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ORIGINAL CONTRIBUTIONS

Coincidental Detection of Gastrointestinal Stromal Tumors During Laparoscopic Bariatric Procedures—Data and Treatment Strategy of a German Reference Center

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Abstract

Introduction Intraoperative pathologic findings during bariatric surgery are relatively rare. Gastrointestinal stromal tumors (GISTs) are commonly located in the stomach and account for < 1% of all neoplasms of the alimentary tract. Coincidental detection of GISTs during bariatric surgery has been reported around 0.8%. We analyzed the incidence of GISTs in bariatric patients and investigated whether simultaneous resection can be oncologically adequate.

Material/Methods A single-center retrospective study of 707 morbidly obese patients, who underwent bariatric surgery (either Roux-en-Y gastric bypass (RYGB), One Anastomosis Gastric Bypass (OAGB), or sleeve resection (LSG) between January 2012 and August 2018). Intraoperative incidental GISTs were recorded and documented for tumor size, localization, immunoreactivity, and mitotic index.

Results Nine (1.27%) patients were identified with GISTs. Seven (78%) tumors were detected in women; mean age 55.6 (range 27–74), mean BMI 51.7 mg/m2 (range 38–71). GISTs were predominantly located in the stomach (78%) and two (22%) within the small bowel; six were found during RYGB vs. three during LSG. No abort of surgery or change of the intended procedure was necessary. All tumors (0.2–3.7 cm) were resected with disease-free surgical margins and displayed low malignancy. No adjuvant therapy was necessary.

Conclusions The incidence of incidental GISTs in our series was higher to what has already been reported. Risk of malignancy was low and resection as part of the bariatric procedure was considered as definitive treatment. Suspicious tumors should be removed and confirmed by histology. In case of GIST histology, tumor resection with negative margins may be weighed as complete oncological treatment if there is low risk of malignancy.

Keywords GIST · Bariatric surgery · Incidental finding · Laparoscopy

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Introduction

Gastrointestinal stromal tumors (GISTs) are rare mesenchymal neoplasms of the gastrointestinal tract with diverse clinical behavior and varying degrees of aggressiveness based on primary tumor location, tumor size, and mitosis rate [1]. GISTs can occur in the entire digestive tract [2]. However, they are most commonly located in the stomach (60%) or small intestine (30%), and less frequently in the colon (10%) or esophagus (5%) [2]. Based on their immunoreactivity for c-kit (CD117), GISTs appear to originate from a common precursor cell, which also gives rise to the interstitial cells of Cajal, commonly known as pacemaker cells who are responsible for peristaltic contractions of the alimentary tract [3]. According to the anatomic distribution of these cells, most frequent locations of GISTs are the gastric cardia and fundus [4]. Based on their differentiation along with the rather frequent specific gain-of-function mutations in the c-kit protein, or in the platelet-derived growth factor receptor alpha (PDGF-α) [5, 6], GISTs appear more aggressive than other GI mesenchymal tumors [7]. Their malignant behavior is determined by the level of mitotic activity, the tumor size, and in some classifications by the location. GISTs are likely to be asymptomatic and if symptoms arise, they are mainly characterized as non-specific. Asymptomatic GISTS are often found coincidentally at the time of radiographic, endoscopic, or surgical evaluation. Upon diagnosis, radical resection with clear resection margins represents the best treatment option, since a high risk of malignancy must be assumed, even in smaller tumors.

Obesity is a major public health and socio-economic burden with an increasing prevalence worldwide [8]. Morbid obesity (body mass index (BMI) > 40 kg/m^2) is frequently associated with metabolic complications, such as type 2 diabetes, hypertension, and dyslipidemia, as well as with an increased risk of developing neoplasms [9–11]. Thus, morbid obesity is recognized to reduce life expectancy and life quality. In the absence of any effective noninvasive treatments, bariatric surgery is at present the most effective treatment for morbid obesity, leading to sustained long-term weight loss, and it has proven to be efficient in preventing and reversing related comorbidities [12, 13]. A number of different surgical methods have been described; however, the sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB) are the two procedures most commonly used in clinical practice. The growing epidemic of obesity has increased the number of bariatric surgical procedures performed worldwide with subsequently more unexpected pathologies to be discovered. In parallel, obese patients present with benign tumors, premalignant conditions, or even malignant lesions before, during, or after the bariatric procedure [14]. Due to the rarity of these conditions, the available evidence is scarce and does not allow one to establish guidelines for proper management. Neoplasms of the upper GI tract may be detected during the preoperative workup by esophago-gastro-duodenoscopy (EGD) or by X-ray but also often during the laparoscopic operation itself and may influence the final bariatric surgical approach [14, 15]. Therefore, every bariatric surgeon should be aware of the management of unexpected pathology.

