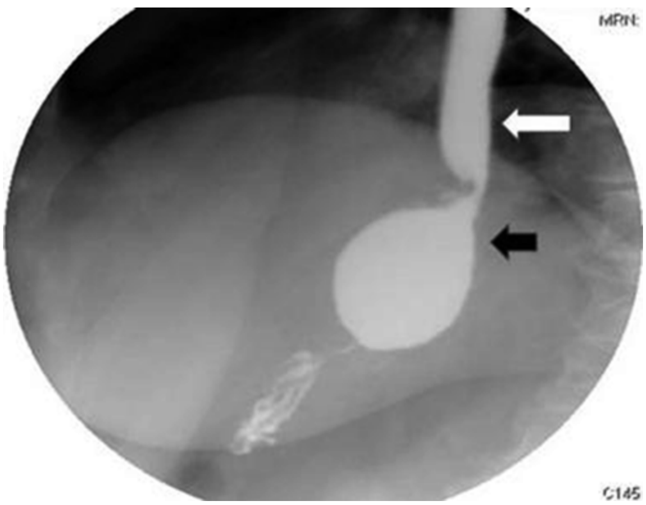

Fig. 28. UGI study revealing a dilated upper part of the sleeve (*black arrow*), with an immediate passage to the lower part. The contrast has retained in the fundus area and reflux up to the mid esophagus was observed (*white arrow*). Reproduced with permission from *OBES SURG 2010*;20:140-147. Dilated Upper Sleeve Can be Associated with Severe Postoperative Gastroesophageal Dysmotility and Reflux.

Since sleeve gastrectomy is still a relatively recent technique, the knowledge regarding the true incidence of new-onset GERD is still evolving. More investigations regarding the physiology of the procedure in terms of emptying, acid production, and reflux mechanisms are needed to draw more conclusions. Until that knowledge is available, a cautious approach to patients with preoperatively suspected motility disorders should be exercised. Patients suspected to have this kind of dysfunction should be studied by esophageal manometry or nuclear emptying studies and may be better candidates for alternative operations, such as the gastric bypass. Patients should be advised preoperatively about the possibility of this complication. If this

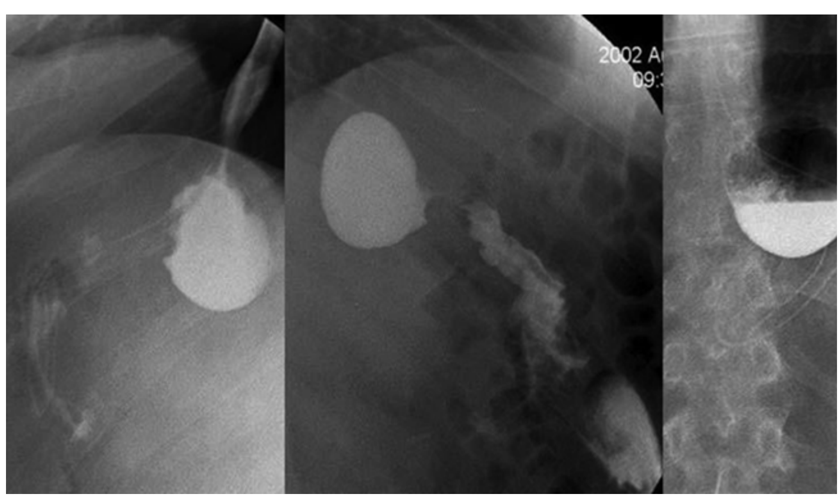

Fig. 29. Retained fundus functioning as diverticula. Reproduced with permission from *OBES SURG 2010*;20:140-147. Dilated Upper Sleeve Can be Associated with Severe Postoperative Gastroesophageal Dysmotility and Reflux.

