

AperTO - Archivio Istituzionale Open Access dell'Università di Torino

## Esophagogastric cancer after bariatric surgery: systematic review of the literature

### **This is the author's manuscript**

*Original Citation:*

*Availability:*

This version is available <http://hdl.handle.net/2318/136200> since

*Published version:*

DOI:10.1016/j.soard.2012.10.002

*Terms of use:*

Open Access

Anyone can freely access the full text of works made available as "Open Access". Works made available under a Creative Commons license can be used according to the terms and conditions of said license. Use of all other works requires consent of the right holder (author or publisher) if not exempted from copyright protection by the applicable law.

(Article begins on next page)



## UNIVERSITÀ DEGLI STUDI DI TORINO

This Accepted Author Manuscript (AAM) is copyrighted and published by Elsevier. It is posted here by agreement between Elsevier and the University of Turin. Changes resulting from the publishing process - such as editing, corrections, structural formatting, and other quality control mechanisms - may not be reflected in this version of the text. The definitive version of the text was subsequently published in [*Surgery for obesity and related diseases*, 9, 1, 2013, 10.1016/j.soard.2012.10.002].

You may download, copy and otherwise use the AAM for non-commercial purposes provided that your license is limited by the following restrictions:

- (1) You may use this AAM for non-commercial purposes only under the terms of the CC-BY-NC-ND license.
- (2) The integrity of the work and identification of the author, copyright owner, and publisher must be preserved in any copy.
- (3) You must attribute this AAM in the following format: Creative Commons BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/deed.en>), <http://dx.doi.org/10.1016/j.soard.2012.10.002>

## **Esophagogastric cancer after bariatric surgery: systematic review of the literature**

- Gitana Scozzari, M.D. Renza Trapani, M.D., Mauro Toppino, M.D., Mario Morino, M.D.

### **Abstract**

#### **Background**

Because the number of patients with a previous bariatric procedure continues to rise, it is advisable for bariatric surgeons to know how to manage the rare event of the development of an esophagogastric cancer. The aim of the study was to perform a systematic review of all reported cases of esophagogastric cancers after bariatric surgery.

#### **Methods**

Systematic review of English and French written literature in MEDLINE and EMBASE database.

#### **Results**

Globally, 28 articles describing 33 patients were retrieved. Neoplasms were diagnosed at a mean of 8.5 years after bariatric surgery (range 2 months–29 years). There were 11 esophageal and 22 gastric cancers; although adenocarcinoma represented most cases (90.6%), a tubulovillous adenoma with high-grade atypia, an intramural gastrointestinal stromal tumor, and a diffuse large B-cell lymphoma of the gastric fundus were also reported. Node involvement was reported in 14 cases, and distal metastases in 5. The most frequently reported symptoms were dysphagia and food intolerance, vomiting, epigastric pain, and weight loss. Surgery was performed in 28 patients, although 4 underwent only chemotherapy and/or radiotherapy and 1 received palliative care. Reported mortality rate was 48.1%.

#### **Conclusions**

To date, it is not possible to quantify the incidence of esophagogastric cancer after bariatric surgery because of the paucity of reported data. Nevertheless, because the main concern is the delay in diagnosis, it is of critical importance to carefully evaluate any new or modified upper digestive tract symptom occurring during bariatric surgery follow-up.

**Keywords:** Obesity, Bariatric surgery, Esophageal cancer, Gastric cancer, Esophagogastric cancer

The number of bariatric surgical procedures has dramatically increased worldwide in the past few years as a result of the increasing prevalence of obesity and because of the excellent results of bariatric surgery in terms of long-lasting weight loss, improvement in obesity-related co-morbidities, and health cost reduction [1].

Because the number of patients with a previous bariatric procedure continues to rise, it is advisable for bariatric surgeons to know how to diagnose and manage the rare event of the development of an esophagogastric cancer in patients who have had bariatric surgery. This is a very rare event, and the literature data are only in the form of isolated case

reports. The aim of the present study was to perform a systematic review of all reported cases of esophagogastric cancers after bariatric surgery.

[Back to Article Outline](#)

## **Methods**

A systematic review of English and French written literature was conducted in the MEDLINE and EMBASE databases. Keywords used were gastric cancer, gastric neoplasm, gastric tumor, gastric carcinoma, gastric adenocarcinoma, esophageal cancer, esophageal neoplasm, esophageal tumor, esophageal carcinoma, and esophageal adenocarcinoma, along with bariatric surgery, obesity surgery, gastric bypass, vertical banded gastroplasty, gastric banding, gastric band, duodenal switch, sleeve gastrectomy, sleeve resection, biliopancreatic diversion, excluded stomach, gastric bypass remnant, bypassed stomach, and gastric fundus.

All abstracts retrieved were screened, and for each one deemed relevant, the full text was obtained. The reference lists of all relevant articles were manually searched to identify any further studies to be included. The search started with the 1990 data, because to the best of our knowledge, the first case was reported in 1991 [2]; the last search was performed on May 31, 2012.

The search was made on human patient studies, and the review included all cases in which the tumor was located in the esophagus, at the esophagogastric junction, in the gastric pouch, or in the bypassed stomach after a bariatric procedure.

[Back to Article Outline](#)

## **Literature review**

Globally, 28 articles describing 33 patients were retrieved [2], [3], [4], [5], [6], [7], [8], [9], [10], [11], [12], [13], [14], [15], [16], [17], [18], [19], [20], [21], [22], [23], [24], [25], [26], [27], [28], [29]; patients' baseline characteristics are summarized in Table 1, Table 2, Table 3. Nineteen patients were females (57.6%) and 14 were males (42.4%); the mean age at diagnosis was 55.1 years (range 38–71 ).

