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REVIEW ARTICLE

Gastro-Intestinal Tract Cancers Following Bariatric Surgery: a Narrative Review

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Abstract

The association between obesity and malignancies has been identified epidemiologically. Meanwhile, the increasing global number of bariatric surgeries is reported annually; bariatric surgery's effect on different types of cancers is not well understood. Unfortunately, nonspecific presentations and difficulties regarding investigations make diagnosis challenging. The aim of this study is to compile available data about gastro-intestinal (GI) cancers, occurring after different bariatric surgeries. Although GI cancers are considered a rare complication of obesity surgery, they do exist, and diagnosis needs a high index of suspicion.

Keywords Bariatric surgery · Gastric neoplasms · Esophageal neoplasms · Colorectal cancer · Gastric bypass · Sleeve gastrectomy

Introduction

The association between obesity and malignancies is identified epidemiologically. The increased risk of the esophageal, gastric, colorectal, liver, gallbladder, pancreas, kidney, endometrial, breast, prostate cancers, non-Hodgkin's lymphoma, and multiple myeloma in obese patients have been studied so far [1–4]. Generally, it is adenocarcinoma, not squamous cell carcinoma, of the esophagus that has increased risk in obese patients [5]. Also, there is a correlation between increased body mass index (BMI) and two-threefold increased risk of gastric cardia adenocarcinoma (unclear for non-cardia adenocarcinoma) [1, 6, 7]. In colorectal cancers (CRC), the relative risk for cancer is.1.5 to 2 (comparing with normal population), when BMI ≥ 28–30 kg/m^2 is present (More obvious in colon cancer and in men) [8]. Meanwhile, the increasing number of bariatric surgeries is reported; the effect of bariatric surgeries on different cancers is not well understood. Bariatric surgery reduces cancer risk along with weight reduction [5, 9, 10]. For example, gastric cancer in obese patients who underwent bariatric surgery is dramatically lower than obese patients not subjected to the surgery (24/100000 versus 306/100000) [10], and a 27% decrease in CRC risk is

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seen after obesity surgery [11], but the issue is not that simple for the following reasons: (1) gastro-intestinal (GI) cancer early symptoms like epigastric discomfort, weight loss, oral intolerance, nausea, and vomiting are quite similar to ordinary post-op symptoms [12–14]. (2) Anatomic alterations make it difficult to use diagnostic modalities. As a result, GI cancer diagnosis after bariatric surgery is challenging, and progressive tumors are frequent. One recent study showed more than a threefold increase in mortality rate in rectal cancer patients with prior obesity surgery [15]. The bariatric surgeon should keep in mind that, though not frequent, GI tract cancers may occur after bariatric surgery and diagnosis needs a high index of suspicion.

Methods

We performed a search in PubMed, Google scholar, Cochrane and science direct, using one or more of the key words including gastrointestinal neoplasms, GI cancer, cancer, GI neoplasm, gastric cancer, gastric neoplasm, gastric tumor, gastric carcinoma, gastric adenocarcinoma, esophageal cancer, esophageal neoplasm, esophageal tumor, esophageal carcinoma, esophageal adenocarcinoma, sleeve gastrectomy, laparoscopic sleeve gastrectomy, SG, SG, OAGB, one anastomosis gastric bypass, LMGB, laparoscopic minigastric bypass, LRYGB, Laparoscopic Roux-en-Y gastric bypass, RYGB, Roux-en-Y gastric bypass, Omega loop gastric bypass, SAGB, single anastomosis gastric bypass, jejuno-ileal bypass, JIB, SASI, single anastomosis sleeve-ileal bypass, SASJ, single anastomosis sleeve-jejunal bypass, SADI, single anastomosis duodeno-ileal bypass, obesity surgery, bariatric surgery, gastric bypass, vertical banded gastroplasty, VBG, gastric banding, gastric band, laparoscopic gastric banding LAGB, duodenal switch, biliopancreatic diversion, excluded stomach, gastric bypass remnant, bypassed stomach and gastric pouch to find all published articles on GI cancers following bariatric surgery.

We excluded non-English language articles and animal model studies and considered all articles published until 30 September 2018. Tumors existing before surgery or at the time of surgery were omitted. Five hundred ninety-three articles were found of which, 22 were duplicates. According to the title, 462 papers were excluded. For 109 articles, abstracts were read which yielded in 40 irrelevant and 6 inaccessible papers. Finally, 63 articles were studied completely and epidemiological, clinical, and pathological data, as well as treatment and prognosis data, were collected and references for each paper were considered to figure out any neglected article.

Results

Jejunoileal Bypass

Historically, jejunoileal bypass (JIB) abandonment occurred early in the 1980s due to severe nutritional and metabolic complications. Nevertheless, clinicians still encounter post-JIB long-term complications [16]. According to our review, there are 4 reports of GI cancers following JIB (Supplementary Table 1). The earliest occurred eight years after JIB, whereas the latest lesion appeared 41 years after the surgery. Two of the cases were female and the mean age of patients was 56.6 years (44–63 years). Rectal bleeding happened in cecal and anal canal tumors but the transverse colon tumor exclusively had vague abdominal symptoms [16–18]. Interestingly, Burton et al. diagnosed the tumor using upper GI endoscopy [17]. Also, Voss et al. reported a squamous cell carcinoma of the upper anal canal, treated by open abdominoperineal resection followed by adjuvant radiation, but the tumors in Morris's and Burton's case reports were, adenocarcinomas of the cecum and transverse colon, orderly [16–18]. Moreover, the transverse colon adenocarcinoma passed away on post-op day 67 for severe pneumonia [16]. In addition to the malignancies mentioned above, McFarland et al. and Sylvan et al. reported polyp formation at the colon following JIB; none were malignant [19, 20].

