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Alkaline Reflux Esophagitis in Patients with Total Gastrectomy and Roux en Y Esojejunostomy

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Abstract

Background and Aims. Alkaline reflux esophagitis is a complication that might develop in patients with total gastrectomy. The aim of the study was to analyze the prevalence and severity of reflux esophagitis and the occurence of complications (Barrett's esophagus and esophageal stenosis) in patients with total gastrectomy and Roux en Y esojejunostomy. **Methods**. 92 patients with total gastrectomy performed for gastric cancer were included in the study. None of the patients had esophagitis prior to gastrectomy. The patients were assessed clinically and endoscopically after a certain interval from surgery. **Results**. An important number of patients (14 out of 92, 15.22%) had reflux esophagitis; 5.43% of the patients had also complications of reflux esophagitis (Barrett's esophagus and benign esophageal stenosis) and 6.52% had local tumor recurrence. Of the 14 patients with reflux esophagitis, the majority (9/14) had Los Angeles (LA) grade C esophagitis. The mean interval between surgery and the endoscopic evaluation was 4.43 years. Barrett's esophagus and benign stenosis were diagnosed after a longer period of time (10.33 and 8 years, respectively) as compared to reflux esophagitis (5.29 years). More than half of the esophagitis patients had reflux symptoms. **Conclusions**. Although Roux en Y esojejunostomy is a reconstructive technique which prevents the reflux, an important percentage of our patients developed alkaline reflux esophagitis. In most cases, the esophagitis was moderate or severe. Complications of alkaline reflux, i.e. benign stenosis and Barrett's esophagus, also occurred after longer periods of time (8 to 10 years) in a small percentage of patients.

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Key words

Alkaline reflux esophagitis – total gastrectomy – Roux en Y esojejunostomy – gastric cancer – Barrett's esophagus – esophageal stenosis.

Introduction

Alkaline reflux esophagitis is a complication occurring after total gastrectomy. Its postoperative incidence depends on the type of reconstructive surgery. Roux-en-Y esophagojejunostomy is the preferred method of reconstruction because it is followed by a lower rate of alkaline esophagitis as compared to other procedures (simple esophagojejunostomy, esophagoduodenostomy) [1-3]. The length of the jejunal loop (i.e., the distance between the esophagojejunostomy and the site where the duodenal content enters the alimentary tract) has a determining role in preventing the reflux. It is considered that the length of the loop must be of at least 35-40 cm, preferably over 50 cm [1, 4, 5]. This type of reconstruction allows the food progression from the esophagus to the intestine and also prevents alkaline reflux into the esophagus [6, 7].

The role of the different components of the refluxate in the pathogenesis of alkaline esophagitis is only partially known. Some studies in animals showed that trypsin, deconjugated bile salts, and lysolecithin are more damaging to the esophagus in the absence of gastric acid [8].

Clinical signs and symptoms such as heartburn, bitter taste, regurgitation suggest the presence of reflux esophagitis. Esophagoscopy is considered the golden standard for the diagnosis of esophagitis. In the absence of esophagitis, the reflux is usually asymptomatic [9].

In the evolution of patients with alkaline reflux esophagitis, certain complications can occur. The most frequent are Barrett's esophagus and stenosis. The acid reflux has been considered to be the main cause for Barrett's esophagus [10], but recent studies revealed that alkaline reflux could also play an important role in the development of this condition [11].

In the present study we analyze the prevalence

and severity of reflux esophagitis in patients with total gastrectomy and Roux en Y esophagojejunostomy, as well as the occurrence of the reflux complications (Barrett's esophagus and esophageal stenosis). We also assessed the prevalence of reflux symptoms and dysphagia, as well as the relationship between their presence and the endoscopic changes.

Material and methods

Patients

Ninety-two patients who had underwent total gastrectomy in a tertiary medical centre (3rd Surgery Clinic, Cluj Napoca) were included in this study. The surgical interventions were performed between January 1984 and December 2006.

The indication for surgery was gastric cancer in all patients. The patients with partial gastrectomy and those with documented reflux esophagitis prior to surgery were excluded from the study. The reconstructive procedure used was Roux en Y esophagojejunostomy. This technique implied sectioning of the jejunum about 40 cm distally to the angle of Treitz and subsequently sectioning of the mesentery, but preserving intact the second grade vessels. The distal loop was brought up either via a precolic or a transmesocolic approach for at least 60 cm and a termino-lateral Y-shaped anastomosis was performed.