**Table 1. Reported cases of esophageal gastric cancer after bariatric restrictive procedures**

Author and publication year	Gender	Age, yr	Previous bariatric procedure	Years after bariatric surgery	Localization of the tumour	Treatment	Histologic pathways	Cancer staging	Follow-up, mo
Sweet, 1996 [3]	F	53	VBG	13	Entire stomach	Surgery: total gastrectomy	ADK, linitis plastica	T4bN2M0	NR
Zirak, 2002 [4]	F	52	SRVBG	2	Gastric pouch	Surgery: total gastrectomy	ADK	T1N0M0	12; disease-free survival
Papakonstantinou, 2002 [5]	M	46	VBG	6	Distal stomach	Surgery: Whipple procedure; adjuvant chemotherapy	ADK	T4bN1M0	6; death
Jain, 2003 [6]	F	67	VBG	15	Gastric pouch	Surgery: total gastrectomy	ADK	T2N2M0	6; disease-free survival
Snook, 2003 [7]	F	50	Gastric band	6	Distal esophagus	Surgery: band removal; esophageal stenting; palliative chemotherapy	ADK	T?N?M1	24; death
Hackert, 2004 [8]	F	62	Gastric band	10	Gastric pouch/cardia	Surgery: palliative high (near total) gastrectomy; adjuvant chemotherapy	ADK	T2bN?M1	NR
Allen, 2004 [9]	F	57	VBG	16	Gastric pouch/cardia	Surgery: total gastrectomy	ADK	NR	15; death
De Roover, 2006 [10]	F	47	VBG	12	Distal stomach	Surgery: total gastrectomy; Imatinib treatment	High-risk GIST		48; asymptomatic with liver and lungs MTS
Chebib, 2007 [11]	M	60	VBG	15	Gastric pouch (and incidental tubular adenoma at the pylorus)	Surgery: total gastrectomy	ADK	T2bN1M0	12; disease-free survival
Melstrom, 2008 [12]	M	65	VBG	5	Distal esophagus	Chemotherapy and RT; esophageal stenting	ADK	T3N1M1	24; death
Stroh, 2008 [13]	F	65	Gastric band	32 mo	Gastric pouch	Exploratory laparotomy: peritoneal carcinomatosis	NR	NR	5 days; death
Korswagen, 2009 [14]	M	43	Gastric band	2	Distal esophagus	RT for osseous metastases	ADK	T?N?M1	“shortly after diagnosis”; death
Belhaj, 2010 [15]	F	54	SRVBG	10	Distal stomach	Neoadjuvant chemotherapy; surgery: subtotal gastrectomy; adjuvant	ADK	T2bN1M0	24; disease-free survival

Author and publication year	Gender	Age, yr	Previous bariatric procedure	Years after bariatric surgery	Localization of the tumour	Treatment	Histologic pathways	Cancer staging	Follow-up, mo
Stauffer, [16]	2011 M	66	Gastric band	23 mo	Distal esophagus	chemotherapy Surgery: band removal; palliative chemotherapy	ADK	T?N+M?	9; death
Scheepers, [17]	2011 F	57	Sleeve gastrectomy	4 mo	Distal esophagus	Chemotherapy and RT	ADK	T2N1Mx	8; disease-free survival

VBG = vertical banded gastroplasty; SRVBG = silastic ring VBG; CT = chemotherapy; RT = radiotherapy; ADK = adenocarcinoma; MTS = metastases; NR = not reported.

**Table 2. Reported cases of esophageal gastric cancer after gastric bypass: esophageal and gastric pouch cancer**

Author and publication year	Gender	Age, yr	Previous bariatric procedure	Years after bariatric surgery	Localization of the tumour	Treatment	Histologic pathways	Cancer staging	Follow-up, mo
Allen, 2004 [9]	M	54	RYGB	21	Distal esophagus	Surgery: esophagectomy	total ADK	T?N0M0	13; death
	M	50	RYGB	14	Cardia	Surgery: esophagogastrectomy	ADK	T1N?M?	72; disease-free survival
Trincado, 2005 [18]	F	52	RYGB	5	Gastric pouch	Surgery: transhiatal esophago-pouchectomy; adjuvant chemotherapy and RT	ADK	T3N1M0	12; disease-free survival
Babor, 2006 [19]	F	61	Loop-GB	29	Gastric pouch	Surgery: gastrectomy	total ADK	T3N0M0	NR
Nguyen, 2006 [20]	F	51	RYGB	5	Cardia	Surgery: esophagogastrectomy	Barrett's metaplasia with a focus of intramucosal carcinoma	T1N0M0	3.5; disease-free survival
Rogers, 2007 [21]	F	53	RYGB	8	Distal to the gastrojejunal anastomosis in the proximal alimentary limb	Surgery: resection of the small bowel and revision of the gastrojejunostomy	Tubulovillous adenoma with high-grade atypia	NR	NR
Sun, 2008 [22]	M	65	RYGB	5	Gastrojejunal anastomosis	Palliative jejunostomy; palliative care	ADK	T?N+M1	2; death
	M	55	RYGB	2 mo	Distal esophagus	Surgery: esophagectomy	ADK	T1N0M0	NR
Melstrom, 2008 [12]	M	58	RYGB	3	Distal esophagus	Surgery: esophagectomy	ADK	TisN0M0	24; disease-free survival
Kuruba, 2009 [23]	M	45	RYGB	20 mo	Distal esophagus	Neoadjuvant chemotherapy and RT; surgery: esophagogastrectomy; adjuvant chemotherapy	ADK	T2N0M?	12; brain MTS

RYGB = Roux-en-Y gastric bypass; RT = radiotherapy; ADK = adenocarcinoma; MTS = metastases; NR = not reported; ? = data not available.

Table 3. Reported cases of gastric cancer after gastric bypass, excluding stomach cancer

Author and publication year	Gender	Age, yr	Previous bariatric procedure	Years after bariatric surgery	Localization of the tumor	Treatment	Histologic pathways	Cancer staging	Follow-up, mo
Raijman, 1991 [2]	F	38	Loop-GB	5	Excluded stomach	Surgery: distal gastrectomy	ADK	T4bN?M?	3; death
Lord, 1997 [24]	F	71	Loop-GB	13	Excluded stomach	Surgery: distal gastrectomy	2 separate polypoid ADK	T1N0M0	3; disease-free survival
Khitin, 2003 [25]	F	57	Loop-GB	22	Excluded stomach	Surgery: distal gastrectomy	ADK	T3N+M0	NR
Escalona, 2005 [26]	F	51	RYGB	8	Excluded stomach	Surgery: total gastrectomy; adjuvant chemotherapy	ADK	T4N3M0	7; survival
Corsini, 2006 [27]	M	57	Banded RYGB	4	Excluded stomach	Surgery: palliative gastroenterostomy	ADK	T4bN+M?	3; death
De Roover, 2006 [10]	M	66	RYGB	3	Excluded stomach	Surgery: distal gastrectomy; adjuvant chemotherapy	Diffuse large B-cell lymphoma		10; clinical and radiologic remission
Harper, 2007 [28]	F	45	Banded RYGB	1	Excluded stomach	Surgery: palliative decompressive gastrostomy tube; palliative chemotherapy and RT	ADK	T4bN+M'	4; death
Watkins, 2007 [29]	M	44	RYGB	18	Excluded stomach	Surgery: distal gastrectomy	ADK	T3N0M0	26; death

RYGB = Roux-en-Y gastric bypass; RT = radiotherapy; ADK = adenocarcinoma; MTS = metastases; NR = not reported ; ? = data not available.