Vertical Banded Gastroplasty Vertical banded gastroplasty (VBG) is less frequent today so all eight articles noting gastric malignant neoplasms after VBG are of last decades (Supplementary Table 2). Three of the patients were male and all the patients were middle-aged, from 44 to 67 years (mean = 55.5 years) [21]. Except for Zirak et al.'s study in which they applied Silastic Ring-VBG, all patients had undergone VBG with mesh placement around the pouch [22]. Totally, cancer developed on an average 10.5 years after VBG (2–16.5 years). In the first study by Sweet et al. (1996), they presented pouch outlet obstruction caused by linitis plastica, though esophago-gastro-duodenoscopy (EGD) biopsies revealed no malignancy [23]. In three cases, the tumor's location was in the pouch, one case in the prepyloric region extending to duodenum's second part (D2), and two cases (including linitis plastica case) in the isolated gastric fundus. Allen and colleagues reported a case of esophagogastric junction (EGJ) cancer with a history of JIB converted to VBG for weight regain and impaired liver function [24]. The lesion in Melstrom's report appeared in the distal esophagus. Generally, surgeons performed laparotomy for all patients (except for Melstrom's case, which underwent chemo-radiotherapy and stenting). In Papakonstantinou et al.'s article, the patient underwent Whipple's pancreaticoduodenectomy due to D2 involvement [21]. Investigations on pathology reports showed aggressive

adenocarcinoma in five cases, but in one case (De Roover et al.), high-grade gastrointestinal stromal tumor (GIST) was the diagnosis [25]. In the early post-op period, one patient experienced anastomosis leak (Jain et al), managed conservatively [26]. The patient underwent Whipple's procedure, passed away six months after the surgery for malnutrition and disseminated metastases. Also, Allen's case died 15 months after the gastrectomy because of the tumor recurrence. The Melstrom's patient died nearly two years after the VBG. The GIST patient had a recurrence at the liver and lung three years post-operation [27].

Laparoscopic Adjustable Gastric Banding

Once being one of the most prevalent bariatric surgeries, laparoscopic adjustable gastric banding (LAGB) is now declining globally, because of its complications like erosion and slippage. Our review showed there are eight cases (five females and three males) of GI malignancies following LAGB (Table 1). Only one of the patients underwent open surgery and surgeons used lapband in most of the cases. The mean age of the patients was 53.9 years (37–66 years). Earliest and latest tumors presented six months and 10 years orderly (mean = 3.4 years). Two cases had lower esophageal cancer, one had EGJ cancer, and three had gastric cancer (one tumor located in the cardia and the other in the pouch just above the band and the last at the incisura angularis). Lower GI tract cancer happened in two patients: one of them was 2 cm above the anal verge and the other was at the recto-sigmoid junction, 18 cm from the anus. The aggressiveness of the tumors was worth noting: most of them were moderately or poorly differentiated adenocarcinomas and all except one had metastatic feature. Metastatic sites were the liver (three patients), vertebrae (one patient), abdominal wall (one patient), and retroperitoneal lymph nodes (one patient). We noticed peritoneal carcinomatosis and ascites in one patient. Four patients received palliative care and four of the patients passed away in the first two years after diagnosis.

Laparoscopic Sleeve Gastrectomy (SG) Up to now, there are only four cases of GI cancers after SG according to our review (Table 2). Scheepers et al. [36] reported the only lower esophageal cancer after SG and all the other three cancers were in the stomach. All the cases were female and the mean age at diagnosis was 51.7 years (44–57 years). The average BMI before SG was 49.6. Tumors appeared 2.2 years after SG on average: one 4 months, one 9 months, and two of the tumors diagnosed four years post-operation. Pre-op EGD was not done in the tumors diagnosed at four months and nine months after the surgery, and they could be present at the time of SG. Three of the patients were smokers and also three had obstructive sleep apnea prior to the surgery. One patient was a pancreas transplant case (immunocompromised). One case has had gastric pacemaker implantation and one case had balloon placement before the SG. Moreover, three cases had dysphagia and food intolerance and one patient had nonspecific abdominal and back pain. Pathology showed two poorly differentiated adenocarcinoma (all four were adenocarcinoma) and two cases had invaded the adjacent structures (T4). The patient with lower esophageal adenocarcinoma underwent definite chemoradiotherapy (Table 1). Kuper et al. reported a case of pancreatic cancer (aside from nesidioblastosis and other endocrine tumors), after SG. The patient was a 52-year-old male with a history of splenectomy, renal cell carcinoma, and asymptomatic pelvic vein thrombosis who underwent SG and then acute pancreatitis repeatedly after the surgery. Investigations identified a tumor in the head of the pancreas and elevated carbohydrate antigen 19–9 (CA19_9), three months post-operation. The patient underwent pylorus-preserving pancreaticoduodenectomy using the gastric sleeve. Pathology report revealed a ductal adenocarcinoma (T3N0M0). There was local recurrence with hepatic metastases nine months after the Whipple's procedure (Kuper) [37].

Roux en-Y Gastric Bypass (RYGB) Our review showed 29 cases (19 female-10 male) of GI cancer after RYGB (Table 3). The average age at the diagnosis was 57.2 years (45–70 years). The mean time between the surgery and cancer diagnosis was 7.9 years (2 months to 28 years). In three patients, RYGB was a redo surgery (VBG: two cases—LAGB: one case). Four patients (13%) were asymptomatic. The most frequent symptom was abdominal pain which occurred in 16 patients (55%), followed by dysphagia, and excessive weight loss (each 17%). Tumor location was the gastric remnant in most cases: one in the fundus, two in the body, and 11 patients in the antrum and pyloric regions. In three patients, the location was the pouch, four in the EGJ and three patients in the distal esophagus, duodenum in two patients, head of the pancreas in two patients, and left colon in one patient. In 20 patients, pathology was adenocarcinoma and nine had different pathologies: Diffuse large B cell lymphoma of gastric remnant in two patients, mucosa-associated lymphoid tissue tumor in one (remnant), GIST of remnant in one, neuroendocrine tumor of duodenum's first part (D1) in one, Krukenberg tumor in one (remnant), and high-grade dysplasia of distal esophagus in one patient. Two patients had linitis plastic: one invaded both the pouch and the remnant and in the other, only pouch infiltration occurred. Five patients had even local or distant metastases at the time of surgery. In four patients, no surgery was done and definite chemo (radio) therapy started while palliative surgery was performed in three patients. Surgeons performed laparotomy in three cases and Ivor-Lewis surgery in three other patients. As a result of periampullary lesions, three patients underwent pancreaticoduodenectomy. Six patients passed away afterwards.