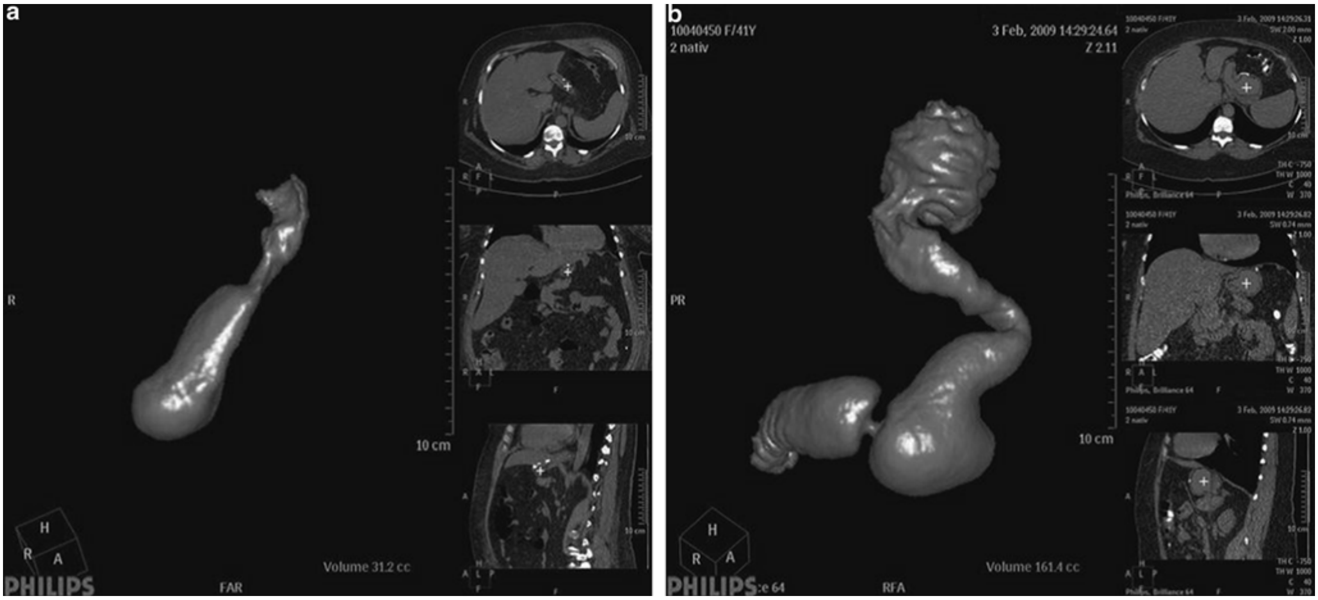

Fig. 30. (**a**) Virtual CT after sleeve gastrectomy third postoperative day: normal finding after calibration with 42-Fr tube. (**b**) Virtual CT after sleeve gastrectomy: surgical mistake with fundus in place (uncompleted resection).

complication has occurred, conservative approach is usually successful, but sometimes, a conversion to other procedure (RYGB) can be curative.

Treatment Post-LSG GERD

Treatment options are divided into conservative therapy, endoluminal modalities, and surgical options. Obviously, the simple fibrotic stricture or complete obstruction should be excluded by swallow study or endoscopy. But even in the absence of complete anatomical occlusion, there may be a functional obstruction, where the propulsive force of the stomach and esophagus is not enough to clear the content downstream. In those cases, endoscopic dilatation may be beneficial. Conservative measures are directed at reducing acid production and improvement of gastric and esophageal motility and acid clearance. Psychological and diet counseling are of utmost importance on the way to success.

Surgical options can be directed at improvement of gastric emptying and decrease of acid production. Since there is no fundic tissue available, the possibility of fundoplication is nonexistent. Ligamentum teres cardiopexy has been described. Re-sleeve will decrease the acid production, but there are no studies reporting objective data of the gastric acidity before and after the sleeve gastrectomy. The best possible operation is probably a conversion to Roux-en-Y gastric bypass. This will improve emptying and divert the acid gastric content to the small bowel. A seromyotomy is an alternative for the mechanical and anatomical stenosis of the sleeve (Fig. 31).

Seromyotomy [38] is a difficult procedure but may resolve the problem of symptomatic dysphagia and appearance of de novo GERD symptoms. During this procedure, dissection is performed by hook electrocautery.

This tool and technique allows for a meticulous dissection of the successive muscular layers of the stomach, with very short electrical bursts near the submucosa area. Usually, bleeding encountered during dissection can be controlled by applying pressure with a closed blunt grasper. The goal is to achieve a myotomy 1 cm beyond the stenosis both proximally and distally. If gastric perforation occurs, it can be treated by interrupted intracorporeal absorbable sutures and omentoplasty. The efficacy of the treatment should be assessed by insufflation of air in the stomach. The edges of the myotomized region should easily open up with air insufflation at the end of the procedure. Symmetry of the SG, by observation of a cylindrical gastric tube, should be achieved (Figs. 32 and 33). If after the seromyotomy, an hourglass deformation still remains, and conversion to another bariatric procedure should be considered.