The previous bariatric operation was a restrictive procedure in 15 patients (45.5%), namely, a vertical banded gastroplasty (VBG) in 9 patients, a gastric band in 5, and a sleeve gastrectomy in 1, and 18 patients (54.5%) underwent a gastric bypass (loop gastric bypass [loop-GB] in 4 patients and Roux-en-Y gastric bypass [RYGB] in 14).

Neoplasms were diagnosed at a mean of 8.5 years after bariatric surgery, ranging 2 months to 29 years. Overall, there were 11 esophageal and 22 gastric cancers. In patients with a previous restrictive procedure, tumors were localized in the esophagus in 5 patients and in the stomach in 10; in patients with a previous loop-GB, all tumors were located in the gastric pouch; in patients who had undergone RYGB, the cancer was localized in the esophagus in 6 and in the stomach in 8; among the latter, 3 were located in the gastric pouch and 5 in the bypassed gastric remnant.

Pathologic findings were reported in 32 patients; although adenocarcinoma represented most cases (29 patients, 90.6%), a tubulovillous adenoma with high-grade atypia [21], an intramural gastrointestinal stromal tumor (GIST) [10], and a diffuse large B-cell lymphoma of the gastric fundus [10] were also reported. Node involvement was reported in 14 patients, and distal metastases was reported in 5. Cancer staging is reported in Table 1, Table 2, Table 3.

Nine studies reported data on preoperative upper endoscopy; in 4 of them [14], [17], [22], [28], a preoperative endoscopy had not been performed, and in 5 studies, a preoperative endoscopy had been performed [7], [9], [13], [20], [27]. Among these studies, there was 1 normal endoscopic appearance [13], 1 patient with gastric pouch ulcerations [7], 1 patient with intestinal metaplasia in the stomach [27], and 2 patients with Barrett's esophagus [9], [20]. In the latter 2, an adenocarcinoma of the esophagogastric junction developed 21 years [9] and 5 years [20] later. In the first patient [9], the upper endoscopy found no atypia in the columnar-lined esophagus 16 years after RYGB, although atypia was found 18.5 years after RYGB. Afterward, the patient failed to have an endoscopic surveillance until dysphagia onset and subsequent adenocarcinoma diagnosis. In the 4 studies reporting that preoperative endoscopy had not been performed [14], [17], [22], [28], cancer



diagnosis was reported at a mean of 25 months after surgery (range 4–60 months), and in the 5 patients with preoperative endoscopy [7], [9], [13], [20], [27], cancer diagnosis was reported at a mean of 92.8 months (range 32–252 ;  $P = ns$ ).

Preoperative detection of *Helicobacter pylori* (Hp) was available only in 4 studies [11], [13], [15], [27]; in 2 of them, Hp testing had not been performed [11], [15], and in 2 studies, it had, proving positive in 1 case [27] and negative in the other [13]. At the cancer diagnosis, Hp detection was reported in 6 patients [6], [10], [11], [22], [24], [27], proving positive in 2 of them [6], [27].

The most frequently reported symptoms were dysphagia and food intolerance, vomiting, epigastric pain, and weight loss; symptom frequency is summarized in Table 4. Reported diagnostic examinations were upper endoscopy, abdominal computed tomography (CT), upper gastrointestinal (GI) contrast series, and less frequently, chest CT, positron emission tomography (PET), magnetic resonance imaging (MRI), endoscopic ultrasound, abdominal ultrasound (US), and x-ray . Surgery was performed in 28 patients, 4 patients underwent only chemotherapy and/or radiotherapy, and 1 patient underwent palliative care.

**Table 4. Frequency of reported symptoms**

<b>Symptoms</b>	<b>Number of patients with reported symptoms</b>
Dysphagia/food intolerance	14
Nausea/vomiting/regurgitation	13
Abdominal/epigastric pain	11
Weight loss	10
Anemia	5
Melena	3
Heartburn	3
Anorexia	3
Fever	2
General malaise	2
Abdominal distention	2
Early satiety	1
Upper gastrointestinal bleeding	1
Left shoulder pain	1
Back pain	1

Follow-up data were available in 27 patients; mean follow-up length was 14.7 months (range 5 days–6 years). Among these 27 patients, death was reported in 13 (mortality rate 48.1%), at a mean of 10.8 months after cancer diagnosis (range 5 days–26 months). Disease-free survival was reported in 11 patients, with a mean follow-up of 17 months (range 3–24 months), whereas 3 patients survived with metastases.

In 8 patients, a tumor was diagnosed within 3 years after bariatric surgery (range 2–32 months). These 8 patients had had a VBG in 1 case [4], a gastric band in 3 [13], [14], [16], a sleeve gastrectomy in 1 [17], and a RYGB in 3 [12], [23], [28]. In this group of patients, preoperative upper endoscopy had not been performed in 3 patients [14], [17], [28] and had been performed in 2 patients [4], [13], revealing normal appearance. In 3 patients, no data were available regarding preoperative workup [12], [16], [23]. Among these 8

patients, disease-free survival was reported in 2 patients [4], [17] and survival with brain metastases was reported in 1 [23]. Mortality was reported in 4 patients [13], [14], [16], [28], and follow-up data were not available in 1 patient. Thus, mortality rate in this group was 57.1% compared with 45.0% in patients who had a tumor >3 years after surgery ( $P = ns$ ).