One Anastomosis Gastric Bypass (OAGB) As our review shows, there is only one report of GI cancer after OAGB

Table 1 Reported cases of GI cancers following laparoscopic adjustable gastric banding (LAGB)

Author (publication year)	Gender (age, year)	Type of previous procedure	EGD before cancer surgery	Time of cancer diagnosis (after bariatric surgery)	Localization of the tumor	Treatment	Pathology	Cancer staging	Follow-up
Snook [28] (2003)	F (58)	Open gastric banding (Kuzmak band)	A fungating lesion arising from an area of Barrett's mucosa	8 years	Lower esophagus	Band removal & stent placement & palliative chemotherapy	Moderately differentiated adenocarcinoma	Stage 4 multiple liver metastases	Died 2 years after band removal
Hackert [29] (2004)	F (62)	LAGB (lap--band)	Intraluminal migration of the gastric band localized to the lesser curvature surrounded by an ulcerating lesion at the cardia	10 years	Cardia & multiple liver metastasis	A palliative high (near total) gastrectomy with end-to-side gastrojejunostomy, lavage and drainage (open) + adj chemotherapy	Poorly differentiated adenocarcinoma (pT2b) with propagation into the perigastric lymphatic vessels and correspondinghep-atic metastases	Stage 4	N/A
Korswagen [30] (2008)	M (43)	LAGB (silicone catheter)	Thickening of the esophageal wall at a length of 10 cm just above the gastric band	2 years	Lower esophagus	Radiotherapy for vertebral metastases	Adenocarcinoma	Stage 4 (multiple vertebral metastases)	Died shortly after diagnosis before chemotherapy being started.
Storth [31] (2008)	F (65)	LAGB (lap--band)	N/A	2 years & 8 months	Gastric cancer concentrated in the pouch above the band	N/A	N/A	Stage 4 (peritoneal carcinomatosis & ascites)	Died on 5th post-op day
Stauffer [32] (2010)	M (66)	LAGB (lap--band)	An obstructing mass at the EGJ	23 months	EGJ	Band removal and chemotherapy	Poorly differentiated adenocarcinoma	An ulcerating, obstructing mass at the distal esophagus with adjacent lymphadenopathy	Died 9 months after cancer diagnosis
Szymnaski [33] (2010)	M (47)	LAGB (pars flaccida technic)	Colonoscopy: 1.5-cm ulceration, 2 cm above anal verge	1 year	1-Rectum 2-Liver metastases: segment four	Rectum: abdominoperineal resection(APR) & adj chemotherapy-liver metastasis: left hemihepatectomy 6 months after APR	Moderately differentiated, tubular rectal adenocarcinomac-ombined partially with mucinous type-liver metastasis: adenocarcinoma	(pT2, N1, Dukes' C stage).	Disease free 12 months after left hemihepatectom-y
Graca [34] (2011)	F (54)	LAGB	Colonoscopy: a polypoid lesion at the rectosigmoidal transition--18 cm from anus	1-Rectum: 14 months 2-Port site met: 28 months	1-Rectosigmoid junction 2-Epigastric mass adjacent to the port	1-Laparoscopic high anterior resection & adjuvant chemotherapy 2-Local excision	1-Rectum: rectal adenocarcinom-a--8 × 6 cm 2-Abdominal wall: metastatic adenocarcinoma-4- × 6 cm	T3N1Mx	N/A

Table 1 (continued)

Author (publication year)	Gender (age, year)	Type of previous procedure	EGD before cancer surgery	Time of cancer diagnosis (after bariatric surgery)	Localization of the tumor	Treatment	Pathology	Cancer staging	Follow-up
Orlando [35] (2014)	F (37)	LAGB	Normal	6 months	A lesion of about 8 mm in the lesser curvature	Open total gastrectomy+ band removal+ Roux en y esophagojejunostomy	Poorly differentiated adenocarcinoma with signet-ring cells	Intramucosal adenocarcinoma of 2 mm, without evidence of perineural and vascular invasion (pT1sN0M0)	Normal 2.5 years after gastrectomy

N/A, not accessible; *EGJ*, esophago-gastric junction; *Adj*, adjuvant; *LAGB*, laparoscopic adjustable gastric banding; *EGD*, esophagogastroduodenoscopy

(Wu et al. 2013): a 51-year-old female with symptoms of melena and abdominal pain and a poorly differentiated adenocarcinoma, located at the excluded stomach' pylorus. Consequently, the resection included the distal two-thirds of the bypassed gastric remnant and surgeons stapled the duodenal stump, performed lymph node dissection, and re-anastomosed the gastric pouch and remnant's fundus. Finally, they constructed a new Billroth II gastrojejunostomy between the proximal gastric remnant and the jejunum. Consequently, the patient received adjuvant chemotherapy [55]. It is clear that 3 other cases considered as "vertical gastric bypass with loop gastrojejunostomy", and Mason's bypass are not categorized as OAGB (Table 4).

Biliopancreatic Diversion (BPD) Fernandez et al. reported a case of a 42-year-old female with a history of BPD six years ago, presented with nonspecific abdominal pain, fatigue and highly elevated carcinoembryonic antigen (CEA), CA19-9, and mild anemia. Subsequently, investigations revealed a moderately differentiated adenocarcinoma of the right colon with invasion to the BPD alimentary limb (Table 5). The patient underwent right hemicolectomy and resection of the infiltrated alimentary limb with the reconstruction of BPD. There were bi-lobar unresectable liver metastases, so adjuvant chemotherapy initiated. However, the patient died eight months after the operation [60]. Adami et al. reported seven cases of colorectal cancer after BPD in 1898 patients for a 26-year follow-up period. Three of seven patients were female and the average age at the time of cancer was 56.4 years (43–66 years). The mean time from BPD was 13 years (6–27 years). Only one case was in the right colon and the rest were left colon cancers. Accordingly, the surgery team performed right hemicolectomy and left hemicolectomy for patients and two patients underwent a second surgery for resection of the liver and lung metastases. Two patients died during the follow-up period and the rest were free of the tumor [61]. Another report by Fernandez et al. was about a metastatic carcinoid tumor in a 58-year-old female with morbid obesity and diabetes mellitus, presented with periodic severe diarrhea three years after BPD. There was an incidental finding of two nodules in the liver's left lobe. Fine needle aspiration of nodules resulted in a metastatic neoplastic lesion of unknown origin. The nodules resected by laparotomy but the primary tumor was uncertain. Afterwards, lab tests showed a carcinoid tumor, so an octroscan was done which located the primary lesion in the pancreas and new hot spots in the liver, i.e., new metastases to the liver, in about 1 month after the surgery. Lastly, somatostatin analogs started with excellent response and the patient was alive at the time of publication [59].

