Obesity Surgery (2019) 29:2660–2669
https://doi.org/10.1007/s11695-019-03951-z

REVIEW ARTICLE

Esophagogastric Neoplasms Following Bariatric Surgery: an Updated Systematic Review

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Published online: 25 May 2019

Abstract

The risk of gastric and/or esophageal cancers after bariatric surgery has been previously discussed in literature. A systematic review was performed to identify articles published between June 2012 and December 2018 reporting new cases of esophageal or gastric cancer not included in previous systematic reviews. Ten gastric malignancies, 28 esophageal cancers, and 2 gastrointestinal stromal tumors (GIST) were identified. Primary bariatric surgery was a restrictive procedure in 26 cases, a purely malabsorptive procedure in 1 subject, and a gastric bypass in 13 patients. Although the vast majority of bariatric procedures seem to present a negligible relationship with any esophagogastric (EG) malignancy, published data remain incomplete. It was however considered of interest to update the number of EG neoplasms arisen following bariatric surgery.

Keywords Mini-bypass · One-anastomosis gastric bypass · Esophageal cancer · Gastric cancer · Bariatric surgery

Introduction

Bariatric surgery is considered the most effective treatment for morbid obesity. Over the years, all the evidences published in literature have demonstrated that bariatric interventions can induce significant and long-lasting weight loss [1]. Several different bariatric procedures are currently recommended by the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) [2]. Despite these excellent results, a systematic review published 6 years ago reported an alarming case series of esophagogastric (EG) cancers arisen following bariatric surgery [3]. These malignancies after

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s11695-019-03951-z) contains supplementary material, which is available to authorized users.

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surgery are considered rare and the vast majority of them were published as sporadic case reports. The main reason for the onset of these malignancies is explained by some EG cancer risk factors, present in morbidly obese patients, as the higher incidence of helicobacter pylori infection and/or the presence of gastroesophageal reflux disease (GERD). Moreover, anatomical modifications after surgery may increase carcinogenesis [3, 4], especially following mini-/one-anastomosis gastric bypass (MGB/OAGB) and sleeve gastrectomy (LSG).

The MGB/OAGB was introduced in 1997 [5], then a revised version has been reported in Spain in 2005 [6]. Although a lot of criticism, understandable at that time, has followed the introduction of these interventions [7], MGB/OAGB has been recently accepted as a standard procedure by IFSO [8, 9] and by the Italian Society for Bariatric and Metabolic Surgery (SICOB) [10]. The main alarming issue, ascribed to MGB/OAGB, was in fact the potential onset of gastric stump or esophageal cancer due to postoperative bile reflux, a well-known drawback following the Billroth II or especially the old Mason's loop bypass, which was soon abandoned for this reason.

Conversely, a recently published study has revealed a worrisome relationship between LSG and the onset of Barrett's lesions in the esophagus [11]. This finding appears to be interesting since LSG remains the most performed procedure worldwide [12].

In the light of this background, the aim of the present study was observing and discussing the epidemiological, histological, and clinical features of unreported cases of EG lesions arisen following a bariatric procedure.

Methods

The present systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement while objectives where reported according to the PICO (Problem, Intervention, Comparison Group and Outcomes) Worksheet and Search Strategy Protocol (see the supplementary material for PRISMA Checklist and PICO protocol) [13, 14].

With the aim to identify eventual new cases of esophageal or gastric cancer not included in the previous reports [3], a systematic review was performed using the PubMed, Cochrane, and Web of Science databases to identify articles published between June 2012 and December 2018. Study search was restricted to data obtained in humans and adults and was conducted using the following keywords: gastric cancer/tumor; esophageal cancer/tumor; bariatric surgery (MeSH terms); Fig. 1 reports in detail the search strategy. Five reviewers (AB, GB, NV, KDL, and DM) screened for appropriateness of title and abstract of potentially relevant studies. Published manuscripts of the selected abstracts were collected and two senior reviewers (MM and GDP) independently performed a second-step selection based on the inclusion criteria. Eventual disagreement was resolved by consensus.