In bariatric surgery, random intraoperative pathologic findings within the gastrointestinal tract are estimated to be around 2% [16]. Among others, GISTs have been presented as a possible unexpected finding during bariatric surgery in several reports with a recorded coincidence of less than 1% [14]. However, this incidence in obese patients undergoing bariatric surgery has been suspected to be markedly higher when compared to the overall population (0.0006 to 0.0015%) [16], assuming a potential association between obesity and this tumor entity [14]. Of note, the tumors described in these series tended to be small with low-risk pathologic features.

The aim of the present study was to analyze the incidence of GISTs in patients undergoing bariatric surgery and to investigate if simultaneous resection can be performed radical and safe from an oncologic standpoint. Secondly, we aimed to compare our findings with previously published reports. Finally, we provide an overview of the literature including a comprehensive discussion on the issue of GISTs as incidentalomas during bariatric surgery.

Materials and Methods

A single-center retrospective study was conducted on prospectively collected data of all morbidly obese patients, who underwent bariatric surgical procedures between January 2012 and August 2018 in the University Hospital, Leipzig, Germany. All cases of incidental GISTs, which were visually detected at the time of laparoscopic exploration and finally confirmed by pathology, were reviewed. All bariatric patients in our center undergo upper GI endoscopy preoperatively. None of those patients with intraoperatively detected GIST had any upper gastrointestinal tract neoplasms found during the EGD or other preoperative diagnostic examinations.

Patient demographic characteristics and clinical characteristics (gender, age, body mass index (BMI), and comorbidities, especially associated with metabolic syndrome, such as type 2 diabetes mellitus, hypertension, and dyslipidemia), tumor characteristics (localization, number, tumor size), including mitotic index and immunoreactivity against c-kit (CD 117), CD 34, DOG-1, Alpha-Smooth Muscle Actin (α-SMA), and S-100 along with the final TNM-pathological classification, operative course (R0-Resection, change of bariatric protocol), and patient follow-up were reviewed.

All operations followed standardized operative protocols and were performed by the same team of bariatric surgeons. These operations were either laparoscopic Roux-Y-Gastric bypass (RYGB), one Anastomosis Gastric Bypass-MiniGastric Bypass (OAGB-MGB) or Sleeve Gastrectomy (SG). Intraoperatively, in SG, the anterior and posterior wall of the stomach were inspected and not the small bowel, while in gastric bypass procedures, the anterior wall of the stomach, the pouch posterior wall, and out of the small bowel only alimentary and biliopancreatic limb were thoroughly inspected. Upon an unexpected abnormal macroscopic finding, this was surgically removed as a full-thickness specimen and with clear macroscopic margins. The specimen was intraoperatively send for frozen section biopsy assessment in order to exclude malignancy such as gastric adenocarcinoma and to verify the clear resection margins. If a sleeve gastrectomy was performed, the tumor was resected along with the specimen, if possible, and sent as a whole for pathological assessment. Following the intraoperative histological assessment, a decision was made whether or not to proceed with bariatric procedure as initially planned.

Results

Between January 2012 and August 2018, a number of 707 patients underwent bariatric surgery at our institution. Nine patients were found to have coincidental GISTs during the bariatric procedure, which was visually detected during the surgical exploration, resected, and finally confirmed in the pathological specimen, resulting in an incidence of 1.27% (13 per 1000). In all patients, the GISTs were removed either as wedge resection during RYGB or along with the specimen during LSG (Fig. 1).

Out of nine patients (Table 1) with coincidental GISTs, seven (78%) were female and two (22%) were male ($p < 0.01$). The mean age was 55.6 ± 14.9 (range 38–74). The mean BMI was 51.7 ± 8.96 mg/m^2 (range 38–71). All patients had hypertension (9/9, 100%), five patients had diabetes (5/9, 56%), and seven had dyslipidemia and steatohepatitis (8/9, 89%). No helicobacter pylori infection was diagnosed, neither in the preoperative gastric biopsies nor in the gastric specimen after sleeve gastrectomy.