Discussion

In contrast to numerous bariatric surgeries performed, just a few cases of GI cancers are post-obesity operations. This is

Table 2 Reported cases of GI cancers following laparoscopic sleeve gastrectomy (SG)

Author (publication year)	Gender (age, year)	Type of previous procedure	EGD before cancer surgery	Time of cancer diagnosis (after bariatric surgery)	Localization of the tumor	Treatment	Pathology	Cancer staging	Follow-up
Scheepers [36] (2011)	F (57)	SG	Lower esophagus lesion	4 months	Lower esophagus	Chemoradiotherapy	Adenocarcinoma	Stage T2N1Mx.	No evidence of tumor 8 months later and her weight was stable
Angrisani [1] (2014)	F (55)	SG	Mass in body and antrum and pylorus	4 years	Body & antrum & pylorus	Total gastrectomy with Roux-en-y esophagojejunostomy with D2 lymphadenectomy and cholecystectomy & adj chemotherapy	Poorly differentiated signet-ring cell adenocarcinoma diffusely infiltrating the body, the antrum, and the pylorus.	pT4aN1, grad, G3	Disease free 8 months after the surgery
Masrur [12] (2016)	F (44)	SG	A tight stricture, 10 cm from EGJ in the stomach	9 months	Stomach body (10 cm from EGJ)	Robot-assisted total gastrectomy with a Roux-en-y esophagojejunostomy, omentectomy, distal esophagectomy, distal splenopancretectomy, tangential colon resection with a feeding jejunostomy & adj chemotherapy	Poorly differentiated and diffused type grade 3 gastric adenocarcinoma	pT4b, pN3a	Bi-basal pleural effusion-well at 8 month follow-up, with no sign of recurrence.
Vlademirov [9] (2017)	F (51)	SG	An ulcer in the antrum of the stomach	4 years	Gastric antrum	Total gastrectomy with Roux-en-y esophagojejunostomy and D2 lymphadenectomy	Mucinous adenocarcinoma	pT1b (sm3), pN0, L0, V0, G3, R0	No evidence of recurrent tumor 2 years postoperative

N/A, not accessible; *EGJ*, esophago-gastric junction; *Adj*, adjuvant; *SG*, laparoscopic sleeve gastrectomy; *EGD*, esophagogastroduodenoscopy

Table 3 Reported cases of GI cancers following Roux en-y gastric bypass (RYGB)

Author (publication year)	Gender (age/ year)	Type of previous procedure	EGD before surgery	Time of cancer diagnosis (after bariatric surgery)	Localization of the tumor	Treatment	Pathology	Cancer staging	Follow-up
Khitin [38] (2003)	F (57)	RYGB	Not done--CT: thickening of the distal antrum causing a gastric outlet obstruction	22 years	Excluded stomach: obstruction by a pre-pyloric mass	The distal two-thirds remnant resected + a loop gastrojejunostomy using the proximal remnant and the jejunum was constructed	Poorly differentiated adenocarcinoma	PT3N0MX.	Uneventful post-op period
Allen [24] (2004)	F (54)	RYGB	Distal, mid- and proximal esophagus + EGJ involvement	21 year	From EGJ to the proximal thoracic esophagus	Total esophagectomy + 50% proximal gastrectomy + jejunal graft between the cervical esophagus and the remnant distally	Adenocarcinoma	N/A	Cancer recurred at 8 months + died 13 months after his operation.
Allen [24] (2004)	M (50)	RYGB	Lesion at the EGJ	14 years	EGJ	Esophago-gastrectomy + a gastric tube was created from the stomach, despite the previous operation on the fundus.	Adenocarcinoma (did not invade the muscularis mucosa)	T1N? M?	Free of recurrent cancer 6 years after his operation
Escalona [39] (2005)	F (51)	RYGB	N/A	8 years	Pyloric region of the remnant	Open TG + RNYEJ + adjuvant chemotherapy	Moderately differentiated adenocarcinoma with signet ring cell	T4N1 (infiltrating into the serosa and extending to the duodenum)	Normal 10 months after surgery
Tricando [40] (2005)	F (52)	RYGB(HX of LAGB: Lap-Ban-d)	N/A	5 years	EGJ + proximal pouch	Transhiatal esophago-pouchectomy + anastomosing the bypassed stomach to the cervical esophagus + adj chemo radiotherapy.	Well-differentiated adenocarcinoma	T3N1M0	Anastomosis dilation due to non-tumoral stenosis 3 months after surgery--no recurrence after 12 months
Corsini [41] (2006)	M (57)	RYGB	Normal	4 years	Antrum of the excluded stomach.	Non-resectable + a gastroenterostomy along the Roux limb for decompression	Poorly differentiated adenocarcinoma	N/A	The patient succumbed3 months after the abdominal exploration
Vanek [42] (2006)	F (56)	RYGB	N/A	10 months	Left colon	Left hemicolectomy & adj chemotherapy and radiation therapy	Poorly differentiated adenocarcinoma	Stage 3 (T3, N2, M0)	Disease-free 8 months post-surgery
Nguyen [43] (2006)	F (N/A)	RYGB (open)	A small just above the EGJ	N/A	EGJ	Laparoscopic and thoracoscopic Ivor Lewis esophago-gastrectomy	Moderately differentiated adenocarcinoma	T1N0M0	No recurrence after 3.5 months
De roover [25] (2006)	M (66)	RYGB	N/A	3 years	Fundus of the remnant	Laparotomy+ sub diaphragm abscess drainage+ excision of the remnant-adj chemo radiotherapy	Diffuse large B cell lymphoma	N/A	Complete remission 10 months after surgery

Table 3 (continued)

