

## Adenocarcinoma of the upper gastrointestinal tract after bariatric surgery. A review of the literature.

Vladimirov M \*, Hesse U, Stein H.J.

Department of General, Visceral and Thoracic Surgery, Paracelsus Medical University Nürnberg, Nuremberg Hospital, Germany

\*Corresponding author: Vladimirov M, Department of General, Visceral and Thoracic Surgery, Paracelsus Medical University Nürnberg, Nuremberg Hospital, Germany. E-mail: [Vladimirov@uni-tuebingen.de](mailto:Vladimirov@uni-tuebingen.de)

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### Abstract

Obesity is associated with an increased risk of cancer development in the upper gastrointestinal tract.

One own case of a female patient with gastric carcinoma after sleeve gastrectomy was the reason to review the literature about the frequency and the genesis of gastric carcinoma after bariatric surgery. Additional to our case 3 further patients with gastric carcinoma after sleeve gastrectomy and 33 patients with carcinomas of the upper gastrointestinal tract after other bariatric operations are reported in the literature. Due to a lack of registry studies the incidence of gastric cancer after bariatric surgery cannot be calculated.

Early diagnostics should be performed in symptomatic patients and in patients with unspecific symptoms after bariatric surgery to avoid a delay of the diagnosis of potential carcinomas of the upper gastrointestinal tract.

**Keywords:** bariatric surgery; gastrointestinal

### Introduction

The frequency of weight-loss surgeries is increasing. After bariatric procedures postoperative complications and a variety of symptoms may occur.

Malignancies after bariatric surgery are rare, but accurate quantification is not available.

The treatment of a female patient with gastric cancer after sleeve gastrectomy was the reason to review the literature about the incidence and etiology of gastric cancer following bariatric surgery.

The literature search was carried out in PubMed for articles published to July 31, 2016. Key words used were gastric cancer, gastric adenocarcinoma, esophageal cancer, esophageal carcinoma, bariatric surgery, gastric bypass, vertical banded gastroplasty, gastric band, sleeve gastrectomy.

Abstracts were reviewed, relevant articles were obtained and their reference lists were searched to identify further relevant studies.

### Results

In addition to one own case 3 further patients with gastric carcinoma after sleeve gastrectomy are reported in the literature (Table 1) (1, 2, 3).

		Author, year of publication		
	Scheepers, A.F. 2011 (1)	Angrisani, L. 2013 (2)	Masur, M. 2016 (3)	Vladimirov, M 2016
Patient (age, gender)	57 years, female	51 years, female	44 years, female	47 years, female
Cancer localisation	lower esophageal adenocarcinoma	body and antrum of stomach,	10 cm from gastroesophageal junction,	antrum of stomach,
Histology	uT2, uN1, cMx	signet-ring cell adenocarcinoma	adenocarcinoma	mucinous adenocarcinoma
		pT4, pN1, cM0	pT4b, pN3a, cM0	pT1b(sm3), pN0, cM0
Time between bariatric surgery	4 months	24 months	9 months	75 months

and diagnosis of cancer				
Preoperative upper endoscopy	no	yes	no	yes

**Table 1.** Case reports of esophagogastric cancer after sleeve gastrectomy

After other bariatric operations additional 33 carcinomas of the upper gastrointestinal tract are described. The majority of the tumors, n = 19, was located in the distal esophagus, at the cardia or within the proximal gastric pouch (Table 2) (4, 5, 6, 7, 8, 9, 10, 11).

Bariatric procedure	Localisaton of the tumor				
	Distal esophagus n	Cardia n	Stomach n	Gastric pouch n	Excluded stomach n
Vertical banded gastroplasty	1		2	3	
Silastic ring vertical banded gastroplasty			1	1	
Gastric banding	3		1	2	
Roux-en-Y gastric bypass	4	2		2	5
Omega loop gastric bypass				1	3
Banded Roux-en-Y gastric bypass					2

**Table 2.** Case reports of adenocarcinomas of the upper gastrointestinal tract after bariatric operations, n = 33 (4, 5, 6, 7, 8, 9, 10, 11) In the 4 patients with gastric adenocarcinoma after sleeve gastrectomy tumors were diagnosed 4, 9, 24 and 75 months after the bariatric procedures had been carried out (Table 1). Esophagogastric cancers after the other bariatric operations (n = 33) listed in Table 2 were diagnosed between 2 months and 29 years postoperatively, at a mean of 8.6 years.