Mean operative time was 170 min (range 85–302 min) and the mean length of hospital stay was 4 days. At the time of hospital admission before surgery, five patients were planned for RYGB and four patients for SG because of comorbidities and BMI.

No change in the initially planned bariatric surgical procedure was necessary upon coincidental detection of GISTs. In one patient receiving RYGB (case no. 2), multiple GISTs were resected from the small bowel (13 tumors in total), either by enterotomy or segmental resection, including parts of the common channel following RYGB. After repair of all sites of resection, including anastomosis, along with pathological verification of clear resection margins, RYGB was finally conducted. There was no perioperative mortality or morbidity, and all patients were discharged according to our standards on postoperative day 4.

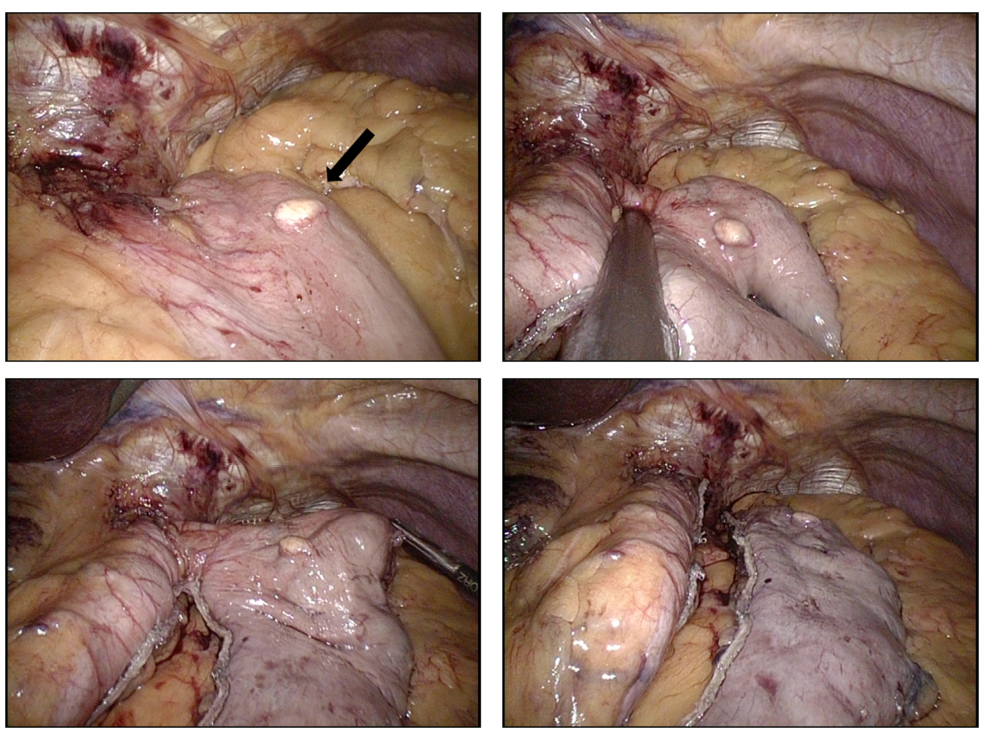

Fig. 1 GIST tumor (black arrow) located on the anterior aspect of gastric fundus, successfully removed along with the specimen during sleeve gastrectomy

Table 1 Patients characteristics

Case	Sex	Age	Weight	BMI mg/m^2	Diabetes mellitus type 2	Hypertension	Dyslipidemia	Steatohepatitis	Operation initially planned	Operation finally performed
No. 1	F	65	140 kg	53	+	+	+	+	RYGB	RYGB
No. 2	F	53	160 kg	56	+	+	+	+	RYGB	RYGB
No. 3	F	27	132 kg	49	−	+	−	−	RYGB	RYGB
No. 4	F	53	187 kg	71	+	+	+	+	Sleeve	Sleeve
No. 5	F	65	123 kg	46	+	+	+	+	RYGB	RYGB
No. 6	M	65	158 kg	50	+	+	+	+	Sleeve	Sleeve
No. 7	F	38	154 kg	54	−	+	+	+	RYGB	RYGB
No. 8	M	74	139Kg	48	−	+	+	+	Sleeve	Sleeve
No. 9	F	60	105 kg	38	−	+	+	+	Sleeve	Sleeve