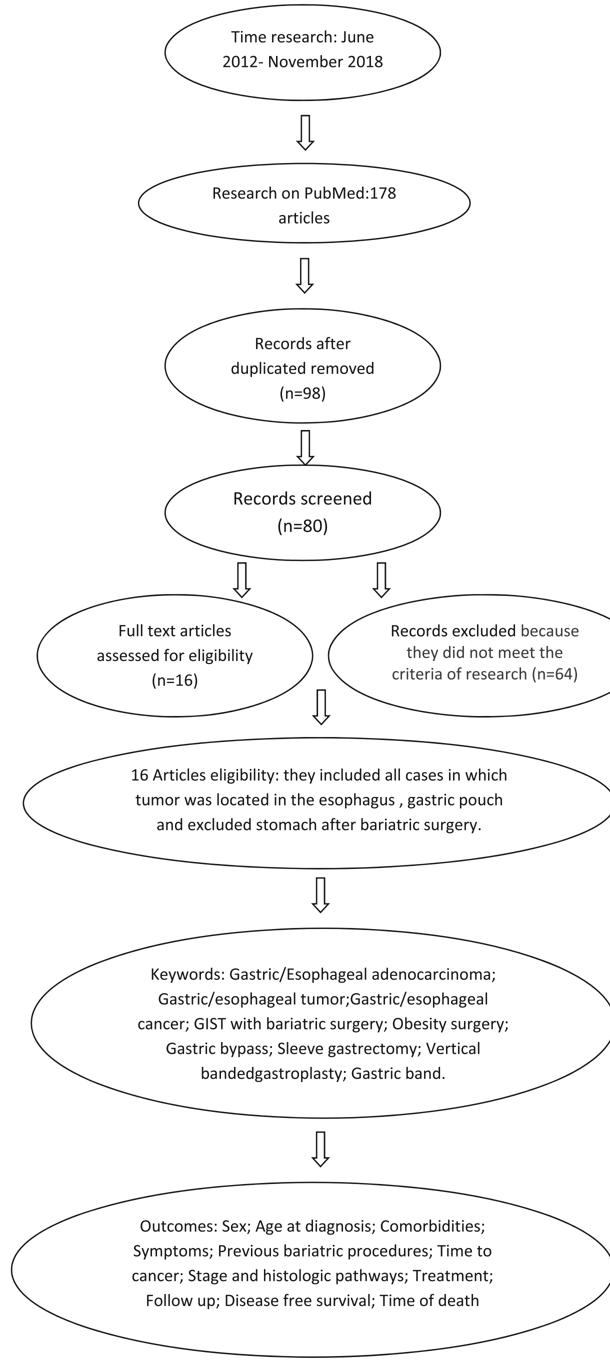

Fig. 1 Search Strategy

Data Extraction and Eligibility

Each study was initially identified considering author, journal, and year of publication. Our data extraction included baseline demographic and clinical information of the study populations. The following outcomes were analyzed: age at the diagnosis, sex, previous bariatric procedures, preoperative comorbidities, reported symptoms, diagnostic procedures, tumor site, histology and stage of neoplasms, elapsed time after bariatric surgery, treatment, follow-up, disease-free survival, and eventual death time. A study was included if all of the following criteria were met: (1) studies reporting the primary bariatric procedure; (2) studies reporting the time lapse between the bariatric procedure and the diagnosis of neoplastic lesion; and (3) studies reporting histology and staging of lesions. Being the majority of papers about a single case report, in the case of literature reviews presenting potential cohort duplication, only unreported cases were included.

Quality Assessment

In order to assess the quality of the selected papers, three parameters were considered: the journal rankings [15], the report of at least 1 year of follow-up, and the confirmation of cancer at final histology (see the supplementary material for the quality assessment).

Results

Forty previously unreported tumors arising in the esophagus or the stomach after bariatric surgery were found in 16 articles [4, 16–30]: 10 gastric cancer, 28 esophageal cancer, and 2 gastro-intestinal stromal tumor (GIST). Data on gender and age were not available for 6 patients; of the other 34 subjects, 17 were males and 17 were females. The mean age at time of diagnosis was 49.8 years old (range 37–74); neoplasms were diagnosed after an interval of 8.7 ± 5.2 years from bariatric surgery (range 6 months to 22 years).