Jorge et al. [37] identified three technical errors that explain most cases of GERD after sleeve gastrectomy: relative narrowing at the junction of the vertical and horizontal parts of the sleeve, dilation of the fundus, and persistence of a hiatal hernia. When they routinely removed the fundus (leaving only enough to allow oversewing), they corrected hiatal hernias when found and avoided relative narrowing or

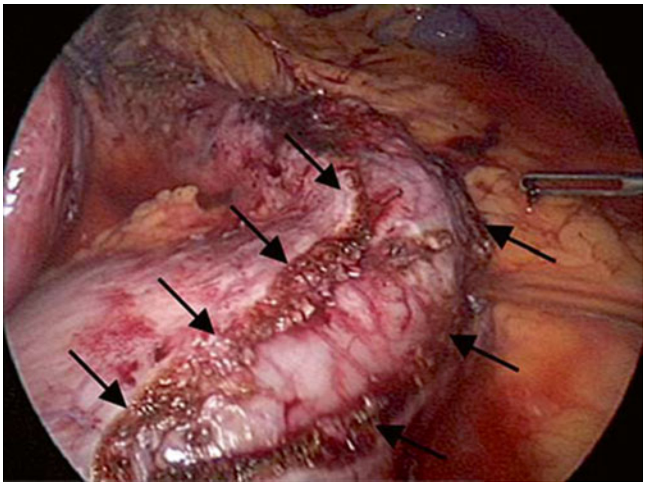

FIG. 31. Final view of laparoscopic seromyotomy. Reproduced with permission from *OBES SURG 2009*;19:495-499. Laparoscopic Seromyotomy for Long Stenosis After Sleeve Gastrectomy with or Without Duodenal Switch.

FIG. 32. Preoperative barium swallow: stricture of the SG at the incisura angularis with GERD symptoms. Reproduced with permission from *OBES SURG 2009*;19:495-499. Laparoscopic Seromyotomy for Long Stenosis After Sleeve Gastrectomy with or Without Duodenal Switch.

torsion of the sleeve; they observed a sharp decrease in the need for postoperative endoscopy to investigate food intolerance or symptoms of GERD. The results of their study

FIG. 33. Postoperative laparoscopic seromyotomy barium swallow: resolution of the stricture. Reproduced with permission from *OBES SURG 2009*;19:495-499. Laparoscopic seromyotomy for long stenosis after sleeve gastrectomy with or without duodenal switch.

show a very low incidence of GERD (1.5 %) at 6–12 months after LSG.

Nutrient Deficiencies After LSG

It has been suggested that LSG has a minimal impact on macronutrients as it does not alter the site of their absorption in the small intestine [39]. Gehrer et al. compared the nutritional deficiencies occurring after LSG and laparoscopic RYGB and observed nutritional deficiencies in 57 % of patients. In particular, after LSG the following deficiencies were observed: folate in 22 %, iron in 18 %, and vitamin B12 in 18 % [40]. Laboratory parameters should be monitored regularly to detect early nutritional deficiencies and to initiate appropriate therapies.

A significant number of patients may develop vitamin B12 deficiency after LSG. Therefore, it is likely that, without supplementation, vitamin B12 deficiencies can occur, especially more than 2 years after operation due to empting of vitamin B12 storage. Therefore, a general vitamin B12 supplementation is advisable to avoid pernicious anemia and to prevent neuropathic pain [41]. This complication could be attributed to fundus resection, which is the most abundant part of the stomach with parietal cells that release intrinsic factor essential for vitamin B12 absorption. Also, PPI (proton pump inhibitor) use might have played an additive role in the development of vitamin B12 deficiency by reducing acidity.

Folate can be absorbed throughout the intestine, especially in the jejunum, and therefore folate deficiency is less common after LSG [42]. A very small amount of folate is stored by the body, and a constant supply of a diet containing foods that are sources of folic acid is necessary to maintain serum concentrations. The best sources of folate are viscera, beans, and green leafy vegetables. Some investigators have reported that low folate levels reflect nonadherence to multivitamin supplementation because the amount of supplemented folic acid properly corrects low serum folate levels. Hakeam et al. reported folate deficiency after surgery, and though patients in this study received a daily supplement containing 0.2-mg folic acid following LSG, folate levels deteriorated throughout the study period. Therefore, patients undergoing LSG might require more than the RDA of folic acid to maintain normal folate levels. This could be attributed to the diet changes after surgery [43]. Also, more attention has to be directed to folic acid and vitamin B12 in females planning to get pregnant after LSG, as folic acid and vitamin B12 deficiency during pregnancy in general population has been linked to the increased risk of neonatal neural tube defects. Close monitoring of vitamin B12 and folate levels is important, and an adequate supplementation is necessary to maintain these parameters in the normal range for all the follow-up period.