The pathology reports from the surgical specimens revealed that all intraoperative-found lesions were GISTs with low or very-low risk of malignancy, with less than five mitoses per 50 high-power fields (HPF) (Table 2). The mean tumor size was 1 cm (range 0.2–3.7) with the majority of tumors (7/9, 85%) to be located in the stomach. All resected margins were disease-free. All tumors were positive for CD117, CD34, and DOG-1 and negative for α-SMA and S100 (Fig. 2). One lesion demonstrated a very weak immunoreactivity for CD117 and only perivascular immunoreactivity for α-SMA, while the expression of the rest of the markers was negative. The final diagnosis of GIST was attributed to this case based on the morphological characteristics and the subsequent molecular analysis of c-kit and/or PDGF-α mutation status.

Following complete resection, as part of the bariatric surgical procedure and final histological assessment, all patients were evaluated in the oncological interdisciplinary tumor board of our Institution. Due to the favorable pathological features and the estimated low risk of recurrence in all resected incidental GISTs, none of the patients received Imatinib adjuvant therapy and only surveillance was recommended.

Mean follow-up was 23.3 months (range 1–67 months). At 1 year, 6/6 patients eligible for follow-up had no evidence of disease progression (100% follow-up). At 2 years, 4/5 patients eligible for follow-up were disease-free, while one was lost from further follow-up (80% follow-up). At 3 years, 1/1 patient eligible for follow-up had no evidence of disease progression. At the time of this report, from the nine patients with incidental GISTs, five patients had oncologic follow-up with no evidence of disease progression, one patient was lost in follow-up, and the remaining three patients have pending surveillance workup.

Given the previous reports on incidental GISTs during bariatric surgery, we proceeded with a review of the existing literature in an effort to compare our data with those from previous patients' cohorts and to estimate the cumulative incidence of unexpected GISTs in bariatric patients (Table 3). In total, 59 cases of incidental GISTS among 8.236 patients undergoing bariatric surgery are reported, representing a cumulative incidence of 0.72% (7 per 1000). Of those, 54% were females (32/59) with a median BMI of 46.1 mg/m^2 and mean age of 55.4 years. The majority of unexpected GISTs were located in the stomach, had size less than 2 cm, and demonstrated very-low mitotic index (< 5 mitoses/50 HPF). All cases reported so far could be removed with clear margins, without changing the bariatric protocol.

Discussion

In this retrospective single-center study, we calculated the incidence of unexpected GISTs encountered during bariatric surgery in morbid obese patients to be 1.27% (13 per 1000). The coincidental GISTs were detected intraoperatively and resected simultaneously during the bariatric operation in all patients. The coincidence of prior undetected GISTs in bariatric surgical cases has been reported to be higher (0.3–1.2%, Table 3) when compared to the overall population (0.0006–0.0015%) [17]. Sanchez et al. described an incidence of 0.8% with 4 GISTs in 517 patients undergoing RYGB [18]. Yuval et al. reported an incidence of 0.6% with 5 GISTs in 827 patients undergoing SG [19], while another study by Crouthamel et al. presented an incidence of 0.8% with 12 GISTs in 1425 patients, who underwent only SG [20]. In the largest case series so far, Chiappetta et al. estimated an incidence of 0.3% with 8 GISTs in 2603 patients undergoing either RYGB or SG [21]. Two further recent reports presented an incidence of coincidental GISTs from 0.5% with 5 GISTs in 915 patients receiving only LSG [22] up to 1.2% with 16 GISTs in 1252 patients undergoing either RYGB or SG [23], respectively. Thus, our study with an incidence of 1.27%, based on a single-institution case series, demonstrates the highest incidence of GISTs associated with bariatric surgery so far. Taken all the reported cases together, an incidence of 0.72% (7 per 1000), with 59 reported incidental GISTs among 8.236 bariatric patients, can be recorded (Table 3). This