Primary bariatric surgery was a restrictive procedure in 26 cases, a purely malabsorptive procedure in 1 subject and a gastric bypass in 13 patients.

Restrictive interventions were as follows: 5 vertical banded gastroplasty (VBG), open in 2 patients and laparoscopic in 3 cases; 5 laparoscopic sleeve gastrectomy (LSG); 16 adjustable gastric banding (AGB), open in 3 patients and laparoscopic in 13 patients.

Bypass procedures were a laparoscopic Roux-en-Y gastric bypass (LRYGBP) in 10 patients, open RYGB in 2 patients, and MGB/OAGB in 1 patient. The malabsorptive technique present in our data was a bilio-pancreatic diversion (BPD). Most frequent comorbidities were type II diabetes mellitus (T2DM), hypercholesterolemia, Barrett's esophagus, GERD, hypertension, obstructive sleep apnea (OSAS), hyperlipidemia, and depression (Table 1).

In 2 patients who underwent open VBG, cancer was found in esophagus, while in 2 patients that received laparoscopic VBG, tumors were located in the lower third of the esophagus and in the distal stomach, respectively.

After LSG, cancer was found in the lower third of esophagus in one patient, in the antrum of the stomach in another patient, in cardiac region in 2 patients (1 was a GIST) and in antrum/body of stomach in the last patient.

Following the open gastric banding, 3 cases of esophageal cancer were detected, while, after LAGB, malignancies were found in the lower third of the esophagus in twelve patients and in the mid-esophagus in one patient.

In 2 open RYGB cases, cancer was found in mid-esophagus, while in LRYGB cases, neoplasms were located in the gastric pouch in 1 patient, in the lower third of the esophagus in 5 patients, in the excluded stomach in 3 patients, and in mid-esophagus in the last patient.

In the patient who underwent MGB/OAGB, cancer was detected in the excluded stomach.

After BPD, cancer was located in the lower third of the esophagus. Notably, this patient had an AGB for 14 years before being converted to BPD (Tables 1 and 2).

The most commonly reported symptoms were dysphagia, abdominal pain, heartburn, reflux, hematemesis, melena, dyspepsia, weight loss, vomiting, iron deficiency, anemia, fullness, syncope, and deficiency of both vitamins D_3 and B_{12}.

During the follow-up, diagnosis and staging were obtained through abdominal CT scan, PET, and EGDS with biopsy. In 10 patients, node involvement was detected, while metastases were found in other 12 cases. In the preoperative study, HP test results were available in 5 patients. Following cancer diagnosis, one patient chose to have no treatment, while six patients underwent palliative care, chemotherapy, and radiotherapy.

Surgery was the treatment of choice for 29 patients (with palliative intent in one case), while 4 patients were treated by endoscopic procedures. Twenty-two patients received adjuvant or neoadjuvant chemotherapy and 3 patients underwent adjuvant radiotherapy.

Follow-up data were available for 28 patients. The mean follow-up was 29.4 months (range 4 months–10 years). During this period, 11 patients died at a mean of 18.5 months after cancer diagnosis (range 4 to 72 months).

Disease-free survival was available in 11 patients with a mean follow-up of 38 months (range 6 months to 10 years). Only in two cases was a recurrent disease found (Table 3). Table 4 reports the histology of each recorded lesion and the original bariatric procedure performed.

Discussion

Obesity is considered an important risk factor responsible to favor the onset of different cancers; malignancies of the prostate, breast, colon (in men), endometrium, gallbladder [31], liver [32], and thyroid [33] are more frequently diagnosed in the obese population. Clinical evidences have finally