Author (publication year)	Gender (age/ year)	Type of previous procedure	EGD before surgery	Time of cancer diagnosis (after bariatric surgery)	Localization of the tumor	Treatment	Pathology	Cancer staging	Follow-up
Watkins [44](2007)	M (62)	RYGB (previous VBG)	N/A	18 years	Antrum of the remnant	Removal of the entire excluded stomach	Adenocarcinoma	Stage 4	Metastasis 18 months after the surgery---died 8 months after initiation of chemo-therapy
Harper [45] (2007)	F (45)	RYGB (open)	Not done	1 year	Gastric remnant	Chemotherapy and radiotherapy	Adenocarcinoma with local extension into the liver and omental metastases	Stage 4	Radiation stricture at the splenic flexure: proximal diverting colostomy _ expired 4 months after surgery
Sun [38] (2008)	M (65)	RYGB	A fungating stricture at the gastrojejunal anastomosis	5 years	Gastric pouch	Laparoscopic jejunostomyfeeding tube (multiple metastaticlesions in the liver)	Poorly differentiated adenocarcinoma	Stage 4 (MRI of the abdomen revealed multiple metastatic liver)	Died in September 2006
Melstrom [27] (2008)	M (55)	RYGB	A distal esophageal nodule (intramucosal carcinoma)	2 months	Distal esophagus	Ivor-Lewis esophagectomy	Grade 2–2.5 cm adenocarcinoma invading into sub mucosa 2.5 cm	Stage IA	Disease free up the time of publication
Melstrom [27] (2008)	M (61)	RYGB	EGD: high-grade dysplasia of the distal esophagus	3 years	Distal esophagus	Transhiatal esophagectomy with esophagogastric anastomosis	High-grade glandular dysplasia/adenocarcinoma in situ	TisN0M0	Disease free after 2 years
Khithani [46] (2009)	F (60)	RYGB	Not done	N/A	Head of pancreas	Pancreaticoduodenectomy (end to side anastomosis)	Adenocarcinoma	N/A	No postop morbidity--no 30 day post-op mortality
Kuruba [47] (2009)	M (45)	RYGB	A nodule at the EGJ	20 months	EGJ	Neo adjuvantchemo radio therapy--open Ivor Lewis esophagogastrectomy--adj chemotherapy	Moderately to poorly differentiated adenocarcinoma.(5 cm –invasion through the muscularis propria)	T2N0M0	Brain metastasis 1 year after the surgery
Khithani [46] (2009)	F (57)	RYGB (previous VBG)	Not done	N/A	Head of pancreas	Pancreaticoduodenoctomy (duct to mucosa anastomosis)	Adenocarcinoma	N/A	No post-op morbidity--no 30 day post-op mortality

Table 3 (continued)

Author (publication year)	Gender (age/ year)	Type of previous procedure	EGD before surgery	Time of cancer diagnosis (after bariatric surgery)	Localization of the tumor	Treatment	Pathology	Cancer staging	Follow-up
Court [48] (2010)	F (65)	RYGB	Laparoscopic remnant gastrostomywith EGD: a duodenal mass(sub mucosal)	7 years	D1	D1 and remnant excision, laparoscopically	Neuroendocrine neoplasm (2 cm)	N/A	Negative octreotide scan at 6 & 12 months post-op
Souriyanarayanane [49] (2011)	F (48)	RYGB	Double-balloon enteroscopy: circumferential mass In the distal part of the duodenum	6 years	Duodenum	Whipple's surgery + adj chemotherapy	Moderately differentiated adenocarcinoma extending to the muscularis propria	T3N1	No recurrence after 22 months
Jawad [4] (2012)	F (70)	RYGB (open)	Not done	21 years	Gastric remnant	Exploratory laparotomy and full thickness stomach biopsy--triple therapy regimen against *H. pylori*	Gastric mucosal-associated lymphoid tumor (MALT) + Helicobacter pylori infection	N/A	Two-month follow-up showed marked improvement in her abdominal symptoms
Kulaylat [50] (2013)	M (62)	RYGB	N/A	6 years	Distal esophagus	Neoadj chemo radiotherapy-Open trans hiatalesophagectomy + pouchectomy +proximal Roux limb resection + cervical esophago -gastrostomy by conduit-adj chemotherapy	Poorly differentiated invasive adenocarcinoma	T3N1	liver metastasis: 15 months after the surgery --died 19 months after the surgery
Kulaylat [50] (2013)	F (54)	RYGB	A 2-cm gastric pouch ulcer	7 years	Pouch & remnant both	TG + previous Roux limb resected + a novel Roux-en-Y reconstruction achieved with end-to-side esophago-jejunostomy	Signet cell adenocarcinoma	T4N1M0	Recurrencefree for 20 months.
Menendez [7] (2013)	F (51)	RYGB	N/A (CT scan revealed a mass in the bypassed stomach)	3 years	Remnant	Neoadj chemotherapy—TG & adj chemotherapy	A metastatic adenocarcinoma in the left fallopian tube and a Krukenberg tumor in the left ovary following TAH + BSO	pT4N2Mx	No evidence of recurrence 6 months after surgery and adjuvant treatment
Abellan [10] (2014)	F (60)	RYGB	Normal	7 years	Greater curvature of the remnant	Gastrectomy of the residual stomach + resection of the left ovarian teratoma.	Serous gastric GIST(T4N0)-15 cm	T4N0	Developed a postoperative collection required radiologic drainage and subsequently did well.
	F (56)	RYGB		9 months		(R-CHOP) chemotherapy		N/A	N/A

Table 3 (continued)

Author (publication year)	Gender (age/ year)	Type of previous procedure	EGD before surgery	Time of cancer diagnosis (after bariatric surgery)	Localization of the tumor	Treatment	Pathology	Cancer staging	Follow-up
Courtney [51] (2014)			An ulcer in the pouch + gastroscopy through the remnant: ulcer at lesser curve ulcer		Lesser curvature of gastric remnant		Diffuse large B cell lymphoma (DLBCL)		
Nau [52] (2014)	F (55)	RYGB	N/A-CT scan: wall thickening of entire remnant sparing the fundus	2 years	Linitis plastica = the entire stomach remnant and pouch was thickened	Chemotherapy and radiotherapy	Poorly adenocarcinoma consistent with linitis plastica	Stage 4 (diffuse peritoneal seeding)	N/A
Magge [53] (2015)	M (69)	RYGB	Mini-laparotomy and push enteroscopy: mass in the remnant	28 years	Excluded stomach	Neo adj chemotherapy-radical intraperitoneal tumor debulking + omentectomy, peritonectomies, subtotal gastrectomy + hyperthermic chemotherapy to the peritoneal cavity---adj chemotherapy	Moderately differentiated mucinous adenocarcinoma	N/A	No recurrence after 6 months
Magge [53] (2015)	F (N/A)	RYGB	Ulcerated mass in the remnant	25 years	Excluded stomach	Subtotal gastrectomy, and proximal duodenectomy + adj chemo RT	Poorly differentiated adenocarcinoma with signet ring cells.	Stage 4 (carcinoma-tosis)	No recurrence after 3 years
Haenen [54] (2017)	F (52)	RYGB	N/A	7 years	Linitis plastica at the gastric remnant mostly antrum and pylorus	Chemoradiotherapy ceased because of tumor progression and clinical intolerance	Signet ring adenocarcinoma-- laparoscopy showed peritoneal metastatic disease of an unknown primary malignancy	T1N0	N/A
Van de vrande [14] (2017)	F (69)	RYGB	A lesion in the gastric pouch, just proximal to the gastroenterosto-my	2 years	Distal gastric pouch	Laparoscopic pouch resection + esophagojejunostomy-no need for remnant resection	Well-differentiated adenocarcinoma	pT3N3b (23/25) M1 (peritoneal seeding).	No recurrence31 after 6 months