Table 2 Tumor characteristics

Case	Size [cm]	Localization	Mitotic index	TNM/UICC-stadium	Margins	CD117	DOG-1	CD34	α-SMA	S-100	Risk of malignancy
No. 1	1.0	Gastric corpus (unifocal)	1 mitose/50 HPF	pT1 pNX M0 L0 V0 Pn0 UICC-stadium IA	R0	+	+	+	–	–	Very-low risk
No. 2	0.2–3.7	Jejunum (multi-focal)	< 5 mitose/50 HPF	pT2 (m) pNX M0 L0 V0 Pn0 UICC-stadium I	R0	+	+	+	–	–	Low risk
No. 3	1.0	Jejunum (unifocal)	1 mitose/50 HPF	pT1 pN0 M0 L0 V0 Pn0 UICC-stadium I A	R0	–	–	–	–	–	Very-low risk
No. 4	0.5	Gastric antrum (unifocal)	1 mitose/50 HPF	pT1 pN0 M0 L0 V0 Pn0 UICC-stadium IA	R0	+	+	+	–	–	Very-low risk
No. 5	0.2	Gastric fundus (unifocal)	1 mitose/50 HPF	pT1 pNX M0 L0 V0 Pn0 UICC-stadium IA	R0	+	+	+	–	–	Very-low risk
No. 6	0.6	Gastric corpus (unifocal)	1 mitose/50 HPF	pT1 pNX M0 L0 V0 Pn0 UICC-stadium IA	R0	+	+	+	–	–	Very-low risk
No. 7	0.4	Gastric fundus (unifocal)	1 mitose/50 HPF	pT1 pNX M0 L0 V0 Pn0 UICC-stadium I	R0	+	+	+	+ (focal)	–	Very-low risk
No. 8	1.1	Gastric fundus (unifocal)	3 mitose/50 HPF	pT1 pNX M0 L0 V0 Pn0 UICC-stadium IA	R0	+	+	+	–	–	Very-low risk
No. 9	0.6	Gastric fundus (unifocal)	1 mitose/50 HPF	pT1 pNX M0 L0 V0 Pn0 UICC-stadium IA	R0	+	+	+	–	–	Very-low risk

incidence is more likely to approach the true incidence of incidental GISTs in obese patients, which, undoubtedly, remains considerably higher than the one in the general patient population [24].

This increased incidence of GISTs in patients with obesity may rely on a strong association at the molecular level between this specific tumor entity and obesity. Obesity is postulated to promote tumorigenesis via (1) increased bioavailability of growth factors and hormones; (b) altered adipocytokine levels such as leptin, adiponectin, and visfatin known to have growth, immune, and tumor-regulatory functions; (c) low-grade inflammation and oxidative stress affecting growth-promoting cytokines and immune modulation; and, more recently, (d) altered microbiomes [25]. Recently, the molecular pathogenesis of GIST has been linked to grehlin [26], a well-known orexigenic hormone that stimulates food intake and appears to be involved in the etiology of obesity [27]. Interestingly, both GISTs and grehlin-producing cells are mainly located in the gastric fundus [26], while GISTs have been found to express grehlin and grehlin receptors [28], suggesting a grehlin autocrine/paracrine loop in GIST tissues, which may explain why the occurrence and the development of GISTs are more frequent in obese patients. Such a molecular link between obesity and GISTs-pathogenesis merits further elucidation.

Another hypothesis for the high incidence of GISTs in obese patients during bariatric surgery may rely on the fact that many small, asymptomatic GISTs are underdiagnosed in the general population. Indeed, 20 to 30% of patients are found to have GISTs incidentally, usually on computed tomography (CT) scan performed for another indication [29], while 22% of GISTs are found at the time of autopsy [30]. In addition to that, there is currently a paucity of literature regarding GISTs found incidentally during other types of operations (laparoscopic hernia or appendectomy), which would allow a more reasonable comparison between different patients' groups with incidental pathology during laparoscopy. But then again, even in cases of removed incidental pathology, retrospective studies carried out using CD117 immunoreactivity as a diagnostic criterion have shown that GISTs are still underdiagnosed [31, 32]. The morphological spectrum of GISTs is nowadays wider than previously recognized. A recent study concluded that the clinical aggressiveness, incidence, and prevalence of GISTs have been historically underestimated [33]. In this study, the annual incidence of GIST was estimated at 14.5 per million per year with the prevalence of all GIST risk groups estimated at 129 per million [33]. A population-based incidence study conducted in Iceland reported a slightly lower incidence of 1.1 per 100,000 per year [34]. However, our current report together with the previous reports (summarized in Table 3) undeniably points to a much higher incidence of incidental GIST in obese patients.