Table 1 Patient comorbidities

Authors	Gender	Age	Procedure	Comorbidity
2018 Gehwolf	N/A	N/A	LAGB (6 cases)	N/A
2018 El Khoury et al.	F	55	LSG	T2DM, hypertension, dyslipidemia, arthritis
2017 Van de Wrande et al.	F	67	LRYGB	T2DM, hypercholesterolemia
2017 Vladimirov et al.	F	47	LSG (gastric pacemaker before)	
2016 Burton et al.	M	57	LAGB	GERD
2016 Burton et al.	M	74	LVBG (LVBG before)	Barrett's
2016 Burton et al.	M	52	LAGB	GERD
2016 Burton et al.	F	53	LAGB (LVBG before)	GERD and Barrett's
2016 Burton et al.	M	65	BPD (LAGB before)	
2016 Burton et al.	M	48	LRYGB	Barrett's
2016 Burton et al.	F	56	LAGB	GERD
2016 Burton et al.	M	59	LAGB	GERD and Barrett's
2016 Tinoco et al.	F	56	LRYGB	
2015 Maret-Ouda et al.	F	51	VBG	
2015 Maret-Ouda et al.	M	63	VBG	
2015 Maret-Ouda et al.	M	71	AGB	
2015 Maret-Ouda et al.	M	64	AGB	
2015 Maret-Ouda et al.	M	74	AGB	
2015 Maret-Ouda et al.	M	64	LAGB	
2015 Maret-Ouda et al.	M	65	RYGBP	
2015 Maret-Ouda et al.	M	60	RYGBP	
2015 Masrur et al.	F	44	LSG	Hypertension, T1DM, hyperlipidemia, bipolar disorder, sleep apnea, vaginal dysplasia, anal condilomatosis
2015 Erim et al.	F	52	LSG	Hyperlipidemia, hypertension
2014 Angrisani et al.	F	51	LSG (intra-gastric balloon before)	Obstructive sleep apnea, hypertension, dyslipidemia, reflux
2014 Orlando et al.	F	37	LAGB	Hypertension
2014 Scozzari et al.	F	50	LVBG	
2014 Scozzari et al.	F	56	LVBG	
2013 Abellan et al.	F	53	LRYGB	
2013 Rossidis et al.	4 M and 1F	57.2	LRYGB	GERD in 2 patients
2013 Wu et al.	F	41	MGB/OAGB	
2012 Menendez et al.	F	51	LRYGB	Basedow disease, depressive disorder

L laparoscopic, *RYGBP* Roux-en-y gastric bypass, *SG* sleeve gastrectomy, *AGB* adjustable gastric banding, *VBG* vertical banded gastroplasty, *MGB/OAGB* mini/one-anastomosis gastric bypass, *BPD* bilio-pancreatic diversion, *GERD* gastroesophageal reflux disease, *T1DM* or *T2DM* type 1 or type 2 diabetes mellitus

demonstrated bariatric surgery to be the ideal approach to achieve satisfactory and durable weight loss [1].

Weight loss achieved after bariatric procedure is also responsible for a reduction of cancer risk in morbidly obese patients [34], and a recent study has associated the use of bariatric procedures with a lower risk of incident cancer [35]. Despite this important achievement, some authors have conversely stressed the risk of esophageal or gastric cancer development following some bariatric procedures, namely the mini-/one-anastomosis gastric bypass (MGB/OAGB) [7, 36–38], while others have detected a worrisome incidence of Barrett's lesions following laparoscopic sleeve gastrectomy (LSG) [11, 39]. This was probably due to the resemblance of MGB/OAGB with two other procedures: the old Mason loop bypass and the Billroth II (B2) reconstruction [40]. Nevertheless, even if all three interventions have in common a loop gastrojejunostomy returning bile and pancreatic juice into the stomach, some technical differences, reflecting into correspondent physiological changes, distinguish the three procedures [41, 42]. Analyzing the results of present study, our attention has been mainly addressed towards two features: the epidemiology and the clinical evolution of the EG cancers that we found within our research. In general, this systematic review, starting from 2012, reports a small number of previously unreported EG cancers arisen following bariatric procedures. Although according to third IFSO global registry report