The case selection was performed from the database of the 3rd Surgical Clinic, a hospital where an average of 28 surgical interventions of this type were performed annually. The patients were contacted and scheduled for investigation by letter or phone.

Only 92 of the selected patients presented for medical examination. All the patients were assessed clinically, by abdominal ultrasonography and by upper digestive endoscopy in the 3rd Medical Clinic, Cluj Napoca between January 2005 and December 2007.

The study was performed in agreement with the Helsinki Declaration and was approved by the Hospital Ethics Committee. A written informed consent was obtained from all the patients.

Method

The medical history included questioning the patients for the presence of the following symptoms: heartburn, bitter taste, regurgitations and dysphagia.

The upper digestive endoscopy evaluated the esophagus, the esojejunostomy anastomosis and the first 20-30 cm of the intestinal loop. The esophagitis lesions were classified according to the Los Angeles (LA) classification: grade A esophagitis: one or more mucosal breaks no longer than 5 mm; grade B esophagitis: one or more mucosal breaks longer than 5 mm, none of which extending between the tops of two mucosal folds; grade C esophagitis: at least one mucosal break that extends betwen the tops of two or more mucosal folds, and involves less than 75% of the esophageal circumference; grade D esophagitis: mucosal breaks which involve at least 75% of the esophageal circumference.

We investigated Barrett's esophagus and benign esophageal stenosis as complications of the jejunoesophageal reflux. The Barrett's esophagus was diagnosed based on the suggestive endoscopic (isles of reddish mucosa going beyond the esojejunal anastomosis) and histological aspect (cylindrical epithelium and goblet cells). Benign esophageal stenosis was diagnosed by the direct view of stenosis covered by normal mucosa with benign histology and confirmed by fluoroscopy.

The diagnosis of local tumor recurrence was established upon the endoscopic description: irregular and/or infiltrated mucosa at the esojejunal anastomosis site. Malignancy was in all cases confirmed by histology.

Statistical analysis

We used Chi square/Fisher tests for the statistical analysis of the qualitative data. We conducted a preliminary distribution testing. The tests were chosen to correlate numerical and qualitative variables, also taking into consideration the approach to Gaussian distribution and the number of non-numerical variable categories. We used Anova/Student and Kruskall-Wallis/ Mann-Whitney U Tests, as the situation required. A $p<0.05$ was considered to have significance for all selected tests. We used the SPSS 13.0 programme (Chicago, II) for data processing.

Results

The demographic and endoscopic features of the patients are displayed in Table I. The mean age of the patients was 58.28 years. Patients were predominantly males. The mean interval between the surgical intervention and the clinical and endoscopic evaluation was 4.43 years. The endoscopic assessment of the 92 patients found that the majority had a normal endoscopic aspect. However, a significant percentage (15.22%) presented reflux esophagitis, 5.43% had reflux complications (Barrett's esophagus or benign esophageal

Table I. Characteristics of patients with total gastrectomy

Characteristics	
Age (years)	58.28±9.59 (range 31 to 75)
Gender: no (%)	
Male	65 (70.65)
Female	27 (29.35)
Interval between surgery and endoscopy (years)	4.43±3.81 (range 1 - 23)
Endoscopic aspect: no (%)	
Normal	67 (72.83)
Esophagitis	14 (15.22)
LA grade A	3 (3.26)
LA grade B	2 (2.17)
LA grade C	9 (9.78)
Reflux complications	
Barrett's esophagus	3 (3.26)
Benign esophageal stenosis	2 (2.17)
Local tumor recurrence	6 (6.52)

stenosis), and 6.52% local tumor recurrence. No patient had hepatic or peritoneal metastases, as assessed by abdominal ultrasonography. Of the 14 patients with reflux esophagitis, most (9/14) had LA grade C esophagitis.

The analysis of the endoscopic changes and the interval between surgery and endoscopy showed that Barrett's esophagus and benign esophageal stenosis occurred after a longer period of time (10.33, respectively 8 years) in comparison with the lesions of esophagitis (5.29 years). The differences, however, were not statistically significant. Local tumor recurrence appeared after a relatively short period of time (Table II).

The patients' age did not influence the endoscopic changes. Reflux esophagitis occurred evenly in male and female patients (Table III). Severe esophagitis (LA grade C), complications (Barrett's esophagus, benign esophageal stenosis) and local tumor recurrence were more frequently present in males, but again without statistical significance ($p>0.05$).

Reflux symptoms (heartburn, bitter taste and /or regurgitations) were present in 28.26% of the patients. In the absence of endoscopic lesions, most of the patients (79.1%) were asymptomatic. More than half of the patients with esophagitis had reflux symptoms. Symptoms were more frequent in patients with LA grade C esophagitis (Table IV).