## Discussion

Several epidemiologic data linking obesity and esophagogastric neoplasms are available to date [30], especially for esophageal cancer. In a meta-analysis of 5000 patients with esophageal or cardia carcinoma, a body mass index (BMI) >25 was associated with increased risk, with odds ratio of 2.0 for women and 2.2 for men [31]. This relationship appears to be related to the significant increase of gastroesophageal reflux disease (GERD) and erosive esophagitis in obese patients [31], [32], with subsequent higher risk of Barrett's esophagus and esophageal carcinoma, and to the carcinogenic effect of hormones, including insulin and insulin-like growth factor, which is typically increased in obese patients [33].

In obese patients undergoing bariatric procedure, the actual incidence of gastroesophageal neoplasm onset is not completely understood because of the scarce literature available. From general surgery literature, it is known that Billroth II gastrectomy is associated with a 3-fold increase in risk in the proximal gastric remnant compared with the general population [34]; however, in a bariatric surgery population, Melstrom et al. [12] reported that in a series of 2875 patients who had bariatric procedures, 3 patients had high-grade dysplasia or adenocarcinoma of the cardia, resulting in an incidence rate of .1%.

From a pathophysiologic point of view, post-bariatric surgery anatomy may increase carcinogenic risk. Gastric mucosal changes have been described after bariatric procedures [35], and the reported cases of gastric carcinoma classically arise in a milieu of intestinal metaplasia, atrophy, and foveolar hyperplasia both in restrictive procedures and in RYGB remnant. In the post-VBG gastric carcinoma reported by Chebib et al. [11], there was florid mucosal atrophy, intestinal metaplasia, and foveolar hyperplasia at the perimeter of the gastric pouch adenocarcinoma and atrophy and metaplasia in the remainder of the pouch and stomach, and in Corsini et al. [27] the mucosa surrounding the antral adenocarcinoma in a patient who had undergone RYGB was found to have intestinal metaplasia.

For esophagogastric neoplasms after restrictive bariatric procedures (i.e., gastric banding, VBG, and sleeve gastrectomy), the main pathophysiologic explanations are chronic GERD, which can promote Barrett's esophagus development [36]; stasis of food and gastric acid in the pouch causing chronic mucosal irritation [6], [9]; and local irritation caused by the presence of the gastric band [8]. Chronic GERD may represent an important risk factor, because the association between restrictive procedures and de novo or worsened GERD symptoms has been clearly described [37]. Chronic GERD may be related to higher incidence of Barrett's esophagus [36]; although the actual incidence of Barrett's esophagus in restrictive procedures is unknown, the link between chronic GERD and metaplasia is well established, as is the fact that patients with >2 cm of Barrett's mucosa are 30–40 times more likely to develop adenocarcinoma of the esophagus than the general population [38]. Also, the presence of the band may have significant effects [35], [39]. Negri et al. [35] reported in a study of 31 VBG patients that, although in most cases the proximal pouch and distal pouch were macroscopically normal, the transitional zone showed pathologic findings. The effects of the mesh may be related not only to the foreign body itself, which can cause adhesion and local reaction [35], but also to the internal pressure against the mucosa and the decreased blood flow with consequent

decrease in parietal cell numbers and metaplastic changes in the mucosa, which may progress to malignancy [6], [10], [39]. Furthermore, the gastric band can induce esophageal dysmotility in the long-term follow-up [40], thus worsening the effects of distal esophagus exposure to gastric acids. Other potential carcinogenic mechanisms after restrictive procedures may be food stasis with impaction and/or friction of the gastric mucosa [3], [8], [35] and the prolonged contact between the gastric pouch mucosa and food or other exogenous carcinogens related to decreased gastric emptying.

RYGB, one of the most widely used bariatric procedures, involves the risk of neoplasms both in the gastric pouch and in the excluded, bypassed stomach; the risk in the latter site is not completely understood, because although the distal stomach is excluded from contact with exogenous carcinogens, it may suffer from prolonged contact with pancreaticobiliary reflux with pooled bile [2], [5], [18], [25], [41], which has been reported to promote intestinal metaplasia and carcinogenesis experimentally [42]. The presence of bile in the excluded stomach is well described. Kuga et al. [43] found bile in the excluded stomach in 68.6% of 35 patients, and Sundbom et al. [44] found scintigraphically bile reflux in 36% of patients. On the other hand, Inoue et al. [45] reported a protective effect of RYGB against diet-induced gastric cancer in a rodent model, with an impressive 4-fold reduction in incidence, explained by the authors by the lack of direct contact with carcinogens, lower bile reflux, and a lower bacteria concentration in the gastric content.

Also, in the RYGB excluded stomach, frequent mucosal changes have been described. A recent study [46] on a rodent model of RYGB reported a higher bacterial and fungal count in the gastric remnant mucosa and a higher incidence of atrophy, intestinal metaplasia, and neutrophilic polymorphonuclear inflammation than in sham-operated rats. In human studies, various type of chronic gastritis (erythematous, erosive, hemorrhagic, and atrophic) have been described in the gastric remnant in percentages of up to 100% of patients [43], [47], and in the 10–12 % of cases histologically confirmed, intestinal metaplasia has been reported [47].

Finally, a specific concern of RYGB is its role in the physiology of esophageal reflux. On one hand, a positive effect on acid reflux is well described, with postoperative clinical and endoscopic improvement [48] to a degree even superior to fundoplication [49], leading some authors to advocate the RYGB as the most effective antireflux procedure. Moreover, in some patients, a regression of Barrett's metaplasia has been reported, both in short-segment and in long-segment Barrett's esophagus [50]. On the other hand, the presence of bile in the gastric pouch has been recently recognized as a possible cause of postoperative pain and dysphagia in patients who have had RYGB [51], [52], and our unpublished personal data on postoperative esophageal impedance-pH have clearly shown the presence of bile reflux after RYGB in most patients. Although the actual effects of Roux-en-Y reconstruction on bile esophageal reflux are still under debate, alkaline reflux is widely accepted as contributing factor for esophagitis [53], Barrett's esophagus [54], [55], and adenocarcinoma development [56], [57], [58], [59], [60].

The role of Hp has been investigated in several studies, which have pointed out that Hp may persist in the excluded stomach after RYGB in up to 20% of patients even if routinely eradicated when present before surgery [43], [47]; this evidence strongly strengthens the indication to preoperative assessment and adequate eradication.