Table 2 Diagnosis, histology, tumor site, and stage of neoplasms

Authors	Time to diagnosis	Histology	Location of tumor	Stage
2018 Gehwolf	14 years*	4 Adenocarcinomas	EG junction	Ia, IIIb, IV,IV
2018 Gehwolf	14 years*	Adenocarcinoma	Lower third of esophagus	IIIa
2018 Gehwolf	14 years*	Undifferentiated	Lower third of esophagus	IV
2018 El Khoury et al.	3 years	Adenocarcinoma	Lower third of esophagus	P T1NO HER2 -
2017 Van de Wrande et al.	2 years	Adenocarcinoma	Gastric Pouch	T1N0 G1
2017 Vladimirov et al.	4 years	Adenocarcinoma mucinous	Antrum of the stomach	pT1b(sm3)N0 G3 R0
2016 Burton et al.	9 years	Adenocarcinoma	Lower third of esophagus	IV T1N2M1
2016 Burton et al.	30/21 years**	Adenocarcinoma	Lower third of esophagus	III T3N1
2016 Burton et al.	15 years	Adenocarcinoma	Lower third of esophagus	III T3N1
2016 Burton et al.	26/6 years**	Adenocarcinoma	Lower third of esophagus	I T1a
2016 Burton et al.	14/8 years**	Adenocarcinoma	Lower third of esophagus	I T1a
2016 Burton et al.	1 year	Adenocarcinoma	Lower third of esophagus	IA T1a
2016 Burton et al.	13 years	Adenocarcinoma	Lower third of esophagus	IV
2016 Burton et al.	12 years	Adenocarcinoma	Lower third of esophagus	IV
2016 Tinoco et al.	10 years	Adenocarcinoma	Excluded stomach	T2N2M1
2015 Maret-Ouda et al.	10 years	Adenocarcinoma	Esophagus	TxN3M1
2015 Maret-Ouda et al.	11 years	Adenocarcinoma	Esophagus	TxNxM1
2015 Maret-Ouda et al.	22 years	Adenocarcinoma	Esophagus	T1N0M0
2015 Maret-Ouda et al.	9 years	Adenocarcinoma	Esophagus	T1N0M0
2015 Maret-Ouda et al.	14 years	Adenocarcinoma	Esophagus	TxN3M1
2015 Maret-Ouda et al.	8 years	Adenocarcinoma	Esophagus	T3N0M0
2015 Maret-Ouda et al.	5 years	Adenocarcinoma	Esophagus	T4bN0M0
2015 Maret-Ouda et al.	4 years	Adenocarcinoma	Esophagus	T3N2M0
2015 Masrur et al.	8 months	Adenocarcinoma Her2 neu positive	Cardiac region of stomach	pT4bN3a
2015 Erim et al.	4 years	GIST	Cardiac region of stomach	–
2014 Angrisani et al.	4 years	Adenocarcinoma	Body and antrum of the stomach	pT4N1 G3
2014 Orlando et al.	6 months	Adenocarcinoma	Antrum of the stomach (lesser curvature)	pT1sN0M0
2014 Scozzari et al.	8 years	Adenocarcinoma	Distal stomach	T4N1M1
2014 Scozzari et al.	3 years	Adenocarcinoma	Distal stomach	T4N0M0
2013 Abellan et al.	7 years	GIST	Excluded stomach	–
2013 Rossidis et al.		Adenocarcinoma	1 mid-esophagus—4 lower third of the esophagus/ EG junction	3-T1N0M0, 1-T2N0M0, 1-T3N1M0
2013 Wu et al.	9 years	Adenocarcinoma	Excluded stomach	pT3N3bM1
2012 Menendez et al.	3 years	Adenocarcinoma	Excluded stomach	pT4N2Mx

EG esophagogastric

*Mean

**Time to diagnosis from first and second bariatric procedure, respectively

2017 [43], regarding the period between 2013 and 2017, a total of 89.662 bariatric procedures have been performed (Table 5); clearly our data cannot be related to IFSO numbers for several reasons. The first one is that even if reported after 2012, a number of EG cancers included in our systematic review was diagnosed and treated before that year. The second is that the past popularity of gastric banding, which was one of the most performed procedure in the first decade of this century [44], might lead to the equivocation that EG cancers are more frequently related with a band placement, and finally, it must be remarked that data from IFSO, for MGB/OAGB procedures performed in last 5 years, are missing, although a thorough recent survey reported this procedure currently being the third most performed bariatric intervention worldwide [11]. If therefore the number of cases of EG cancers following a primary bariatric procedure is too small to attempt any

Table 3 Diagnostic approach, treatment, follow-up, eventual death time, and disease-free survival

