Gallbladder stones formation in relation to different operations for weight reduction

Mohamed El-Saeed[1], Doaa Omar Refaat[1], Amr Ibrahim[1], Walid A. Mawla[1]
[1]: General surgery Department, Zagazig University, Egypt

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Abstract:

Background: Cholelithiasis is a common complication after bariatric surgery. Pure restrictive procedures such as sleeve gastrectomy and gastric banding theoretically should result in less gallstone formation because the food continues to follow the normal gastrointestinal transit, maintaining the enteric–endocrine reflex intact. Gallstone diseases are one of the most common complications of obesity and after bariatric surgery with multiple risk factors. The role of prophylactic cholecystectomy at the time of bariatric surgery remains controversial. The fact that pathologic evidence of gallbladder diseases has been found in more than 75% of routinely resected specimens supports those who advocate prophylactic cholecystectomy.

Keywords: Gallbladder, Stones, Weight reduction, Operations.

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Introduction:

Based on a survey through The International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) The total number of surgical and endoluminal procedures performed in 2018 in the world was 696,191. Sleeve gastrectomy (SG) remained the most commonly performed bariatric procedure ($N = 386{,}096$; 55.4%). Among the total reported bariatric/metabolic interventions (SG, RYGB, OAGB, BP), 604,223 (86.8%) were primary surgical and 29,167 (4.2%) primary endoluminal operations; 62,801 (9%) were revisional procedures (both surgical and endoluminal). **(Angrisani L. et al., 2021).**

Roux-en-Y gastric bypass (RYGB):

The gastric bypass procedure was developed in the late 1970s and consisted of a horizontal partitioning of the upper stomach to create a small gastric pouch. Gastrointestinal continuity was reestablished with a gastrojejunostomy. A shift to Roux-en-Y reconstruction of continuity soon followed due to a high incidence of complications of bile reflux associated with the loop procedure **(Seeras, et al., 2021).**

Gastric bypass has evolved over the 30 years following its initial description to include multiple modifications. The size of the gastric pouch has gradually been reduced to the present 20 – 30-mL capacity **(Wolfe et al., 2016).**

Historically, the incidence of new gallstone formation following gastric bypass surgery ranges from 32% to 42%, and about one-third to one-half of those patients became symptomatic. Increased gallstone formation in RYGB patients is caused by supersaturation of bile with cholesterol secondary to a reduction in bile acid secretion because of the caloric restriction. Another reason is limited gallbladder contractility and emptying secondary to a reduction in the secretion of cholecystokinin-8 (CCK-8) due to the bypassed duodenum. Most gallstones are formed within the first 6 months postoperatively **(Seeras, et al., 2021).**

Single-Anastomosis Sleeve-Ileal Bypass (SASI):

Single-anastomosis sleeve ileal (SASI) bypass is a simplification of sleeve gastrectomy with transit bipartition. Both share a metabolic foundation through early postprandial ileal brake, and SASI bypass has the advantages of shorter operative time and less incidence of internal herniation **(Khalaf and Hamed, 2021).**

In a recent study, they assessed the outcome of SASI against two standard procedures recognized by the major bariatric societies, the sleeve gastrectomy and one-anastomosis gastric bypass (OAGB). The study concluded that SASI bypass was associated with greater weight loss, better improvement in DM, and more longterm nutritional complications than the other two procedures**.** The size of gastroileal anastomosis should be 2–3 cm because an anastomosis measuring less than 2 cm is more liable to stenosis and obstruction. Although Mahdy et al. recommended the size of the anastomosis to not exceed 3 cm, and the common channel length to be 250–300 cm**,** other reports combined heterogeneous groups of patients with anastomosis size of more than 3 cm and common channel length of up to 350 cm **(Mahdy et al., 2021).** To eliminate such heterogeneity in the technique, the world consensus meeting statement standardized the common channel length to be 300 cm, measuring upwards from the ileocecal junction **(Bhandari et al., 2019).**