N/A, not accessible; *EGJ*, esophago-gastric junction; *Adj*, adjuvant; *VBG*, vertical banded gastroplasty; *LAGB*, laparoscopic adjustable gastric banding; *TG*, total gastrectomy; *TAH-BSO*, total abdominal hysterectomy-bilateral salpingo-oophorectomy

Table 4 Reported cases of GI cancers following one anastomosis gastric bypass (OAGB) and its older versions

Author (publication year)	Gender (age/ year)	Type of previous procedure	EGD before surgery	Time of cancer diagnosis (after bariatric surgery)	Localization of the tumor	Treatment	Pathology	Cancer staging	Follow-up
Wu [55] (2013)	F (51)	OAGB	Not done-CT scan: wall thickening of the distal antrum, which was causing gastric outlet obstruction	9 years	Remnant mass + LAP positive peritoneal seeding	Resection of remnant's distal two third + re-anastomosis between pouch and fundus + lymph-adenectomy + adj chemotherapy	Poorly differentiated adenocarcinoma	T4N3M1	N/A
Lord [56] (1997)	F (71)	Vertical gastric bypass with loop gastro--enterostomy	Gastroscopy through the afferent limb of the loop gastro-enterostomy: two tumors in the bypassed gastric antrum	13 years	Excluded stomach (two tumors)	Distal gastrectomy	First tumor: adenocarcinoma invaded sub mucosa Second tumor: tubulo-villous adenoma	N/A	Remained well and hemoglobin was stable at 13.3 g/dL, 3 months post-surgery
Raijman [57] (1991)	F (38)	Mason's bypass	Normal	5 years	Body of the remnant-Exten-ded to the liver	Resection of the excluded stomach	Adenocarcinoma	Tumor infiltrating through the gastric muscle wall into perigastric fat and adjacent lymph nodes	Died 3 months after discharge
Babor [58] (2006)	F (61)	Mason's bypass	A lesion obstructing the gastric pouch outlet	29 years	Gastric pouch out let	TG + resection of invaded transverse colon and jejunom + Roux-en-y gastric bypass	Adenocarcinoma with a predominance of signet ring cells	N/A (metastases at the liver)	N/A

N/A, not accessible; *EGJ*, esophago-gastric junction; *Adj*, adjuvant; *LAP*, lymphadenopathy

Table 5 Reported cases of GI cancers following biliopancreatic diversion (BPD)

Author (publication year)	Gender (age/year)	Type of previous procedure	EGD before surgery	Time of cancer diagnosis (after bariatric surgery)	Localization of the tumor	Treatment	Pathology	Cancer staging	Follow-up
Fernandez [59] (2007)	F (58)	BPD	N/A	3 years	Pancreas with metastatic liver lesions	Resection of the liver metastases & somatostatin analogue	Carcinoid tumor	pT4bN2aM1a; stage Iva	Excellent response to somatostatin analogue
Fernandez [60] (2014)	F (42)	BPD	No EGD was done--colonoscopy: tumor in the ascending colon	6 years	Right colon + ileo-cecal valve + infiltration to the alimentary limb of BPD	Right hemicolectomy and resection of the alimentary limb with reconstruction of BPD + Adj chemotherapy	Moderately differentiated adenocarcinoma	N/A	Metastases to the lung, liver, and scalp--Died 8 months after the surgery

N/A, not accessible; *EGJ*, esophago-gastric junction; *Adj*, adjuvant; *BPD*, biliopancreatic diversion

probably due to a decrease in risk factors, firstly elevated BMI. Also, pre-operative investigations appear to play an essential role [25].

Colorectal Cancer as a Complication of JIB Regional and systemic etiologies (notably enteroglucagon) may play a role for GI cancers after JIB. Anatomic changes following JIB alters bowel transit time, increases bile flow to the distal small bowel and colon (10 times increase in bile flow to the colon), and changes gut flora. Also, fat, carbohydrate, and protein intake changes dramatically [19]. Silverman et al. studied microbial flora of patients who underwent JIB, but the result did not support a carcinogenic role for gut flora [20]. Compensatory mechanisms after JIB are studied well in rat bowel and similar changes may be present in man. Bristol et al. reported a 17% increase in colorectal length, a 29% increase in wet weight, and an 86% increase in cecal weight. Also, crypts were 25% deeper in the distal third of the colon. Crypt cell proliferation rates (CCPR) more than doubled in the middle third of the colorectum and trebled in the distal third, following JIB [62]. Moreover, hyperplasia of sialomucin cells occurs in man after JIB [63]. In one animal model study, considering CRC, nearly 75% of the tumors happened in the distal half of the colorectum, 28% were malignant, and most were polypoid, while, in the small bowel, most of the tumors occurred in the proximal duodenum or upper jejunum, all were sessile and 60% were malignant [62]. Sylvan et al. propose long-term colonoscopic follow-up after JIB [20].

Esophagogastric Cancers and VBG According to Mason, several factors may be responsible for esophagogastric carcinoma after VBG: (1) Barrett's esophagus as a result of chronic reflux gastritis. Barret's metaplasia is present in about 28% of redo VBGs has done for severe reflux [64]. (2) Too large pouch has impaired motility and results in chronic irritation of the outlet mucosa and (3) mucosal irritation and ischemia caused by the mesh surrounding the outlet [21, 65]. Negri et al. reported mucosal hyperplasia and metaplasia at the outlet of the VBG [21]. Generally, underlying stomach carcinoma should be suspected in any late gastric outlet stenosis in a VBG patient [26]. Surveillance EGD after VBG is controversial; however, De Roover et al. recommend endoscopic surveillance for patients symptomatic for gastro-esophageal reflux disease (GERD) and also after 15 years following VBG [66, 67].