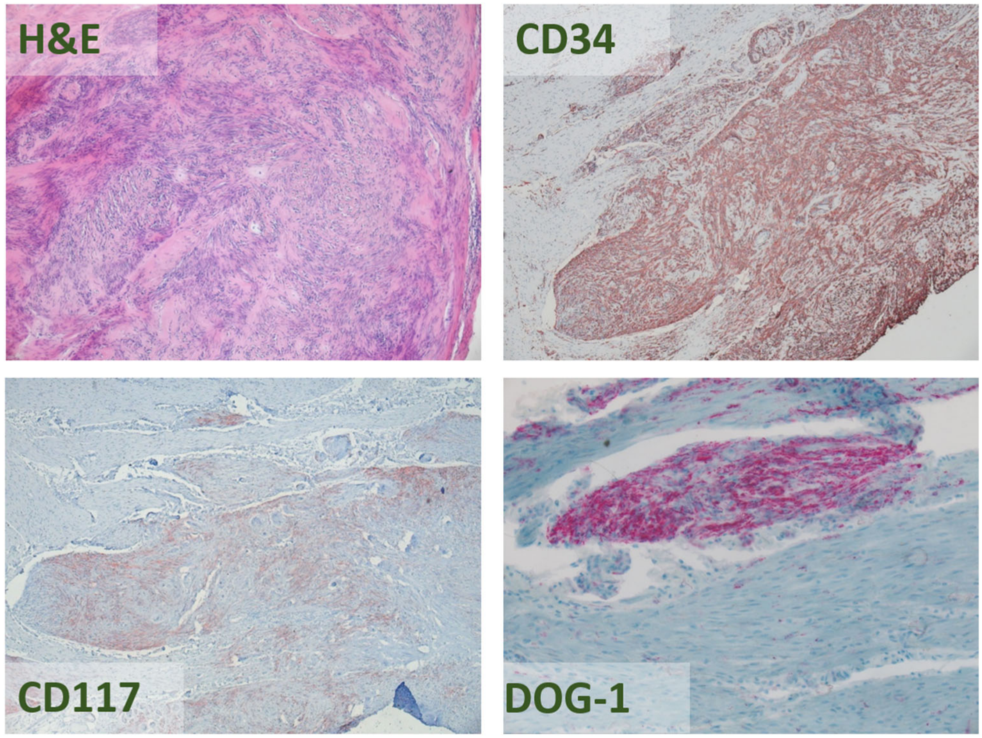

Fig. 2 Typical histopathological findings from GIST removed during laparoscopic bariatric procedure demonstrating positivity for CD34, CD117, and DOG1

Since we do not routinely run the small bowel during SG, or the common channel during RYGB, which would justify a more frequent detection of incidental findings, we attribute the highest so far reported incidence (1.27%) of unexpected GISTs associated with bariatric surgery in our study, to the fact that our cohort included more severe morbid obese patients, as shown by higher BMI (mean BMI 51.7 mg/m^2) and the higher prevalence of comorbidities (56% type 2 diabetes mellitus, 100% hypertension, 85% dyslipidemia, 85% fatty liver). An association of the increased incidence of GIST with the patient's geographical origin cannot be assumed, since epidemiology of GIST demonstrates consistent features across geographical regions and if we consider a previous case series, which demonstrated a fewer incidence of GISTs, was also based on German bariatric patients cohort [21]. The mean age of our patients was 55.6 years, similar to the previous reports. With an estimated mean age of 55.4 years of all reported GIST cases across the literature, it appears that GISTs are encountered in younger age in obese patients than in the general population, where GISTs are more likely to be diagnosed in the older age group (> 60 years) [35]. This may relay on the younger age of obese patients admitted to bariatric procedure. Notably, in our study, more female patients are recorded (78%). However, based on the previous reports, it appears that GISTs have a relative equal sex distribution between obese patients, similar to general population [36]. Positive helicobacter pylori (HP) gastritis was not addressed in any of our patients in the preoperative esophago-gastro-duodenoscopy, which comes in line with the previous conclusion that no association between positive HP and GISTs can be done [21].