**Discussion**

Cohort studies have shown a positive association between obesity and the incidence of malignancies of the esophagus, the gallbladder, the breast, the ovaries, the pancreas, the prostate, the colon, the endometrium, the kidney and leukemia (12). Obesity is involved in 16% (12) of all types of cancer. Obesity and gastric cancer are strongly related, particularly a BMI  $\geq 25$  kg/m<sup>2</sup> (odds ratio = 1.55) (13) was associated with an increased risk

of gastric cancer of the cardia. One proposed pathway is that increased body weight may increase gastroesophageal reflux which has been associated with adenocarcinoma in Barrett’s esophagus. Obesity in adolescence at an age of 18 with a BMI  $\geq 25.3$  kg/m<sup>2</sup> was associated with a higher risk of gastric cancer (14). Other mechanisms (Table 3) are discussed such as alterations in insulin resistance, increased insulin and IGF levels (insulin-like growth factor), the levels of adiponectin and leptin (13, 14, 15, 16, 17, 18).

Stomach	Localisaton of the tumor Gastric pouch	Excluded stomach
BMI at adolescence	GERD	Biliary pancreatic reflux
Insulin resistance	Mucosal irritation for stasis	Intestinal metaplasia
IGF level Estrogen level Helicobacter pylori	Presence of gastric band	

**Table 3** Gastric cancer etiology. Pathophysiology and risk factors (13, 14, 15, 16, 17, 18)

BMI = body mass index; GERD = gastroesophageal reflux disease; IGF = insulin-like growth factor

Bariatric surgery is an effective treatment of obesity and related with a significant reduction in incidence of cancer (5), but carcinogenesis cannot be prevented completely. In a retrospective review 3 of 2875 patients (0.1 %) were reported who had undergone bariatric operations and developed adenocarcinoma of the distal esophagus (19). Due to a lack of registry studies the incidence of gastric cancer after bariatric surgery cannot be calculated.

Pathophysiologic explanations for esophagogastric cancer after restrictive bariatric procedures are chronic gastroesophageal reflux with development of Barrett's esophagus (20), stasis of food and gastric acid in the gastric pouch causing mucosal irritation (9), increased exposure of the vulnerable lower esophagus to carcinogens unavoidably placed closer to the esophagus within a gastric pouch (11), and local irritation caused by implanted gastric bands (10).

After Roux-en-Y gastric bypass cancer may develop within the gastric pouch as well as in the excluded stomach. The exclusion of the bypassed part of the stomach eliminates its contact with exogenous carcinogens and may be cancer protective. In an experimental rat model Roux-en-Y gastric bypass reduced the risk of dietary-induced gastric cancer (21). On the other hand bile reflux into the excluded stomach is proven, which is discussed to be carcinogenic (22, 23). Also as a potential carcinogen, *Helicobacter pylori*, even if eradicated before restrictive bariatric surgery, may persist in the bypassed part of the stomach (23).

In the here reported 37 cases of upper gastrointestinal cancers the malignancies were diagnosed at a mean of 95 months (7.9 years) after bariatric surgery, ranging from 2 months to 29 years. In patients not undergoing preoperative endoscopy, time intervals between bariatric surgery and cancer diagnosis were shorter than in patients with preoperative endoscopy. In some patients with reported intervals less than 24 months after surgery it can be speculated, whether the tumors had existed at the time of the bariatric procedures. In these cases routine preoperative endoscopy might have been able to detect the malignancies. Regardless of the possible link between bariatric procedures and subsequent cancer development, we recommend early esophagogastroduodenoscopy in symptomatic patients and in patients with unspecific symptoms after bariatric surgery to avoid a delay in the diagnosis of potential cancer of the upper gastrointestinal tract.

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