Dysphagia was present in 12 of the 92 patients (13.04%). Of these, 2 had local tumor recurrence, 1 had benign stenosis, 2 had reflux esophagitis (LA grade A or C) and 7 had a normal endoscopic aspect. No significant correlation was found between the presence of dysphagia and the endoscopic changes (Table V).

Discussion

The reconstruction of the alimentary tract after total gastrectomy has been the subject of many controversies in the past and over 50 reconstructive procedures are described in the medical literature [12, 13]. Roux en Y esophagojejunostomy is considered to be the most efficient procedure that also ensures the prevention of reflux.

The postgastrectomy reflux consists of the passage of jejunal content into the esophagus [9]. This can be accompanied by reflux symptoms: heartburn, regurgitations and/or bitter taste. The reflux can be assessed by scintigraphic methods, bilimetry (the measurement of bilirubin concentration in the esophagus) and 24-hour intra-esophageal pH monitoring (Holter) to confirm the alkaline pH in the esophagus [6, 14]. Alkaline reflux esophagitis, a complication of the jejunoesophageal reflux, consists of inflammatory lesions of the mucosa. It occurs only in some patients with reflux and is diagnosed at upper digestive endoscopy.

Table II. The relation between endoscopic changes, interval from surgery, and age of the patients

Endoscopic aspect	The interval between surgery and endoscopy (years)			Age (years)		
	Mean± SD	Min	Max	Mean± SD	Min	Max
Normal	4.5±3.28	1	20	57.63±9.98	31	75
Esophagitis						
LA grade A	5.33±3.79	1	8	63.0±3.0	60	66
LA grade B	3.00±1.41	2	4	66.50±0.71	66	67
LA grade C	5.78±4.09	1	11	60.89±10.04	47	71
Barrett's esophagus	10.33±9.97	4	23	53.67±7.09	46	60
Benign esophageal stenosis	8.00±2.83	6	10	59.50±14.85	49	70
Local tumor recurrence	2.67±1.97	1	6	58.50±7.48	47	65
	p=0.083			p=0.70		

Table III. The relation between endoscopic lesions and gender

Endoscopic aspect	Male (%)	Female (%)	Number of patients
Normal	48 (71.67)	19 (28.36)	67
Esophagitis	7 (50.0)	7 (50.0)	14
LA grade A	0 (0)	3 (100.0)	3
LA grade B	1 (50.0)	1(50.0)	2
LA grade C	6 (66.66)	3 (33.33)	9
Complications (Barrett's esophagus, benign stenosis)	4 (80.0)	1 (20.0)	5
Local tumor recurrence	6 (100.0)	0 (0)	6
Total number of patients	65	27	92
	χ^2=10.43; df=5; p=0.06		

Table IV. The relation between endoscopic lesions and reflux symptoms

Endoscopic aspect	Patients without reflux symptoms (%)	Patients with reflux symptoms (%)	Total number of patients
Normal	53 (79.10)	14 (20.90)	67
Esophagitis	6 (42.86)	8 (57.14)	
LA grade A	2 (66.67)	1 (33.33)	3
LA grade B	2 (100.0)	0 (0)	2
LA grade C	2 (22.22)	7 (77.78)	9
Complications: Barrett's esophagus, benign stenosis	3 (60.0)	2 (40.0)	5
Local tumor recurrence	4 (66.67)	2 (33.33)	6
Number of patients	66	26	92
	χ^2=13.91; df=5; p=0.48		

Table V. The correlation between dysphagia and endoscopic lesions

	Endoscopic changes				Number of patients		The interval between surgery and endoscopy			
	Normal	Esophagitis	Complications	Local tumor recurrence			Mean±SD	Min	Max	
Patients with dysphagia (%)	7 (58.33)	2 (16.67)	1 (8.33)	2 (16.67)	12	χ^2=2.8; df=3; p=0.42	3.25±2.14	1	8	p=0.25
Patients without dysphagia (%)	60 (75)	12 (15)	4 (5)	4 (5)	80		4.61±3.98	1	23	
Total number of patients	67	14	5	6	92		-	-	-	-

