



Remnant Gastric Cancer After Roux-en-Y Gastric Bypass: Narrative Review of the Literature

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Abstract

Background The Roux-en-Y gastric bypass (RYGB) is one of the most commonly performed procedures for surgical weight loss. It has been shown that overweight may be associated with an increased risk of gastric cancer. However, the risk of remnant gastric cancer after RYGB has not been defined yet and the development of neoplasm in the excluded stomach remains a matter of concern.

Methods PubMed, EMBASE, and Web of Science databases were consulted. Articles that described the diagnosis and management of remnant gastric cancer after RYGB were considered.

Results Seventeen patients were included. The age of the patient population ranged from 38 to 71 years. The most commonly reported symptoms were abdominal pain, nausea/vomiting, and anemia. Abdominal computed tomography was used for diagnosis in the majority of patients. The neoplasm was located in the antrum/pre-pyloric region in 70% of cases and adenocarcinoma was the most common tumor histology (80%). An advanced tumor stage (III–IV) was diagnosed in almost 70% of patients and 40% were considered unresectable. Gastrectomy with lymphadenectomy was performed in 9 cases (53%). Post-operative morbidity was 12%. The follow-up ranged from 3 to 26 months and the overall disease-related mortality rate was 33.3%.

Conclusion The development of remnant gastric cancer after RYGB is rare. Surgeons should be aware of this potential event and the new onset of epigastric pain, nausea, and anemia should raise clinical suspicion. Further epidemiologic studies are warranted to deeply investigate the post-RYGB-related risk of remnant gastric cancer development in high-risk populations.

Keywords Roux-en-Y gastric bypass · Remnant gastric cancer · Early diagnosis

Introduction

The Roux-en-Y gastric bypass (RYGB) is one of the most commonly worldwide-performed procedures for surgical weight loss. Because of its standardization and excellent

results, the laparoscopic RYGB is considered by many the gold standard to treat morbid obesity [1]. However, the diagnosis and treatment of developing diseases in the gastric remnant are challenging and represent a major limitation [2].

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The epidemiologic association between excess body weight and gastric cancer is debated. It has been shown that overweight and obesity may be associated with an increased risk of gastric cancer and the strength of this association increases with BMI [3]. However, the risk of gastric cancer after bariatric surgery has not been established and the onset of neoplasm in the excluded stomach after RYGB remains a great concern in the western and eastern countries.

The purpose of this narrative review [4] was to evaluate the reported incidence of remnant gastric cancer after RYGB and to summarize the current knowledge on diagnostic and treatment workup.

Materials and Methods

An extensive literature review was performed to identify all English-written published case reports and case series on the development of remnant gastric cancer after RYGB. PubMed, EMBASE, and Web of Science databases were consulted matching the terms “cancer,” “tumour,” “adenocarcinoma,” “stomach,” “gastric,” “bariatric surgery,” and “gastric bypass” with “AND” and “OR” until 31st of December 2018. All abstracts were evaluated and full text acquired for relevant studies. The search was completed by consulting the listed references of each article. Non-human studies, reports of neoplasm after bariatric surgery different from RYGB, cancer of the esophagus, gastric pouch, alimentary limb, or other sites different from the remnant stomach were excluded.

Two authors (ST and AA) independently extracted data from eligible studies. Data extracted included study characteristics (first author name, year, and journal of publication), number of patients included in the series, time frame, clinical and demographic characteristics of patients’ population, type of surgical procedure, and outcomes.

Results

Fifteen papers were included in the narrative review for a total of 17 patients (Table 1). There were 3 case series and 12 case reports. The age of the patient population ranged from 38 to 71 years and 76.5% were females. The median time from RYGB to tumor diagnosis was 9.3 years (range 1–22). The duration of symptoms was reported in 10 papers and ranged from 1 month to 6 years. The most commonly reported symptoms were abdominal pain (76.5%), especially in the epigastric region (35.3%), nausea and vomiting (35.3%), abdominal distention (29.4%), anemia, excessive weight loss, and gastrointestinal bleeding (17.6%) (Table 2). An abdominal computed tomography was performed for diagnosis in 70.5% of patients. Other exams include trans-gastric endoscopy, double-balloon enteroscopy, endoscopic ultrasonography (EUS),

positron emission tomography (PET), and technetium-99m-labeled red blood cell scan.