GI Cancers after LAGB As a whole, probable mechanisms in pathogenesis of esophagogastric carcinoma after LAGB are (1) prolonged contact of exogenous carcinogen containing food in the gastric pouch, (2) increased intraluminal pressure, (3) erosion and ischemia caused by the band (incidence:1.6%) (4) Helicobacter pylori (H.pylori) infection and (5) increased GERD after LAGB [28, 29, 31, 33–35, 68]. As LAGB augments lower esophageal sphincter, it may relieve GERD

symptoms especially, in the early post-op period, as reported by some studies. However, Forsell et al. (in 326 patients who had undergone LAGB) found GERD is the most common complication requiring re-operation [69]. Consequently, all LAGB candidates should have an exact EGD and if Barret's esophagus is found or the patient is high risk for gastrointestinal cancer or has GERD symptoms, then, it is wise to change the plan to RYGB rather than LAGB [31, 32].

GI Cancers Following SG SG has become the most prevalent bariatric surgery, done worldwide, and available literature show only 4 cases of upper GI cancer after this surgery [1, 9, 12, 36]; hence, SG is probably the safest bariatric surgery in terms of GI tract cancers, though it should be investigated in complementary studies [12]. As our review shows, all post SG cancers are adenocarcinomas at the distal esophagus or the sleeve. Kant and colleagues stated that unlike RYGB, there is no increase in mucosal biomarkers of CRC at 6 months following SG [70]. One of the scenarios frequently seen during SG is facing a GIST. Yuval et al. stated in their cohort that the incidence of GIST in SG (1%) is much higher than that of previous reports, but was nearly comparable with the incidence of incidental GISTs found in RYGB patients. All GISTs were near the lesser curvature. Also, tumors were more prevalent in lower BMI and older patients. As a rule, the surgeon should check the entire stomach before resection and all GISTs should be removed. Also, all liver and peritoneal surfaces should be examined for metastases. Finally, they reported the presence of a GIST on the lesser curvature may change the surgical plan from SG to RYGB or even abort the procedure [71, 72]. One of the technical challenges after SG is conducting an esophagectomy to treat esophageal or proximal gastric cancers. The gastroepiploic arch is usually damaged or detached from the stomach so conduit creation, using the sleeve, is rarely possible and colon interposition should be considered [5]. Lastly, two of the cancers after SG happened four months and nine months post-op and EGD was not done before the surgery in these patients. This fact may necessitate pre-op EGD in SG patients.

GI Cancers Following LRYB According to the published literature, it seems that bariatric surgery, especially LRYGB, causes a real decrease in esophageal and gastric cancers [10, 24, 73–75]. The incidence of gastric cancer is 306/100000/year in obese patients while it reduces to 24/100000/year in patients who underwent the surgery [10]. The probable causes of this reduction in GI cancers may be as follows: (1) LRYGB is a potent antireflux surgery and is an excellent remedy for Barret's metaplasia (one study reported 57% regression of Barret's esophagus and 100% resolution of symptoms in the study group, underwent LRYGB after 2 years [40, 45, 74]); (2) the lack of food content (carcinogens) in the excluded stomach [38, 73, 76]; (3) minimal or no acid production in the small gastric pouch [48, 74]; (4) minimal or no bile reflux into the pouch or distal esophagus; (5) lower bacteria concentration in the gastric content [77]. So, GI cancer following LRYGB is rare, but it may happen after the surgery and the patient must be completely attentive prior to the operation. Unfortunately, most of the gastric tumors occur in the remnant; thus, the clinical symptoms are vague and conventional EGD cannot diagnose them easily [10, 51, 53]. Pathogenesis and etiology of these tumors are not well understood but these factors may play a role in pathogenesis: (1) chronic bile reflux into the gastric remnant: duodenal reflux happens in the remnant of 36–68% of LRYGB patients [6, 39, 52]. Also, 97% of patients have superficial and 94% have pan gastritis at the excluded stomach [52]. (2) Intestinal metaplasia at the remnant: approximately, it occurs in 6.5–19% of patients who underwent LRYGB [6, 52, 54]. (3) H. pylori infection: in one study, 20% of cases were seropositive for H. pylori and in another study, a high proportion of patients were H. pylori positive. So, H. pylori screening is essential for all patients and we should treat any infection before the operation [6, 52]. Interestingly, pepsinogen I, pepsinogen II, and gastrin anti-Helicobacter pylori antibodies have some relations to atrophic gastritis and may be useful for prediction of neoplastic changes of gastric mucosa in LRYGB patients and also for cancer surveillance after the surgery [39]. As noted before, investigation of the gastric remnant is very difficult and most of the tumors are diagnosed in late stages. Unfortunately, conventional EGD is possible, only in cases with very short Roux limb [39, 46]. As a result, various diagnostic modalities have been proposed for investigation of the gastric remnant and duodenum after LRYGB: (1) insertion of a gastrostomy tube in the remnant and also placement of a radio-opaque marker around the gastrostomy site enabling performance of contrast study, (2) the use of a pediatric colonoscope or a long retrograde endoscope, (3) double-balloon endoscopy (DBE), (4) virtual computed tomography (CT) scan. Also, positron emission tomography-CT (PET-CT) has a sensitivity of 94% in the diagnosis of excluded stomach tumors (5) introducing a trocar in the remnant laparoscopically and performing endoscopy through the trocar [7, 41, 44, 49, 52, 56]. Hereon, Inoe stated that LRYGB is a safe remedy for obesity even in areas with high incidence of gastric cancer [77]. Braghetto et al. declared that resection of the excluded stomach does not increase morbidity after LRYGB. In general, they recommended routine resection of the gastric remnant in high-risk situations including (1) high-risk populations such as Asia, Latin-America, Eastern Europe, and some areas of Western Europe; (2) pathologies found in screening EGD, especially adenomatous polyps, dysplasia, intestinal metaplasia, and Menetrier's disease; (3) a family history of gastric cancer, hereditary non-polyposis colon cancer (HNPCC), and the Li-Fraumeni syndrome; (4) bile reflux and bacterial overgrowth [6, 39]. In contrast, Ghanem and colleagues propose SG instead of