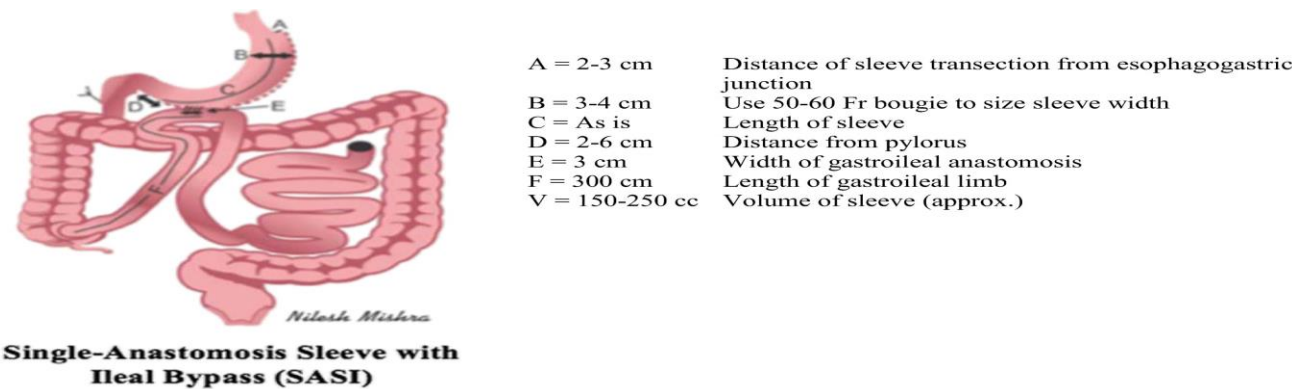

Figure 1: Single-anastomosis sleeve with ileal bypass (SASI) (Bhandari et al., 2019).

Sleeve Gastrectomy

Bariatric surgery has been recognized as the most effective long-term treatment modality for severe obesity. Among various bariatric procedures, laparoscopic Sleeve gastrectomy (SG) remained the most commonly performed bariatric procedure among the total reported bariatric/metabolic interventions. **(Angrisani L. et al., 2021).**

LSG entails resecting the greater curvature and fundus of the stomach; the partial gastrectomy is oriented vertically, parallel to the lesser curvature of the stomach. Originally described in the 1990s as the "Magenstrasse and Mill procedure," the principle of LSG derives from the physiologic "Magenstrasse" (German for "street of the stomach"), which conveys food from the esophagus to the antral "Mill" to be ground and propelled into the duodenum (figure 2) **(CornejoPareja et al., 2019).**

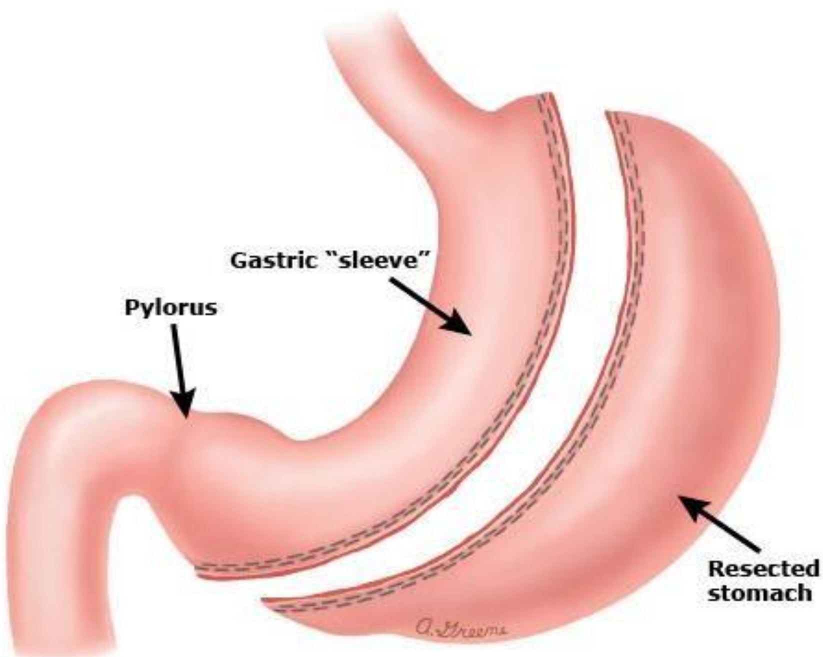

Figure 2: sleeve gastrectomy ***(Kheirvari et al., 2020)***

Although LSG was initially regarded as a purely restrictive procedure, we now know that it also promotes weight loss by inducing anorexia through removal of most ghrelin-producing cells located in the gastric fundus. Overall, LSG results in excellent weight loss and remission of most obesity-related comorbidities. LSG is also less morbid than some of the other bariatric operations, such as laparoscopic Roux-en-Y gastric bypass, because of its technical simplicity and its limited alteration of the normal anatomy. The American Society for Metabolic and Bariatric Surgery (ASMBS) recognizes LSG as either a primary bariatric procedure or the first part of a staged approach in high-risk patients **(Kang et al., 2014).**

Indications:

Like other bariatric operations, LSG is indicated in all patients meeting the 1991 National Institutes of Health (NIH) consensus conference criteria.