The tumor was located in the antrum/pre-pyloric region in 12 patients (70.5%), in the gastric body in two patients (11.7%), and in the gastric fundus in one patient (5.9%). Two patients (11.7%) were diagnosed with *linitis plastica*. Overall, 5 papers recorded the examination for *Helicobacter pylori* (HP) in the specimen, with one positive histologic result. Other reported risk factors for gastric cancer were smoking, family history of upper GI neoplasm, alcohol abuse, and vitamin D₃ deficiency.

Gastric adenocarcinoma was the most frequent tumor histology (88.2%), followed by gastric lymphoma (5.9%), and gastrointestinal stroma tumor (GIST) (5.9%). The pathological tumor stage was reported in 15 patients: Tis was diagnosed in 13.3%, stage IA in 6.6%, stage IIB in 6.6%, stage IIIB in 33.3%, and stage IV in 40% of patients.

At the operation, seven patients had an unresectable tumor and underwent palliative chemotherapy (41%). Decompressive gastroenterostomy and surgical gastrostomy were performed in two patients. Overall, nine patients underwent subtotal gastrectomy with lymphadenectomy while another patient underwent trans-gastric laparoscopic resection of a pre-pyloric degenerated polypoid lesion. Post-operative complications occurred in two patients (11.7%) with one intra-abdominal abscess managed with percutaneous drainage and one pneumonia managed with antibiotics. The 30-day mortality was 0%. The follow-up was reported in 15 studies (range 3–26 months) and the disease-related mortality rate was 33.3%.

Discussion

Morbid obesity has become a worldwide health problem probably because of the change in dietary habits and sedentary lifestyle [20]. Concomitantly, bariatric surgery has gained growing popularity because of its long-term effectiveness in weight loss and comorbid resolution [21]. Because of its standardization and excellent results, the laparoscopic RYGB is considered by many the gold standard to treat morbid obesity, and the American Society for Metabolic and Bariatric Surgery (ASMBS) estimated that almost 20% of the 228,000 bariatric procedures performed in 2017 were constituted by RYGB <https://asmbs.org/>[22]. The RYGB combines a restrictive, malabsorptive, and metabolic effect with a steady reduction of BMI. However, the difficult endoscopic evaluation of the gastric remnant is a matter of concern particularly in countries where the high incidence of gastric cancer mandates the necessity to perform upper endoscopy screening exams [23]. Even if limited by patients’ number and follow-up, different surgical alternatives to the classical RYGB have been

Table 1 Demographic, clinical, and operative data of the patient population

	Nation	Age (years)	Sex	Years from RYGB	Symptom duration	Treatment	Tumor location	Histology	Staging
Rajjman 1991 [5]	USA	38	F	5	Nr	Explorative laparotomy	Body	Adenocarcinoma	IIIB
Lord 1997 [6]	Australia	71	F	12	6 years	Distal gastrectomy	Antrum	Adenocarcinoma	IA
Khiin 2003 [7]	USA	57	F	22	2 months	Distal gastrectomy	Antrum	Poorly differentiated adenocarcinoma	IIIB
Escalona 2005 [8]	Chile	51	F	8	2 months	Resection of the excluded stomach	Antrum	Signet ring cells adenocarcinoma	IIIB
De Roover 2006 [9]	Belgium	66	m	3	6 months	Resection of the excluded stomach	Fundus	Diffuse large B cell lymphoma	Nr
Corsini 2006 [10]	Brazil	57	m	4	4 months	Decompressive gastroenterostomy	Antrum	Poorly differentiated adenocarcinoma	IV
Watkins 2007 [11]	USA	44	m	14	4 years	Resection of the excluded stomach	Antrum	Adenocarcinoma	IIIB
Harper 2007 [12]	USA	45	F	1	Nr	Decompressive gastrostomy	Antrum	Adenocarcinoma	IV
Swain 2010 [13]	USA	66	F	21	Nr	Resection of the excluded stomach	Pylorus	Early gastric cancer	0 (Tis)
	USA	69	F	20	Nr	Resection of the excluded stomach	Pylorus	Adenocarcinoma	Nr
Abellan 2013 [14]	Spain	57	F	4	Nr	Resection of the excluded stomach	Body	GIST	IIIB
Nau 2013 [15]	USA	55	F	4	1 month	Explorative laparoscopy	Limitis plastica	Poorly differentiated gastric carcinoma	IV
Tinoco 2015 [16]	Brazil	56	F	10	2 month	Resection of the excluded stomach	Antrum	Adenocarcinoma	IIIB
D'Antonio 2017 [17]	Italy	58	F	4	Nr	Laparoscopic trans-gastric resection of the polyp	Antrum	Early gastric cancer	0 (Tis)
Ali 2018 [18]	USA	40	F	13	Nr	Chemotherapy	Antrum	Signet cell gastric adenocarcinoma	IV
	USA	50	F	6	9 months	Explorative laparoscopy	Antrum	Poorly differentiated gastric carcinoma	IV
Haenen 2018 [19]	Belgium	52	F	7	1 month	Explorative laparoscopy	Limitis plastica	Adenocarcinoma	IV