GISTs demonstrate varying degrees of aggressiveness based on primary tumor location, size, and rate of mitoses. Notably, all incidental GISTs reported in bariatric patients are found mainly located in gastric fundus, having a small size (> 2 cm) and presenting low-risk pathologic features (Table 3). Similarly, in our cohort, the majority of GISTs were unifocal, mainly located in the stomach (with the exception of two intestinal GISTs), had small size (< 1.1 cm), and presented low mitotic index (< 1 mitose/50HPF). It is still unknown what contributes to the favorable pathologic characteristics and the low-risk malignancy of the GISTs encountered in bariatric patients. A recent study attempted to reversely assess the impact of obesity on pathologic and short-term outcomes in patients with resected GISTs. Interestingly, obese patients tended to have a superior prognosis than leaner counterparts [37]. The size of GISTs demonstrated an overall negative association with BMI (kg/m^2), while obese patients appeared to have smaller and surgically more manageable GISTs. Further, patients with lower BMI (< 30 kg/m^2) were reported to undergo more often multi-visceral resections for GIST removal than the more obese patients (BMI > 30 kg/m^2) [37]. Therefore, GISTs may represent another example of "obesity paradox," in which obesity provides a protective effect. Such an inverse relationship between obesity and favorable outcomes has been previously introduced for other types of malignancies [38–40]. Yet, it remains unclear which role obesity and body fat composition play in the tumor biology of GISTs.

Table 3 Review of existing studies and comparison

Study	Incidence (n)	Type of operation	Patients characteristics				Tumor characteristics			
			Mean age	Mean BMI	% Female	Diabetes mellitus	Tumor localization (stomach)	Size (cm)	Mitotic index	R0
Leipzig	1.27% (9/707)	RYGB/LSG	55.6	51.7	(7/9) 78%	56%	(7/9) 85%	0.2–3.7	< 5/50 HPF	100%
Waledziak et al. (2017)	1.2% (16/1252)	RYGB/LSG	55.5	48.9	(6/16) 37.5%	nm	(16/16) 100%	0.3–2	< 5/50 HPF	100%
Viscido et al. (2017)	0.5% (5/915)	LGS	59.6	50.5	(4/5) 80%	nm	(5/5) 100%	0.5–1.5	< 5/50 HPF	100%
Chiappetta et al. (2015)	0.31% (8/2603)	RYGB/LSG	54	48.5	(4/8) 50%	38%	(8/8) 100%	0.5–1.3	< 5/50 HPF	100%
Crouthamel et al. (2015)	0.8% (12/1415)	LSG	55	44.6	(9/12) 75%	nm	(12/12) 100%	0.3–2.9	< 5/50 HPF	100%
Yuval et al. (2014)	0.6% (5/827)	LSG	55.4	36	(1/5) 20%	60%	(5/5) 100%	0.32–1.3	< 5/50 HPF	100%
Sanchez et al. (2005)	0.8% (4/517)	LSG	52.7	44.75	(1/4) 25%	25%	(4/4) 100%	0.4–1	< 5/50 HPF	100%
Summarized results	0.72% (59/8236)	RYGB/LSG	55.4	46.1	54% (32/59)	46.2% (12/26)	97% (57/59)	0.2–3.7	< 5/50 HPF	100%

The incidence of unsuspected GISTs during bariatric surgery underscores the need for bariatric surgeons to be aware of this condition, in order to properly manage it. GISTs are difficult to diagnose via endoscopy, since they do not present mucosal involvement [41]. The preoperative workup with EGD may detect tumors that are larger than 2 cm, but will miss small ones, unless they are submucosal [42]. All our bariatric patients undergo preoperative EGD (reviewer no. 1, comment no. 6) during which none of the reported incidental GISTs were detected. All tumors were detected intraoperatively and were located on the serosal side of the stomach. Therefore, incidental pathology found during the abdominal exploration in bariatric procedures should be surgically removed, due to the increased possibility of GIST in those patients. The extent of the abdominal exploration is still in debate. It has been suggested that a thorough abdominal exploration should be mandatory and always performed by force [42]. In SG, such an exploration is always performed as part of the procedure itself, whereas in gastric bypass procedures, usually, only the anterior portion of the stomach is laparoscopically inspected, with the other posterior half to be overlooked. On the other hand, gastric bypass enables a more thorough exploration of the jejunum compared to sleeve gastrectomy. However, the reported elevated incidence of GIST in bariatric patients should not justify a more extended exploration intraoperatively. Evaluation of the entire small bowel, when sleeve gastrectomy is planned, or by force inspection of the posterior stomach during RYGB is most likely to lengthen the operation time and increase morbidity. The detected GISTs in our cohort were detected during our routine exploration of the entire stomach in case of SG, and the thorough inspection of the anterior stomach along with exploration only of the proximal jejunum, as part of the RYGB.