Authors	Reasons for detection	Diagnostic approach	Treatment	Follow-up	Death time	Disease-free survival
2018 Gehwolf	N/A	N/A	3 palliative, 3 Ivor-Lewis	N/A	N/A	N/A
2018 El Khoury	Vomit, Barrett's surveillance	Upper gastrointestinal opacification, EGDS	Endoscopic mucosectomy	N/A	N/A	N/A
2017 Van de Wrande et al.	Vomit, dysphagia, weight loss of 8 kg	EGDS, CT scan abdominal	Total gastrectomy, chemotherapy	6 m	N/A	6 m
2017 Vladimirov et al.	Abdominal pain	EGDS, CT scan abdominal	Total gastrectomy D2	2 y	N/A	2 y
2016 Burton et al.	Reflux	CT scan abdominal, PET total body	Chemotherapy, surgery	1 y	1 y	N/A
2016 Burton et al.	Barrett's surveillance	CT scan abdominal, PET total body, EGDS	Extended total gastrectomy, chemotherapy	8 m	8 m	N/A
2016 Burton et al.	Reflux	CT scan abdominal, PET total body	Ivor-Lewis, chemotherapy	5 y	N/A	Recurrent disease
2016 Burton et al.	Screening EGDS	CT scan abdominal, PET total body, EGDS	Minimally invasive Ivor-Lewis	10 y	N/A	10 y
2016 Burton et al.	Incidental investigation of iron deficiency	CT scan abdominal, PET total body	Endoscopic mucosal resection	2 y	N/A	2 y
2016 Burton et al.	Barrett's surveillance	CT scan abdominal, PET total body, EGDS	Endoscopic mucosal resection	1 y	N/A	N/A
2016 Burton et al.	Reflux	CT scan abdominal, PET total body, EGDS	Palliative chemotherapy and radiotherapy	11 m	11 m	N/A
2016 Burton et al.	Hematemesis	CT scan abdominal, PET total body, EGDS	Palliative chemotherapy and radiotherapy	10 m	10 m	N/A
2016 Tinoco et al.	Abdominal pain, melenic stool, vitamin deficiency	CT scan abdominal	Total gastrectomy D2, adjuvant chemotherapy	N/A	N/A	8 m
2015 Maret-Ouda et al.	Epigastralgia, nausea	EGDS, CT scan abdominal	Surgery	1 y	1 y	N/A
2015 Maret-Ouda et al.	Melena, anemia	EGDS, CT scan abdominal	Chemotherapy, radiotherapy	1.2 y	1.2 y	N/A
2015 Maret-Ouda et al.	Dysphagia and weight loss	EGDS, CT scan abdominal	Chemotherapy, surgery	8.7 y	N/A	8.7 y
2015 Maret-Ouda et al.	Screening EGDS	EGDS, CT scan abdominal	Surgery	6 y	6 y	N/A
2015 Maret-Ouda et al.	Nausea and vomit	EGDS, CT scan abdominal	None	1 y	1 y	N/A
2015 Maret-Ouda et al.	Melena	EGDS, CT scan abdominal	Surgery, chemotherapy, radiotherapy	5.2 y	N/A	5.2 y
2015 Maret-Ouda et al.	Heartburn	EGDS, CT scan abdominal	Chemotherapy, surgery	1.8 y	1.8 y	N/A
2015 Maret-Ouda et al.	Dysphagia	EGDS, CT scan abdominal	Chemotherapy, surgery	2.5 y	2.5 y	N/A
2015 Masrur et al.	Dysphagia to solids and liquid intolerance	EGDS, CT scan abdominal	Total gastrectomy D2 extended, adjuvant chemotherapy	8 m	N/A	N/A
2015 Erim et al.	Dyspepsia	CT scan abdominal	Submucosal endoscopic dissection	N/A	N/A	N/A
2014 Angrisani et al.	Vomiting after ingestion solid food, dysphagia, epigastric pain, asthenia	EGDS, CT scan abdominal	Total gastrectomy D2, adjuvant chemotherapy and radiotherapy	8 m	N/A	8 m
2014 Orlando et al.	Screening EGDS	EGDS	Total gastrectomy	3 y	N/A	3 y
2014 Scozzari et al.	Vomit, dysphagia, weight loss	RX transit, EGDS, CT scan abdominal	Explorative laparotomy and palliative digiunostomy, adjuvant chemotherapy and adjuvant radiotherapy	4 m	4 m	0