Hakeam et al. found a low incidence of iron deficiency (4.9 %) and of anemia (1.6 %) 12 months after surgery [43]. After 1 year, the impact of this bariatric surgery on iron indices was negligible. Therefore, iron supplementation appears unnecessary in nonanemic patients undergoing LSG at least in the interval of 6–12 months after surgery.

Bone metabolism can change during the first year after LSG. Part of this change is explained by the weight loss itself due to the loss of pressure on the weight-bearing bones, thus losing a potent stimulant for bone preservation. Furthermore, normal levels of vitamin D are essential for an adequate intestinal calcium uptake. A shortage in vitamin D eventually leads to a negative calcium balance and causes a compensatory rise in PTH to promote bone resorption. Aarts et al. reported normal calcium levels 1 year after LSG but suboptimal levels of vitamin D, although on daily multivitamin supplementation [44]. Calcium supplementation is important in the first 6 months in the multivitamin formula and it is sufficient to maintain normal plasma values during the follow-up period. Patients with deficiencies in albumin, vitamin D, or calcium have a higher risk of developing osteoporosis; therefore, it is recommended that appropriate supplementations be initiated, even if the concentrations of these parameters are only slightly decreased. PTH levels should be determined to diagnose secondary hyperparathyroidism.

Moreover, supplementation of zinc should be based on symptoms (hair loss, immune deficiency, dry skin). High zinc intake reduces absorption of copper and iron. Zinc and calcium should be taken at different times because zinc reduces calcium absorption. Supplementation of selenium is not generally necessary because postoperative deficiencies normalize on their own without supplementation, and an adequate, varied food intake seems to be sufficient.

Regular determination of laboratory parameters should be performed 3 and 6 months after the operation and semiannually thereafter; if the patient's weight stabilizes, laboratory parameters should be determined once a year.

Conclusion

LSG is an accepted bariatric procedure that can be used for many different patient populations. It has been effectively used as part of a staged risk-management strategy for high-risk patients and has gained popularity as a primary bariatric procedure. The evidence supporting the safety and efficacy of SG continues to increase and long-term data are emerging that report excess weight loss greater than 50 %. There is not yet a standard technique for this procedure. Heterogeneity includes the size of the bougie, beginning site of resection, and reinforcement of the staple line. The solution may lie in finding a suitable size at which the pressure of the tube is not excessive and the restriction is sufficient for obtaining good weight loss results without increasing the risk of complications.

Attractive features of LSG are rapid weight loss, comorbidity reduction, and avoidance of long-term complications of bypass procedures or implantable devices. Concerns remain regarding the risks of leaks, the long-term incidence of GERD symptoms, and the weight loss durability beyond 5 years. Management of leaks after LSG is a formidable challenge for the bariatric surgeon, and early diagnosis followed by a multidisciplinary treatment strategy is key.

Review Questions and Answers

Questions

1. What are the potential causes of post-LSG gastric leak?
   (a) Large hiatal hernia
   (b) Use of a large-size bougie
   (c) Mid-sleeve stenosis
   (d) Staple line near GE junction
   (e) Staple on the migratory crotch staple

2. What are the signs and symptoms of post-LSG GL?
   (a) Persistent hiccups and chronic cough
   (b) Persistent dysphagia with nausea and vomiting
   (c) Diffuse abdominal tenderness
   (d) Unexplained tachycardia (>100/min)
   (e) Localized abdominal tenderness

3. What are the common sites of post-LSG bleeding?
   (a) Mesocolon
   (b) Sleeve staple line
   (c) Short gastric vessels
   (d) Spleen
   (e) Liver

4. What are the treatment options of post-LSG obstruction?
   (a) EGD + dilatation ± stent
   (b) Laparoscopic strictuloplasty
   (c) Laparoscopic RYGB
   (d) Laparoscopic feeding jejunostomy
   (e) Laparoscopic seromyotomy

Correct Answers

1. c, d, e
2. a, c, d, e
3. b, c, d
4. a, b, c, e

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