Table 2 Patients' symptoms. Data are reported as numbers and percentages (%)

Symptoms	n (%)
Abdominal pain	13 (76.5)
Epigastric pain	6 (35.3)
Nausea/vomiting	6 (35.3)
Abdominal distention	5 (29.4)
Anemia	3 (17.6)
Weight loss	3 (17.6)
GI bleeding	3 (17.6)
Fever	2 (11.8)
Hyporexia	2 (11.8)

described in an attempt to overcome the limitations of the original procedure [24, 25].

Data on the development of remnant gastric cancer after RYGB are scarce and the real-world incidence is unknown. In the last 10 years, there has been a significant increase in the number of literature-reported cases probably because of the concomitant increase of RYGB procedures or previous underreporting. The exact pathological mechanism remains unclear. Flickinger et al. conducted a study to evaluate the gastric remnant in 53 patients after RYGB. The presence of bile reflux was documented in all patients while 17 patients were diagnosed with chronic gastritis and 5 with gastric metaplasia. The authors concluded that the chronic alkaline reflux, not washed out by meals or gastric peristalsis, may act as a chronic inflammatory stimulus possibly causing intestinal metaplasia and dysplasia [26]. Additionally, family history of gastric cancer, intestinal metaplasia, or dysplasia has been proposed to be associated with an increased risk of remnant gastric cancer.

The diagnosis is usually late because symptoms are aspecific, puzzled, and could be interpreted as physiological consequences of the bariatric operation. Weight loss up to 40% EWL is expected after a RYGB, abdominal pain could be related to the presence of post-operative peritoneal adhesions, and anemia may be caused by iron, and folate or vitamin B₁₂ malabsorption. However, the new onset of symptoms in patients with a regular post-bariatric course and the concomitant presence of the triad abdominal pain, excessive weight loss, and nausea/vomiting should alarm clinicians. The diagnostic workup and the definitive histological diagnosis are troublesome. Abdominal CT scan with intravenous iodine contrast was used in the majority of patients and may be useful to detect gastric wall thickening, remnant gastric distention with outlet obstruction, lymphadenopathies, metastasis, free fluid, and signs of peritoneal carcinomatosis. However, these radiological signs may not be present in early tumor stages. Direct endoscopic examination is feasible and safe in the presence of a short limb loop or through a surgical-

assisted trans-gastric endoscopy, and double-balloon enteroscopy has been proven useful in reaching the remnant in selected patients [27, 28]. Despite all these procedures being valuable options, they are costly, time-consuming, limited by patients' post-operative adhesions/strictures, and not suitable for screening purposes [29]. For all these reasons, the definitive diagnosis is challenging and usually completed in a late stage when curative resection is not feasible with palliative chemotherapy or decompressive gastric surgery being the only therapeutic options. If feasible, surgical resection of the gastric remnant with celiac lymphadenectomy has been shown to be feasible and safe and should be considered as a definitive treatment.

Principal limitations of this narrative review are the small number of patients and the possible background selection bias related to the heterogeneity of the included studies and methodological quality. It is worthwhile that the development of remnant gastric cancer after RYGB should be further investigated in high-risk populations and reported in long-term follow-up datasets.

Conclusion

Data on the development of remnant gastric cancer after RYGB are scarce and the real incidence is unknown. Because of the increasing number of bariatric operations, surgeons should be aware of this potential event. The new onset of epigastric pain, nausea, and sense of abdominal distention should always raise clinical suspicion to obtain an early diagnosis and achieve definitive treatment. Further epidemiologic studies are warranted to deeply investigate the risk of post-RYGB remnant gastric cancer development especially in high-risk populations.

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Author Contribution AA and ST did the literature search. AA and DB formed the study design. Data collection were done by A.A, ST, and D.B. AA and GB analyzed the data. AA, GB, and DB interpreted the data. ST, PGB, and AA wrote the manuscript. AA, GM, and DB critically reviewed the manuscript.

Compliance with Ethical Standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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

Informed Consent Not applicable.

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