## **Diagnostic assessment**

The main concern in esophagogastric neoplasms after bariatric procedures is the delay in diagnosis, because the symptoms may be attributed by the patient to the effects of surgery; furthermore, the patient may be happy with further weight loss, thus delaying the access to medical assessment.

When a patient who has had previous bariatric surgery presents with symptoms suggestive of esophagogastric neoplasms, it is vital to exhaustively study the upper GI. Upper endoscopy has a critical importance in the diagnostic evaluation. During this evaluation, it is important to obtain a complete dilation of any strictures that could hamper the evaluation of the whole stomach. In the case reported by Sweet et al. [3], endoscopy found a marked stenosis of the pouch outlet with no evidence of mass or ulceration within the pouch, but once the outlet was dilated, a narrowed outlet with suboptimal filling of the remainder stomach could be seen on the subsequent contrast study, leading to surgical exploration.

In the case of RYGB, the postoperative anatomy renders the distal stomach difficult to access by conventional endoscopic and radiologic investigation, and this has led several authors to describe different techniques allowing the bypassed stomach to be studied.

CT can be used to evaluate any distention of the gastric remnant, but mucosal abnormalities cannot be assessed, and the use of oral contrast will not opacify gastric remnant; thus, small or early lesions can be misdiagnosed [29]. A virtual gastroscopy approach was described by Silecchia et al. [61] in 2002. By percutaneous puncture, the excluded stomach was filled with saline solution or air, enabling a thin slice image acquisition of the distended stomach and duodenum to be obtained, which gave, in the opinion of the authors, an excellent intraluminal view. More recently, Alva et al. [62] described a similar technique that was completely noninvasive. The authors obtained the distention of the excluded stomach by means of ingested effervescent granules, thought to act by generating gas with the potential to reflux in the excluded stomach. Although more detailed than standard CT, virtual gastroscopy has the same limitations as the former, because it may not reveal fine mucosal details, thus misdiagnosing early lesions, and it is impossible to obtain samples for histologic evaluation.

Post-RYGB endoscopic evaluation has been described, both via a retrograde approach and with double-balloon technique. Retrograde endoscopy via the biliopancreatic limb has been reported [24], [41], with several authors reporting the use of a pediatric colonoscope [41]. Failures of this approach can result from too narrow of a gastrojejunostomy or from the inability to advance the endoscope beyond the angulations of the jejunojejunostomy or the ligament of Treitz. The double-balloon endoscopy was described by Yamamoto et al. in 2001 [63]. This method involves the use of 2 balloons, 1 attached to the tip of the endoscope and the other at the distal end of the overtube; when inflated, the balloons make it possible to straighten the small bowel, preventing loop formation and avoiding postoperative abdominal adhesions. In 2005, Sakai et al. [64] reported successfully reaching the excluded stomach in 5 of 6 patients, and both Kuga et al. [43] and Safatle-Ribeiro et al. [47] reported a success rate of 87.5%.

Endoscopic evaluation of the bypassed stomach has also been described by a percutaneous approach. This approach involves creating a percutaneous route by a long-needle puncture of the excluded stomach under radiologic CT or US guidance followed by percutaneous endoscopy through a gastrostomy [65] or a gastrostomy tube introduced into the excluded stomach by a radiopaque marker inserted during the RYGB operation and allowing radiologic localization of the bypassed stomach [66]. More recently, Watkins et al. [29] recommended performing routinely a gastropexy of the antral area on the inside surface of the abdominal wall, encircling the edges of the site by a radiopaque marker. Other authors have also described laparoscopic-assisted transgastric endoscopy [67].

To overcome the potential problems arising from the bypassed stomach, Cariani et al. described in 2003 a functional RYGB where a band surrounding the gastrogastic outlet allows access from the stapled gastric pouch into the distal stomach [68], [69]. This technique, also called gastric bypass-on-VBG, acts functionally like a standard RYGB, with similar reported weight loss results [70], but allows access from the gastric pouch to the

gastric fundus, which can be easily evaluated by endoscopic and radiologic studies. Given the clinical delay, technical difficulties, and diagnostic power limits of the available diagnostic tools, most authors recommend continual periodic endoscopic surveillance after bariatric procedures [4], [5], [11], [17], [19], [22], [43].

## **Preoperative screening**

Several authors recommend routine preoperative upper endoscopy before bariatric surgery [12], [13], [14], [16], [22], because a consistent percentage of patients may have preoperative pathologic features that should be treated before surgery or involve changing the type of surgery. For instance, a patient who is positive for Hp preoperatively can be treated before surgery; as also recommended by other authors [26], in our department the preoperative evaluation of patients undergoing bariatric procedures routinely includes upper GI endoscopy and eradication of Hp, if detected. Moreover, preoperative biopsy findings can indicate strict postoperative follow-up, such as in the case of mucosal metaplasia [12]. In patients in whom intestinal metaplasia is detected before RYGB, some authors recommend the resection of the bypassed stomach to reduce the risk of future complications [71]. Some cases of esophagogastric neoplasms may also be present before surgery, thus leading to a change in surgical plans. Recently, a case of esophageal carcinoma discovered after laparoscopic sleeve gastrectomy was described only 4 months after surgery [17], underlining the critical importance of extensive preoperative evaluation. In the present review, patients who had not undergone preoperative endoscopy were diagnosed with cancer at a shorter follow-up time than those with preoperative endoscopic assessment (25 versus 93 months); although not statistically significant, this difference has an undeniable clinical significance.

The actual percentage of pathologic findings in preoperative endoscopy is still being debated but seems to be consistent. In a retrospective analysis of 169 patients who had undergone upper endoscopy before RYGB, Barrett's esophagus was present in 1.3% of patients and other pathologic features, such as esophagitis, in 66.6% [72]. Sharaf et al. [73] reported a clinically significant lesion in 61.5% of 195 patients undergoing preoperative upper endoscopy. One of the few prospective studies [74], based on 626 patients, found endoscopic abnormalities in 46% of patients, with the most common findings being gastritis (21%) and esophagitis (16%). Also, a case of gastric cancer was found, thus underlining once again the importance of preoperative evaluation. An important aspect of this study was that the patients' ages were associated with abnormal endoscopy, as the patients with abnormal endoscopy were significantly older than those with normal endoscopic findings. Boru et al. [75], in a wide retrospective analysis of cancer incidence in more than 1330 obese patients, reported 2 GISTs with borderline malignancy, 1 diagnosed intraoperatively and 1 preoperatively, and a case of gastric adenocarcinoma diagnosed during preoperative evaluation.