Besides being a primary bariatric operation, LSG has also been used as a bridging procedure in super morbid obese patients (BMI of 50 kg/m2 and above) before biliopancreatic diversion with duodenal switch. Additionally, LSG is also a good revisional procedure for patients who fail laparoscopic adjustable gastric banding **(Jeffrey I. et al., 2013).**

Laparoscopic adjustable gastric banding (LAGB).

LAGB procedures are routinely done using a laparoscopic approach, although an open approach can be used if necessary (Figure 3). In these procedures, a band or collar is placed around the upper stomach 1–2 cm below the gastroesophageal junction, thereby creating an approximate 30-mL upper gastric pouch. The degree of constriction of the stomach is variable and may be adjusted by modifying the amount of saline injected into a subcutaneous port, which is linked to a balloon within the confines of the band. The capacity to adjust the degree of constriction is believed to be responsible for the superior outcomes associated with this procedure compared to the largely abandoned VBG **(Billeter et al., 2014).**

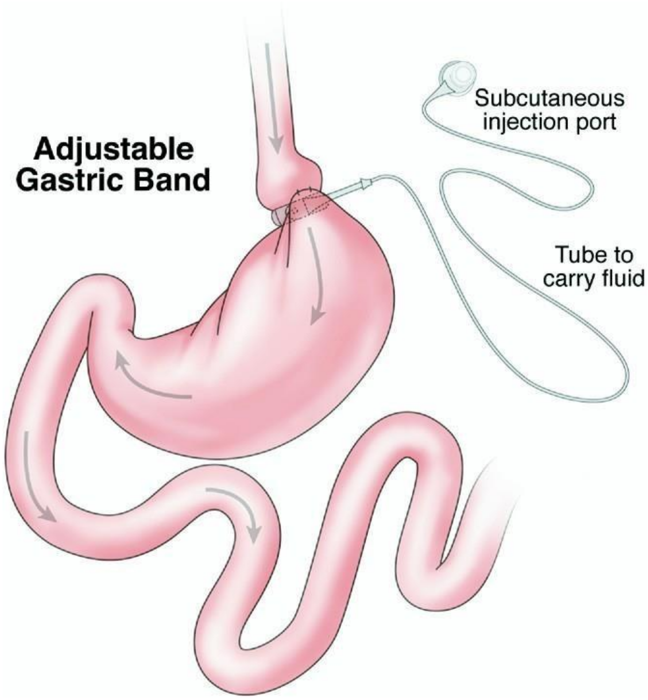

Figure 3. Adjustable gastric band ***(Wolfe et al., 2016).***

Biliopancreatic diversion.

Scopinaro developed the biliopancreatic diversion, creating malabsorption but avoiding the stasis associated with the intestinal bypass by maintaining a flow of bile and pancreatic juice through the biliopancreatic limb **(Scopinaro N, et al, 2005).**

The extent of malabsorption is thought to be a function of the length of the common channel, varying from 50 –125 cm above the ileocecal valve. This procedure is combined with a subtotal gastrectomy as described by Scopinaro **(Seeras, Sankararaman, et al., 2021).**

A modification known as the biliopancreatic bypass with duodenal switch (BPD/DS; Figure 4) consists of a sleeve gastrectomy in which the greater curvature of the stomach is resected creating a tubular section along the lesser curvature of the stomach. The pylorus is preserved, and an ileoduodenostomy is constructed distal to the pylorus. The alimentary and biliopancreatic limbs are generally of approximately equal length **(Seeras, Sankararaman, et al., 2021).**

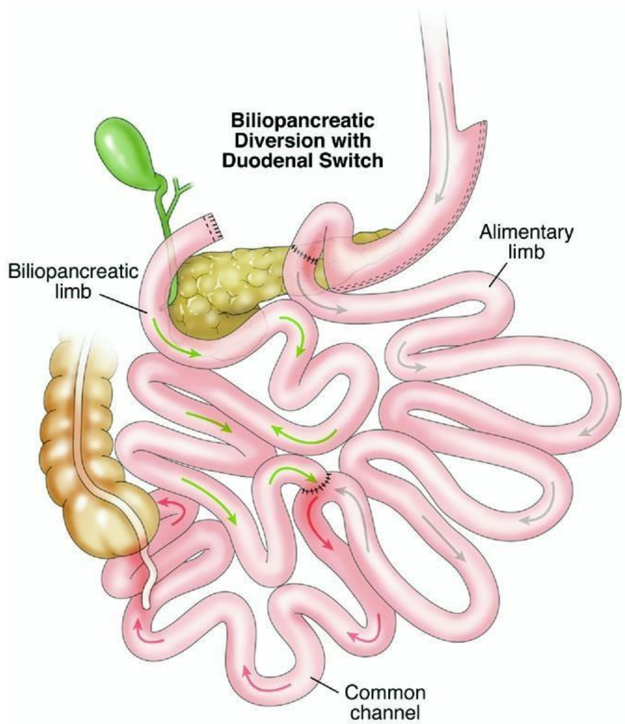

Figure 4. Biliopancreatic diversion with duodenal switch **(Wolfe et al., 2016).**