Table 3 (continued)

Authors	Reasons for detection	Diagnostic approach	Treatment	Follow-up	Death time	Disease-free survival
2014 Scozzari et al.	Dysphagia, hematemesis, weight loss	EGDS, CT scan abdominal	Total Gastrectomy D1, adjuvant chemotherapy	5 y	N/A	N/A
2013 Abellan et al.	Incidental	CT scan abdominal	Gastrectomy of residual stomach	N/A	N/A	N/A
2013 Rossidis et al.	N/A	PET total body, CT scan abdominal	5 total esophagectomy, 2 neoadjuvant chemotherapy	9 m (mean)	N/A	N/A
2013 Wu et al.	Abdominal pain, fullness	EGDS, CT scan abdominal	Subtotal gastrectomy D2, adjuvant chemotherapy	N/A	N/A	N/A
2012 Menendez et al.	Dysphagia, vomit, syncopal, Krukenberg tumor left ovary	CT scan abdominal, RX transit	Total gastrectomy D2, neoadjuvant chemotherapy, hysterectomy with bilateral salpingo oophorectomy	6 m	N/A	N/A

eventual etiological correlation with the surgical technique, conversely, it may be however of interest to observe epidemiological data about the prevalence of esophageal or gastric cancer in a standard non-obese population. A recent survey about cancer incidence and mortality in Europe [45], analyzing 25 major cancers for 40 countries, estimated the onset of 53×10^3 new esophageal cancer and 133×10^3 new cases of gastric cancer per single year in a standard population. The same authors, expanding their research worldwide, have reported the onset of 572×10^3 new esophageal cancer and over 1000×10^3 of new cases of gastric cancer per single year. Nevertheless, it remains very interesting to observe the age standardized derived age-, sex-, and site-specific rates $\times 10^5$ person/year (ASRs) analyzed by GLOBOCAN [46]. According to these data, the estimates of incidence for esophageal cancer are 9.3 new cases per year every 10^5 persons for male patients and 3.5 new cases per year per 10^5 persons for female patients. Procedures reported by IFSO in this time lapse seem to present a negligible relationship with esophageal or gastric cancer we found in our review. Even if we observe the 15 new cases of esophageal cancer occurred after a LAGB, and we consider the alarming relationship between esophageal cancers and LAGB use already reported in an interesting survey from Austria [30], caution should be recommended in the interpretation of these findings, and not only for the above discussed reasons. If in fact morbid obesity, especially central adiposity, is per se related to increased risk of esophagitis, metaplasia, and esophageal adenocarcinoma [47], it should be reminded that the denominator to which those 15 cancers correlate remains undefined.

One final observation regarding the clinical evolution of EG cancers reported in our series may be attempted. In a standard non-obese population, the rate of distant metastases identified for esophageal cancer at initial diagnosis ranges from 37 to 42% [48], while it decreases at 35% for gastric cancer [49]. In our series, it was 8/40 (20%) for esophageal cancer and 4/40 (10%) for gastric cancer. Similarly, the survival rate in our series, when available at follow-up, was of 20.6% at 5 years for esophageal cancer (6/29 patients). This appears to be in line with data from a standard population not submitted to any bariatric procedure, in which the average survival rate from diagnosis is 15–20% at 5 years for esophageal cancer [50]. These numbers seem to suggest a lower aggressiveness in our subset of EG cancer detected after bariatric surgery, as already hypothesized in the previous systematic review [3]. However, it is actually difficult to assess if certain cases of cancers, as they have occurred a few months postoperatively, in most cases without preoperative endoscopy, are really caused by bariatric surgery or if they were most likely present at the time of bariatric surgery and were missed. On the other hand, bariatric patients usually follow a strict follow-up after the procedure; therefore, some cases can be

Table 4 Histology of each recorded lesion and the original bariatric procedure performed