LRYGB in high-risk patients [78]. In terms of EGJ and distal esophagus cancers following LRYGB, some considerable points are present according to the existing literature; first, both minimally invasive transhiatal esophagectomy and Ivor Lewis surgeries are feasible. Second, all patients should have a mechanical bowel preparation prior to the surgery. Third, computed tomography angiography (CTA) of the mesenteric vessels is compulsory before the surgery. Even if CTA of mesenteric vessels is normal, the surgeon should start the dissection from the remnant to evaluate its blood supply sufficiency. Fourth, pyloroplasty is controversial and some protocols do not recommend this manipulation. And last but not the least, the part of the alimentary limb between the resected pouch and jejunojejunal anastomosis should not be resected because aside from the absorptive role, it can be used for feeding jejunostomy placement [5, 14, 43, 47, 50, 74]. As noted before, 2 cases of gastric lymphoma are reported post-LRYGB. Basically H. pylori eradication is the mainstay of treatment if the patient has the infection. Close follow-up and EGD with biopsies is vital up to 3 years which is difficult for excluded stomach lymphoma. In such cases, adding local radiotherapy may help overcome this problem [4]. According to our review, except for 1 tubulovillous adenoma with atypia which occurred 8 years after LRYGB near the gastrojejunal anastomosis [13], no case of small bowel cancer is reported following LRYGB. Although there are rare reports about increased colorectal epithelial cell proliferation and Crypt fission associated with Roux-en-y gastric bypass [8.78], no case of CRC following LRYGB is reported currently.

OAGB and GI Cancers In one study conducted by Mahawar et al., regarding objections to OAGB, 50.9% of respondents stated that OAGB will result in an increase in the risk of gastric cancer while 45.4% was apprehensive about esophageal cancer risk increase after OAGB [79]. There is only one case of cancer reported in an Asian patient, 9 years after OAGB, located in the gastric remnant [55]. The impact of acid reflux on Barret's esophagus and esophageal cancer is clear, but whether bile reflux induces esophageal cancer is controversial [80–82]. Bruzzi et al. reported a strong association between chronic biliary reflux, Barret's metaplasia, and esophageal carcinoma in obese patients that have not undergone bariatric surgery [80]. In contrast, Carbajo's study concluded there is no significant clinical association between bile reflux and increased esophageal cancer risk [81]. Some studies have reported few cases of gastroesophageal cancer, 20–30 years after Billroth II gastrectomy, but the situation is quite different for OAGB because there is a long narrow pouch and also biliary and pancreatic content dilution occurs at 1.5 m (at least) from the ligament of Treitz [82]. Also, no increase in esophagogastric cancer risk is seen after Mason's loop gastric bypass, which has some similarities to OAGB [57, 83]. Babor et al. recommend regular endoscopies for cancer surveillance, starting 20 years after Mason's loop gastric bypass [58]. Though, there is not enough evidence for GI cancer screening following OAGB, every OAGB patient, suffering from unusual complaints, is at risk for upper GI malignancies and proper investigation is crucial [55].

Colorectal Cancer After BPD Theoretically, anatomic changes that happen after BPD may make large bowel prone to malignancies because increased contact with food carcinogens and biliary content along with an alteration in microflora may occur [59]. Adami and colleagues stated that only a substantial increase in CRC take place after BPD, which is related to the years passed after BPD, and age and gender are not major determinants [60, 61].

Carcinoid Tumors and Bariatric Surgery A global increase in carcinoid tumors has transpired recently, due to environmental factors, diet alterations, and longer life expectancy [84]. Furthermore, multiple reports have stated that compared with the general population, carcinoid tumors have a higher incidence in obese patients [84, 85]. Also, malignant gastric carcinoid tumors are more prevalent in obese patients [86]. The increased incidence of these tumors may be due to hormonal changes that happen in obese people. Moreover, screening pre-op EGD results in a more precise diagnosis of the asymptomatic tumors [87]. Also, it is shown that hypergastrinemia occurs after SG in the animal model. Hypergastrinemia plays a major role in type 1 gastric carcinoid tumor pathogenesis; hence, we should be aware of probable increased carcinoid tumor risk after SG [87]. Moreover, intraoperative recognition of a gastric remnant carcinoid tumor, during gastric bypass, mandates excluded stomach resection [88]. Another issue is increased prevalence of appendix carcinoid tumors (ACT), in obese patients, and, when faced intraoperatively, seems challenging. Ordinarily, they are more frequent in female, young, and high-BMI bariatric surgery candidates [3]. Crea and colleagues recommend routine appendectomy or, at least, investigation of appendix during each obesity surgery. In addition, they stated that it neither causes additional complications nor increases the operation time significantly. If appendectomy is necessary and the patient is scheduled to undergo LAGB, then according to Crea, we should change the surgery plan. As a rule, simple appendectomy is sufficient for tumors less than 2 cm in diameter that have not involved mesoappendix or serosa, but if the tumor is greater than 2 cm or has involved mesoappendix or serosa, whether grossly or histopathologically, then right hemicolectomy is essential as the adjuvant surgery [3].

Finally, although hundreds of thousands of bariatric surgeries are done up to now, only these few cases are present as post-op GI malignancies, so there is not conclusive evidence about the correlation of obesity surgery and GI cancers, the epidemiologic features of the subjects and their clinical and

paraclinical presentations. As a result, complementary studied are still demanded.

Conclusion

Bariatric surgery reduces the risk of obesity-related malignancies. Generally, GI cancers are rare following bariatric surgery but they may occur at any time after the operation. Unfortunately, their presentations are nonspecific and are mistaken with expectable symptoms arising in the post-op period. Also, anatomic alterations make investigations quite harder in these patients. As a result, most tumors appear in advanced stages and have a poor prognosis. All clinicians who deal with these patients should keep in mind that unusual complaints after bariatric surgery may be due to tumors and proper work-up should be done. Finally, there is growing evidence in favor of pre-op screening EGD. This modality makes the bariatric team capable of early diagnosis of precancerous and malignant lesions and helps to make the best decision both in bariatric and oncosurgical aspects.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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