On the other hand, in 448 consecutive preoperative endoscopy studies in bariatric patients, positive findings leading to a change in medical treatment were found in 18% of patients, and a change in the timing or surgical technique was needed in only 1% of patients [76].

## **Conclusions**

We recognize as a main limitation in the present study the fact that the evidence level of the available literature is low, because all reported cases were in the form of isolated case reports. Consequently, given the lack of prospective epidemiologic data, it was not possible to analyze the real incidence of esophagogastric cancer in bariatric patients,

because the reported cases were derived from bariatric series of unknown size and came from different countries, thus no incidence comparisons could be made with the general population. Furthermore, the limited sample size did not allow identification of patient- or procedure-related risk factors. Despite these limits, the present study is the first to systematically review all the reported cases of esophagogastric cancer in patients who have had bariatric surgery.

We can conclude that, in light of the available literature, it is not possible to quantify the incidence of esophagogastric cancer after bariatric surgery because of the paucity of reported data. Although the risk appears to be low, considering the number of reported cases compared with the number of bariatric procedures performed annually worldwide, it may be affected by the retrospective, anecdotal report of cases, thus strongly underlining the need for wider, epidemiologic studies. Furthermore, because it is possible that a number of esophagogastric cancer cases have not been reported, it is advisable that the bariatric community makes all efforts to publish all cases encountered and share its experience to allow a more precise comparison between the post-bariatric surgery and general population. Although the incidence of esophagogastric cancer in patients with a previous bariatric procedure, namely in patients with an excluded stomach, does not seem to be greater than in the general population, it is critically important to bear in mind that patients who have had bariatric surgery represent an ever-increasing population that includes many adolescents.

The main concern in esophagogastric neoplasms after bariatric procedures is the delay in diagnosis, because the symptoms may be attributed to the effects of surgery. Because the investigation of new or modified upper GI symptoms may allow earlier diagnosis, it is of critical importance to carefully evaluate any new or modified upper digestive tract symptom occurring during bariatric surgery follow-up. Furthermore, although preoperative endoscopy may detect abnormalities and guide future evaluations, several authors also recommend long-term follow-up, with periodic endoscopic surveillance.

## References

1. Sjöström L, Lindroos AK, Peltonen M, et al. **Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery.** *N Engl J Med.* 2004;351:2683–2693
2. Rajjman I, Strother SV, Donegan WL. **Gastric cancer after gastric bypass for obesity. Case report.** *J Clin Gastroenterol.* 1991;13:191–194
3. Sweet WA. **Linitis plastica presenting as pouch outlet stenosis 13 years after vertical banded gastroplasty.** *Obes Surg.* 1996;6:66–70
4. Zirak C, Lemaitre J, Lebrun E, Journé S, Carlier P. **Adenocarcinoma of the pouch after silastic ring vertical gastroplasty.** *Obes Surg.* 2002;12:693–694
5. Papakonstantinou A, Moustafellos P, Terzis I, Stratopoulos C, Hadjiyannakis EI. **Gastric cancer occurring after vertical banded gastroplasty.** *Obes Surg.* 2002;12:118–120
6. Jain PK, Ray B. **Royston CM. Carcinoma in the gastric pouch years after vertical banded gastroplasty.** *Obes Surg.* 2003;13:136–137
7. Snook KL, Ritchie JD. **Carcinoma of esophagus after adjustable gastric banding.** *Obes Surg.* 2003;13:800–802
8. Hackert T, Dietz M, Tjaden C, Sieg A, Buchler MW, Schmidt J. **Band erosion with gastric cancer.** *Obes Surg.* 2004;14:559–561
9. Allen JW, Leeman MF, Richardson JD. **Esophageal carcinoma following bariatric procedures.** *JLS.* 2004;8:372–375

10. De Roover A, Detry O, de Leval L, et al. **Report of two cases of gastric cancer after bariatric surgery: lymphoma of the bypassed stomach after Roux-en-Y gastric bypass and gastrointestinal stromal tumor (GIST) after vertical banded gastroplasty.** *Obes Surg.* 2006;16:928–931
11. Chebib I, Beck PL, Church NG, Medlicott SA. **Gastric pouch adenocarcinoma and tubular adenoma of the pylorus: a field effect of dysplasia following bariatric surgery.** *Obes Surg.* 2007;17:843–846
12. Melstrom LG, Bentrem DJ, Salvino MJ, Blum MG, Talamonti MS, Printen KJ. **Adenocarcinoma of the gastroesophageal junction after bariatric surgery.** *Am J Surg.* 2008;196:135–138
13. Stroh C, Hohmann U, Urban H, Manger T. **Gastric cancer after laparoscopic adjustable gastric banding.** *Obes Surg.* 2008;18:1200–1202
14. Korswagen LA, Schrama JG, Bruins Slot W, Hunfeld MA. **Adenocarcinoma of the lower esophagus after placement of a gastric band.** *Obes Surg.* 2009;19:389–392
15. Belhaj A, Memmo L, Mehdi A, Mboti F, Closset J. **[Gastric adenocarcinoma following "silastic vertical ring gastroplasty": case report].** *Rev Med Brux.* 2010;31:459–462
16. Stauffer JA, Mathew J, Odell JA. **Esophageal adenocarcinoma after laparoscopic gastric band placement for obesity.** *Dis Esophagus.* 2011;24:E8–10
17. Scheepers AF, Schoon EJ, Nienhuijs SW. **Esophageal carcinoma after sleeve gastrectomy.** *Surg Obes Relat Dis.* 2011;7:e11–e12
18. Trincado MT, del Olmo JC, García Castaño J, et al. **Gastric pouch carcinoma after gastric bypass for morbid obesity.** *Obes Surg.* 2005;15:1215–1217
19. Babor R, Booth M. **Adenocarcinoma of the gastric pouch 26 years after loop gastric bypass.** *Obes Surg.* 2006;16:935–938
20. Nguyen NT, Tran CL, Gelfand DV, et al. **Laparoscopic and thoracoscopic Ivor Lewis esophagectomy after Roux-en-Y gastric bypass.** *Ann Thorac Surg.* 2006;82:1910–1913
21. Rogers AM, Capen J, Galka E, Cooney RN. **Tubulovillous adenoma with atypia found at gastrojejunal anastomosis 8 years after gastric bypass for morbid obesity.** *Surg Obes Relat Dis.* 2007;3:559–560
22. Sun C, Jackson CS, Reeves M, Rendon S. **Metastatic adenocarcinoma of the gastric pouch 5 years after Roux-en-Y gastric bypass.** *Obes Surg.* 2008;18:345–348
23. Kuruba R, Jawad M, Karl RC, Murr MM. **Technique of resection of esophageal adenocarcinoma after Roux-en-Y gastric bypass and literature review of esophagogastric tumors after bariatric procedures.** *Surg Obes Relat Dis.* 2009;5:576–581
24. Lord RV, Edwards PD, Coleman MJ. **Gastric cancer in the bypassed segment after operation for morbid obesity.** *Aust N Z J Surg.* 1997;67:580–582
25. Khitin L, Roses RE, Birkett DH. **Cancer in the gastric remnant after gastric bypass: a case report.** *Curr Surg.* 2003;60:521–523
26. Escalona A, Guzmán S, Ibáñez L, Meneses L, Huete A, Solar A. **Gastric cancer after Roux-en-Y gastric bypass.** *Obes Surg.* 2005;15:423–427
27. Corsini DA, Simoneti CA, Moreira G, Lima SE, Garrido AB. **Cancer in the excluded stomach 4 years after gastric bypass.** *Obes Surg.* 2006;16:932–934
28. Harper JL, Beech D, Tichansky DS, Madan AK. **Cancer in the bypassed stomach presenting early after gastric bypass.** *Obes Surg.* 2007;17:1268–1271