Incidental tumors during bariatric procedures should be analyzed histologically in frozen sections in order to rule out malignancy, such as gastric cancer. If the histopathology of GIST is confirmed or suspected, the surgical removal is the mainstay of therapy, with the goal of achieving negative microscopic resection margins (R0-Resection). Lymph node metastasis is rare; hence, radical lymphadenectomy is not recommended [43]. According to NCCN and ESMO guidelines, complete tumor excision is mandatory for GISTs with size > 2 cm, with the laparoscopic wedge resection to be a feasible and safe approach [43]. The laparoscopic approach should be clearly discouraged in patients with large tumors because of the risk of tumor rupture, which is associated with high risk of relapse [43]. The management of small incidental GISTs with size less than 2 cm is a matter of controversy. According to the most recent ESMO guidelines (2018), small nodules <2 cm, if diagnosed as GISTs, will be either low-risk or entities whose clinical significance remains unclear. Therefore, surveillance with endoscopic ultrasound and not immediate excision should be considered [43]. This recommendation concerns

GISTs discovered during endoscopy or ultrasonography, in which the risk of morbidities associated with invasive surgical resection is not justified by the low risk of malignancy of the lesions. However, intraoperatively discovered small nodules consist a different condition, and their excision should be performed, unless major morbidity if expected. This notion becomes more urgent, if we consider that even small GISTs (smaller than 1 cm) with low-risk features have shown potential for recurrence and metastasis [44]. As reported in all patients, incidental GISTs could be safely removed laparoscopically during bariatric surgery with negative microscopic resection margins, providing an oncologically adequate tumor removal, without changing the intentionally bariatric strategy. The risk of peritoneal contamination is negligible if the procedure is properly carried out (no manipulation of the nodule, usage of extraction bags). If a sleeve gastrectomy is being performed, the tumor can be resected along with the specimen if possible. Specimen after sleeve gastrectomy should not be discarded and promptly visually and digitally inspected on the table, with additional suture markings of any small nodularity for the pathologists [42]. Subsequently, sleeve gastrectomy is being increasingly recognized as a concomitant treatment option for obesity and GIST.

GISTs have unpredictable behavior and long-term follow-up is essential for all patients, independent of their benign or malignant characteristics according to standard guidelines [43]. An optimal follow-up schedule for the small, low-risk GIST encountered in bariatric patients in conjunction with their weight loss is not known. The frequency of surveillance should be dependent on the risk as judged by a consensus of the treating multidisciplinary team [45]. It is suggested that after clinical assessment, very-low-risk tumors may warrant no scans and routine follow-up. Low-risk tumors should have a single CT at baseline (3 months after surgery) then clinical assessment only with no further scans unless indicated. However, these recommendations concern all GIST patients regardless of their BMI. Undoubtedly, in bariatric patients, the altered anatomy should be taken into consideration during follow-up and clinical assessment. A recurrent GIST in the excluded stomach following RYGB may not give the typical symptoms as a GIST in a person with intact anatomy. Thus, in such cases, a more frequent surveillance program may prove beneficial for those patients.

Conclusion

The incidence of unexpected GISTs in obese patients, as shown based on bariatric surgery series reports, appears higher than in the general population. Therefore, the aspect of obesity should be taken into consideration during laparoscopic procedures, regardless of the scope, and incidental pathologies should be surgically removed, due to the higher risk for GIST pathology. However, additional unnecessary exploration besides the scopes of the actual planned operation can contribute to morbidity and should be avoided. Concomitant bariatric surgery and complete tumor resection in case of coincidental GIST are feasible, without compromising the objectives of each. All reported cases of incidental GISTs in obese patients found during bariatric procedure so far are small in size and have favorable pathological features with low or very-low risk of malignancy. The bariatric surgeon should be aware of this entity and prepared to manage it properly whenever encountered intraoperatively with R0 resection. Postoperatively, a multidisciplinary decision-making is warranted for further treatment or follow-up based on the risk assessment.

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Compliance with Ethical Standards

Statement Regarding Ethics and Consent For this type of study, formal consent is not required.

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

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