<u>Complications</u>

There are numerous complications that may arise following any of the bariatric surgical procedures that require understanding and delineation of the specific anatomy of the operation performed. These complications may include nutrient deficiencies or GI pathology **(Lim et al., 2018).**

Nutrient Deficiencies

Any operative procedure that dramatically alters or reduces the anatomic pathways of nutrient intake will necessarily affect the intake of specific nutrients.

Gastric restrictive procedures may lead to nutrient deficiencies due to inadequate intake or nutrient loss because of frequent vomiting, but malabsorption is not an issue **(Sawaya et al., 2012).**

Anastomotic leak

Most commonly occurs at the site of the gastrojejunostomy, but leaks involving the jejunojejunostomy, closure of the gastric staple lines, secondary to other GI injury, may also occur. Most leaks occur in the early postoperative interval and require prompt intervention for resolution **(Seeras, et al., 2021).**

Transluminal endoscopic suturing

Such defect has been attempted, although the efficacy of such intervention remains unknown. The surgical approach is generally to divide the communicating structures and close both sides of the fistula separately. Any GI anastomosis may be followed by development of a stricture. The incidence of stricture of the gastrojejunostomy appears to be higher following laparoscopic gastric bypass than following the open procedure (**Connell, M., et al., 2022).**

Rapid weight loss is a known cause of development of gallstones. Rapid weight loss following bariatric surgery may occur in approximately 30% of gastric bypass patients who retain their gallbladder. Routine oral bile salt administration has been demonstrated to substantially decrease the frequency of this complication. As a result, most bariatric surgery programs advise bile salt supplementation for the first 6 months following gastric bypass. A diagnosis of cholelithiasis should be in mind in any post-bariatric surgery patient with a clinical profile suggesting this diagnosis, even if the gallbladder was known to be free of gallstones before surgery **(Connell, M., et al., 2022)**.

Mechanism of gallstone formation after bariatric surgery:

Lithogenesis is modified following bariatric surgery. Post-bariatric modifications include cholesterol hypersaturation of bile (through cholesterol mobilization from fatty tissues enhancing cholesterol crystallization), decreased secretion of biliary acids (caloric restriction), increased mucin production (enhancing crystallization) and last, gallbladder hypomotility (secondary to decreased cholecystokinin secretion related to the hypocaloric diet, or obesityrelated resistance to cholecystokinin, to gastroduodenal exclusion, or due to intraoperative injury to the hepatic branches of the vagus nerves) **(Leyva-Alvizo et al., 2020).**

During rapid weight loss, the risk for cholesterol gallstone formation increases further in obese subjects. Patients with the highest body mass index (BMI) before weight loss and those who lose weight most rapidly seem to be at the highest risk for gallstone formation. This finding was true in subjects on a weight-reducing diet as well as those subjects undergoing surgical treatment. The mechanism for gallstone formation during rapid weight loss is not quite clear, although different factors have been suggested. According to several studies, cholesterol saturation of bile increases during weight reduction **(Stokes & Lammert, 2021).**

Increased amounts of pronucleating proteins and mucin in the gallbladder, which may predispose to gallstone formation, have also been observed. Poor gallbladder emptying and gallbladder stasis, which allows crystals to grow, have been reported during rapid weight loss by means of certain very low caloric diets. However, most of these studies have been performed on bile samples obtained by duodenal drainage, leading to dilution of the bile and contamination with duodenal content **(Wuttiporn M. et al., 2016).**