29. Watkins BJ, Blackmun S, Kuehner ME. **Gastric adenocarcinoma after Roux-en-Y gastric bypass: access and evaluation of excluded stomach.** *Surg Obes Relat Dis.* 2007;3:644–647
30. Yang P, Zhou Y, Chen B, et al. **Overweight, obesity and gastric cancer risk: results from a meta-analysis of cohort studies.** *Eur J Cancer.* 2009;45:2867–2873
31. Hampel H, Abraham NS, El-Serag HB. **Meta-analysis: obesity and the risk for gastroesophageal reflux disease and its complications.** *Ann Intern Med.* 2005;143:199–211
32. Corley DA, Kubo A, Levin TR, et al. **Abdominal obesity and body mass index as risk factors for Barrett's esophagus.** *Gastroenterology.* 2007;133:34–41
33. Nilsson M, Lagergren J. **The relation between body mass and gastro-oesophageal reflux.** *Best Pract Res Clin Gastroenterol.* 2004;18:1117–1123
34. MacDonald WC, Owen DA. **Gastric carcinoma after surgical treatment of peptic ulcer: an analysis of morphologic features and a comparison with cancer in the nonoperated stomach.** *Cancer.* 2001;91:1732–1738
35. Negri M, Bendet N, Halevy A, et al. **Gastric mucosal changes following gastroplasty: a comparative study between vertical banded gastroplasty and silastic ring vertical gastroplasty.** *Obes Surg.* 1995;5:383–386
36. Näslund E, Stockeld D, Granström L, Backman L. **Six cases of Barrett's esophagus after gastric restrictive surgery for massive obesity: an extended case report.** *Obes Surg.* 1996;6:155–158
37. Tutuian R. **Obesity and GERD: pathophysiology and effect of bariatric surgery.** *Curr Gastroenterol Rep.* 2011;13:205–212
38. Fitzgerald RC. **Molecular basis of Barrett's oesophagus and oesophageal adenocarcinoma.** *Gut.* 2006;55:1810–1820
39. De Roover A, Detry O, Desaive C, et al. **Risk of upper gastrointestinal cancer after bariatric operations.** *Obes Surg.* 2006;16:1656–1661
40. Suter M, Dorta G, Giusti V, Calmes JM. **Gastric banding interferes with esophageal motility and gastroesophageal reflux.** *Arch Surg.* 2005;140:639–643
41. Sinar DR, Flickinger EG, Park HK, Sloss RR. **Retrograde endoscopy of the bypassed stomach segment after gastric bypass surgery: unexpected lesions.** *South Med J.* 1985;78:255–258
42. Miwa K, Fujimura T, Hasegawa H, et al. **Is bile or are pancreaticoduodenal secretions related to gastric carcinogenesis in rats with reflux through the pylorus?.** *J Cancer Res Clin Oncol.* 1992;118:570–574
43. Kuga R, Safatle-Ribeiro AV, Faintuch J, et al. **Endoscopic findings in the excluded stomach after Roux-en-Y gastric bypass surgery.** *Arch Surg.* 2007;142:942–946
44. Sundbom M, Hedenström H, Gustavsson S. **Duodenogastric bile reflux after gastric bypass: a cholescintigraphic study.** *Dig Dis Sci.* 2002;47:1891–1896
45. Inoue H, Rubino F, Shimada Y, et al. **Risk of gastric cancer after Roux-en-Y gastric bypass.** *Arch Surg.* 2007;142:947–953
46. Cunha Medeiros A, Meneses Rego A, Medeiros Azevedo I, Ferreira Carvalho M, Brasil Medeiros V, Araujo-Filho I. **Metabolism and gastric remnant changes after Roux-en-Y gastric bypass in rats.** *J Invest Surg.* 2011;24:109–114
47. Safatle-Ribeiro AV, Kuga R, Iriya K, et al. **What to expect in the excluded stomach mucosa after vertical banded Roux-en-Y gastric bypass for morbid obesity.** *J Gastrointest Surg.* 2007;11:133–137