Features	VBG	Open VBG	LSG	LAGB	Open AGB	LRYGBP	Open RYGBP	MGB/OAGB	BPD
Tumor histology									
Adenocarcinoma of stomach	2		3	1		3		1	
Adenocarcinoma of esophagus	1	2	1	12	3	6	2		1
GIST			1			1			
Tumor location									
Esophagus		2		1	3		2		
Mid-esophagus						1			
Lower third esophagus				10		5			1
Siewert II	1		2	1					
Gastric pouch						1			
Body and antrum of stomach			1						
Antrum of stomach	2		1	1					
Excluded stomach						3		1	
Total	3	2	5	13	3	10	2	1	1

VBG vertical banded gastroplasty, *LSG* laparoscopic sleeve gastrectomy, *LAGB* laparoscopic adjustable gastric banding, *AGB* adjustable gastric banding, *LRYGBP* laparoscopic Roux-en-Y gastric bypass, *MGB/OAGB* mini-/one-anastomosis gastric bypass, *BPD* bilio-pancreatic diversion

diagnosed at an early stage. Furthermore, some details regarding the reported cases of neoplasms should also be underlined in order to understand better possible relationship between surgery and cancer. El Khoury [29] reported a sleeve that was performed on a patient that had Barrett's esophagus, a known contraindication to this surgery. Masrur [23] published a case of gastric adenocarcinoma, only 12 months after sleeve, in a transplant patient on immunosuppression. The neoplasm reported by Erim [22] was a gastric carcinoid, which is a submucosal lesion that has never been associated before with bariatric surgery.

The cases of cancers after sleeve, described by Vladimirov [27] and Angrisani [21], occurred in patients who had previously undergone other gastric procedures (an anterior pacemaker and a gastric balloon, respectively).

Our study presents important limitations. The major comes from the heterogenicity of the collected data. If on one side, we systematically reviewed all cases of EG cancers published starting from 2012 and until 2018, published data from IFSO are available only for the 2013–2017 5-year period. Again, published IFSO data are sometimes incomplete. This depends on the fact that in some countries, national registries are available, while conversely in some other countries, data are collected by a single institution. Probably the most important issue is that not all centers performing bariatric surgery report their numbers to the corresponding national society or to the institution collecting the data. Even if the suggested time lapse to detect a gastric stump cancer following a Billroth II reconstruction ranges from 17.5 to 34.6 years [51]. It is also interesting that published evidences regarding MGB/OAGB,

Table 5 Primary surgery in the calendar years 2013–2017 [43]

Operation*	Number of procedures	Rate (%)	Esophageal cancers**	Gastric cancers**
Gastric band	5389	6.0	15	1
Gastric bypass	41,508	46.3	8	3
Sleeve gastrectomy	39,137	43.6	1	3
Duodenal switch	50	0.1	n/a	n/a
Duodenal switch with sleeve	321	0.4	n/a	n/a
Bilio-pancreatic diversion	474	0.5	n/a	n/a
Other	2783	3.1	1	n/a
All	89,662	100	n/a	n/a

*No data available for vertical banded gastroplasty (VBG) and mini-/one-anastomosis gastric bypass (MGB/OAGB)

**Years 2012 to 2018 included

22 years after its introduction, report only 4 cases of gastric cancer. Three were detected in previous systematic review [3] and the last one presented in this paper [19]; all these malignancies were located in the excluded stomach and therefore not related to the loop reconstruction. Although recommended only 12 years ago as a single step procedure [52] and despite recent warnings [11, 39], also for LSG, data deriving from the comparison of our results with IFSO report do not raise any special alarm about an eventual relationship of this procedure with EG cancer.

In conclusion, the goal of this systematic review remains to address all those surgeons called to evaluate the onset of an EG malignancy following bariatric surgery. It must be however recognized that an accurate conclusion about the eventual relationship of some bariatric procedures with EG cancer cannot be reached. If on one side, we have incomplete data from IFSO (inaccurate or undefined denominator), leading to a potential overestimation of reported malignancies, conversely, probably not all EG cancers following bariatric surgery have been published (incomplete numerator), causing an underestimation of the onset of cancer.

Compliance with Ethical Standards

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

Ethical Approval Statement This article does not contain any study with human participants or animals performed by any of the authors.

Informed Consent Statement Does not apply.

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