Twenty-six normal-weight volunteers (body mass index [BMI} less than 30) were compared with 14 morbidly obese patients (BMI greater than 40). Gallbladder volumes were measured ultrasonographically, after fasting and following stimulation with intravenous cholecystokinin-octapeptide (CCK-8) Preoperatively, fasting gallbladder volume and residual volume after CCK stimulation were both two times greater in the obese group ($P<0.02$ versus controls). Gallbladder refilling was four times higher in the obese patients ($P<0.01$). By six weeks postoperatively, the obese patients lost 1.4±0.1% body weight per week. Gallbladder emptying decreased 18.4% (80.3±3.9% to 65.5±6.9%; $P<0.05$); residual volume rose one-third (not significant), and refilling fell 60.5% (0.43±0.09 to 0.26±0.04 mL/min; $P=0.07$). Three patients with weight losses of greater than 1.7% per week developed- gallstones; gallbladder emptying fell outside the 95 percentiles. By six months, weight loss slowed to 0.5±0.1% per week; gallbladder motility improved modestly. No further stones developed **(Di Ciaula A., et al., 2019).**

Compared with women whose weight changed less than 4 kg, women who lost 4 to 10 kg had a 44% increase in the risk for gallstone disease with the weight loss, and women who lost more than

10 kg had a 94% increase in the risk for gallstone disease when controlling for BMI and other risk factors for gallstones **(Stinton & Shaffer, 2012).**

Clinical studies of persons having rapid weight loss using very low-calorie diets have provided strong evidence of an increased risk for gallstones among the obese who lose large amounts of weight **(Stokes et al., 2014).**

In a study in Italy, gallstones developed in none of 34 obese persons undergoing a 500 kcal/d diet for 90 days within 6 months despite an average 6.6 kg/m reduction in BMI. Maintenance of gallbladder motility was considered the main protective factor. New gallstones developed in only 2 of 38 participants in a study with a more relaxed diet of 800 to 840 kcal/d (15% to 25% from fat), although the study duration was only 10 weeks **(Cunningham R. M., et al., 2021).**

However, it has not been possible to evaluate the effect of weight loss independently of the multiple effects of major abdominal surgery. Weight loss also tends to be greater after surgery. Nevertheless, it is reasonable to assume that the risk for gallstone formation with weight loss dieting would be no greater than the 37.8% risk observed from a compilation of the two surgical series with ultrasound follow-up **(Gutt et al., 2020).**

Follow-up among the surgical patients was longer than among the diet-treated patients, but nearly all the new cases of gallstones probably occurred within the first few months of surgery. Further, the natural history of gallstones, once formed, is probably similar for diet-treated patients .To summarize the experience of the few clinical studies of weight loss dieting and gallstone formation, 12.1% of patients (47 of 390) developed gallstones during the 8 to 16 weeks of supervised very low-calorie diets or shortly thereafter. This risk was less than that found after gastric bypass surgery, in which gallstones developed in 37.8% (42 of 111) of patients within 12 to 18 months of follow-up. Most persons developed gallstones concurrent with dietary therapy or with the period of greatest weight loss after gastric bypass surgery **(Pak M., & Lindseth G., 2016).**

The probability of gallstone formation during these periods was much higher than that expected of equally obese persons who were not losing weight. Approximately one third of patients on a diet and those who were surgically treated became symptomatic within a few months of gallstone formation. Among perhaps half of the asymptomatic patients, gallstones spontaneously disappeared within 1 to 2 years **(Stinton & Shaffer, 2012).**

From these few studies, a rough estimate of the probability of the development of symptomatic gallstones would be about 4% to 6% within 6 months to a year of the initiation of substantial weight loss. However, this estimate is largely determined by the results of one large study in which only 10.9% of dieting patients developed gallstones **(Tanaja et al., 2021).**

The cholesterol saturation index increased on average in some studies, but results among individual patients have varied considerably, with the occurrence of both large increases and decreases during weight loss. The effects of very low calorie and low-fat diets on biliary lipid composition depend on the balance of increased hepatic uptake of cholesterol, diminished dietary intake of cholesterol, and changes in hepatic cholesterol synthesis and bile acid secretion **(Seid & Rosenbaum, 2019).**

As a result, the biliary lipid pattern may become more favorable to gallstone formation during a hypocaloric diet, but this is not a universal effect. Contrary to the mixed findings with low calorie diets, the cholesterol saturation index decreased among nearly all patients during a fast of at least several days. In addition, with weight stabilization after a hypocaloric diet, the cholesterol saturation index decreased to a level lower than the level before weight loss, primarily a result of diminished cholesterol secretion **(Smelt, 2010).**

Nucleation time decreased during weight loss concurrent with an increase in bile glycoprotein concentration. Very low-calorie, low-fat diets may also have increased fasting and residual gallbladder volumes among the obese, consistent with gallbladder hypomotility. The diets that have been associated with gallstone formation in most clinical studies did not have enough fat or protein to maximally stimulate gallbladder contraction **(Garvey W. T., 2016).**

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