48. Nelson LG, Gonzalez R, Haines K, Gallagher SF, Murr MM. **Amelioration of gastroesophageal reflux symptoms following Roux-en-Y gastric bypass for clinically significant obesity.** *Am Surg.* 2005;71:950–954
49. Csendes A, Smok G, Burdiles P, Braghetto I, Castro C, Korn O. **Effect of duodenal diversion on low-grade dysplasia in patients with Barrett's esophagus: analysis of 37 patients.** *J Gastrointest Surg.* 2002;6:645–652
50. Houghton SG, Romero Y, Sarr MG. **Effect of Roux-en-Y gastric bypass in obese patients with Barrett's esophagus: attempts to eliminate duodenogastric reflux.** *Surg Obes Relat Dis.* 2008;4:1–5
51. Swartz DE, Mobley E, Felix EL. **Bile reflux after Roux-en-Y gastric bypass: an unrecognized cause of postoperative pain.** *Surg Obes Related Dis.* 2009;5:27–30
52. Gagné DJ, Germaine N, Urbandt JE. **Laparoscopic revision of Roux-en-Y gastric bypass for dysphagia and bile reflux.** *Surg Obes Relat Dis.* 2010;6:551–553
53. Byrnes CK, Bahadursingh A, Akhter N, et al. **Duodenal reflux produces hyperproliferative epithelial esophagitis: a possible precursor to esophageal adenocarcinoma in the rat.** *J Gastrointest Surg.* 2003;7:172–180
54. Kawaura Y, Tatsuzawa Y, Wakabayashi T, Ikeda N, Matsuda M, Nishihara S. **Immunohistochemical study of p53, c-erbB-2, and PCNA in Barrett's esophagus with dysplasia and adenocarcinoma arising from experimental acid or alkaline reflux model.** *J Gastroenterol.* 2001;36:595–600
55. Hak NG, Mostafa M, Salah T, et al. **Acid and bile reflux in erosive reflux disease, non-erosive reflux disease and Barrett's esophagus.** *Hepatogastroenterology.* 2008;55:442–447
56. Attwood SE, DeMeester TR, Bremner CG, Barlow AP, Hinder RA. **Alkaline gastroesophageal reflux: implications in the development of complications in Barrett's columnar-lined esophagus.** *Surgery.* 1989;106:764–770
57. Gillen P, Keeling P, Byrne PJ, West AB, Hennessy TP. **Implication of duodenogastric reflux in the pathogenesis of Barrett's esophagus.** *Br J Surg.* 1988;75:540–543
58. Attwood SE, Smyrk TC, DeMeester TR, et al. **Duodeno-esophageal reflux and the development of esophageal adenocarcinoma in rats.** *Surgery.* 1992;111:503–510
59. Miwa K, Segawa M, Takano Y, et al. **Induction of oesophageal and forestomach carcinomas in rats by reflux of duodenal contents.** *Br J Cancer.* 1994;70:185–189
60. Fein M, Peters JH, Chandrasoma P, et al. **Duodenal esophageal reflux induces esophageal adenocarcinoma without exogenous carcinogen.** *J Gastrointest Surg.* 1998;2:260–268
61. Silecchia G, Catalano C, Gentileschi P, et al. **Virtual gastroduodenoscopy: a new look at the bypassed stomach and duodenum after laparoscopic Roux-en-Y gastric bypass for morbid obesity.** *Obes Surg.* 2002;12:39–48
62. Alva S, Eisenberg D, Duffy A, Roberts K, Israel G, Bell R. **A new modality to evaluate the gastric remnant after Roux-en-Y gastric bypass.** *Surg Obes Relat Dis.* 2008;4:46–49
63. Yamamoto H, Sekine Y, Sato Y, et al. **Total enteroscopy with a nonsurgical steerable double-balloon method.** *Gastrointest Endosc.* 2001;53:216–220
64. Sakai P, Kuga R, Safatle-Ribeiro AV, et al. **Is it feasible to reach the bypassed stomach after Roux-en-Y gastric bypass for morbid obesity? The use of the double-balloon enteroscope.** *Endoscopy.* 2005;37:566–569

65. Gill KR, McKinney JM, Stark ME, Bouras EP. **Investigation of the excluded stomach after Roux-en-Y gastric bypass: the role of percutaneous endoscopy.** *World J Gastroenterol.* 2008;14:1946–1948
66. Fobi MAL, Chicola K, Lee H. **to the bypassed stomach after gastric bypass.** *Obes Surg.* 1998;8:289–295
67. Ceppa FA, Gagné DJ, Papasavas PK, Caushaj PF. **Laparoscopic transgastric endoscopy after Roux-en-Y gastric bypass.** *Surg Obes Relat Dis.* 2007;3:21–24
68. Cariani S, Vittimberga G, Grani S, Lucchi A, Guerra M, Amenta E. **A functional Roux-en-Y gastric bypass to avoid gastric exclusion: 1-year results.** *Obes Surg.* 2003;13:788–791
69. Cariani S, Amenta E. **Three-year results of Roux-en-Y gastric bypass-on-vertical banded gastroplasty: an effective and safe procedure which enables endoscopy and X-ray study of the stomach and biliary tract.** *Obes Surg.* 2007;17:1312–1318
70. Cariani S, Palandri P, Della Valle E, et al. **Italian multicenter experience of Roux-en-Y gastric bypass on vertical banded gastroplasty: four-year results of effective and safe innovative procedure enabling traditional endoscopic and radiographic study of bypassed stomach and biliary tract.** *Surg Obes Relat Dis.* 2008;4:16–25
71. Braghetto I, Csendes A, Korn O, et al. **Laparoscopic resectional gastric bypass in patients with morbid obesity: experience on 112 consecutive patients.** *J Gastrointest Surg.* 2011;15:71–80
72. Zeni TM, Frantzides CT, Mahr C, et al. **Value of preoperative upper endoscopy in patients undergoing laparoscopic gastric bypass.** *Obes Surg.* 2006;16:142–146
73. Sharaf RN, Weinshel EH, Bini EJ, Rosenberg J, Sherman A, Ren CJ. **Endoscopy plays an important preoperative role in bariatric surgery.** *Obes Surg.* 2004;14:1367–1372
74. Muñoz R, Ibáñez L, Salinas J, et al. **Importance of routine preoperative upper GI endoscopy: why all patients should be evaluated?.** *Obes Surg.* 2009;19:427–431
75. Boru C, Silecchia G, Pecchia A, et al. **Prevalence of cancer in Italian obese patients referred for bariatric surgery.** *Obes Surg.* 2005;15:1171–1176
76. Loewen M, Giovanni J, Barba C. **Screening endoscopy before bariatric surgery: a series of 448 patients.** *Surg Obes Relat Dis.* 2008;4:709–712