The studies of jejunoesophageal reflux after total gastrectomy with Roux en Y esophagojejunostomy have had a variable design: some evaluated the reflux symptoms and others the reflux itself, demonstrated by scintigraphic methods, bilimetry or intraesophageal pH monitoring. There are few studies analyzing the endoscopic changes of alkaline reflux esophagitis, these include a relatively small number of patients and the reported results are variable. We found in our study that 15.22% of the patients had reflux esophagitis. We also included in the study the patients presenting complications (Barrett's esophagus and benign stenosis), who presumably had previous esophagitis (5.43%). Schrock et al reported in 1978 a very low percentage of reflux esophagitis after total gastrectomy and Roux en Y esophagojejunostomy (4.76%), as compared to other reconstructive types (100% after simple esophagojejunostomy, 57% after esophagoduodenostomy) [2] (Table VI). Donovan et al noted the presence of reflux esophagitis in 45% of the cases [4]. The reflux was present only in patients having a loop length shorter than 35 cm. Feussner et al found mild esophagitis in 14.28% of the patients with total gastrectomy and Roux en Y procedure [15]. In another study, reflux esophagitis was reported in 28.6% of the cases [16]. Recently, Kim et al published a high incidence of esophagitis secondary to total gastrectomy, without exactly stating the type of reconstruction [17]. The variability in the incidence of alkaline reflux esophagitis after Roux en Y esophagojejunostomy may depend on the surgical technique and especially on the length of the jejunal loop, which should be at least 35 cm.

Reflux esophagitis has been shown to be present in about 2-3% of the general population, although some studies found a higher prevalence - 15.5% in the Kalixanda study [18]. We excluded, as accurately as possible in a retrospective study, those patients with esophagitis prior to the surgical intervention.

Of our 14 patients with reflux esophagitis, most had LA grade C esophagitis. However, the small number of patients in our group did not allow conclusions of statistical significance regarding the severity of esophagitis following this type of surgery.

We analyzed the relationship between the endoscopic changes and the interval between surgery and endoscopic evaluation, and found that Barrett's esophagus and benign esophageal stenosis occurred after a longer period than the lesions of esophagitis, but the difference was not statistically significant. There is still debate in the literature regarding the period of time elapsed between the onset of alkaline reflux and the diagnosis of Barrett's esophagus. Some studies noted that Barrett's esophagus followed after a long period of alkaline reflux [11], while others considered Barrett's esophagus to be the final stage of reflux esophagitis, without any relation with the period or the grade of reflux [19]. It is not exactly known which component of the esophageal content causes Barrett's esophagus. Bile acids are considered to contribute [20]: taurine-conjugated bile acids were demonstrated by combined pH measurement and bilimetry (BILITEC 2000) to induce esophageal lesions. It has also been demonstrated in animal models that pancreatic juice can induce Barrett's esophagus and esophageal cancer [21, 22].

Table VI. Studies assessing the alkaline reflux after total gastrectomy

Author	Year	Reference number	Number of patients	Reflux symptoms	Reflux diagnosis (scintigraphy, bilimetry, esophageal pH monitoring)	Esophagitis (endoscopy) (%)
Schrock TR	1978	2	42	-	-	2 (4.76%)
Donovan JA	1982	3	20	-	25%	9 (45%)
Feussner H	1988	11	7	28.57%	-	1 (14.28%)
Adachi S	2003	12	10	50%	-	
Yumiba T	2005	13	7	-	-	2 (28.6%)
Kim EM	2009	14	54	-	-	~ 60%
Present study	2010	-	92	28.26%	-	14 (15.22%)

The prevalence of gastroesophageal reflux disease and Barrett's esophagus increases with age, even more so after the age of 40 [9, 10]. However, we did not find a significant correlation between alkaline reflux esophagitis after gastrectomy and the patients' age (Table II) or gender. Severe esophagitis (LA grade C) and complications (Barrett's esophagus and benign esophageal stenosis) seemed to be more frequent in male patients, but again without statistical significance. Some studies showed an increased prevalence of gastroesophageal reflux disease and Barrett's esophagus in males [9, 10, 23], but the correlation between alkaline esophagitis and gender has been less investigated.

Reflux symptoms were present in approximately 25% of our patients with total gastrectomy and Roux en Y reconstruction. Similar results were published by Feussner et al (Table VI), but other studies mentioned the presence of heartburn in more than 50% of patients after gastrectomy and Roux en Y esojejunostomy [24].

In the absence of endoscopic lesions, most of our patients were asymptomatic and more than half of those with esophagitis had reflux symptoms. The symptoms occurred more frequently in patients with LA grade C esophagitis. Most studies on gastroesophageal reflux disease found no correlation between symptoms and the severity of morphological lesions [9].

Although dysphagia usually suggests the development of stenosis [6, 9], we did not find a significant correlation between dysphagia and the endoscopic lesions in our patients. Of the 12 patients having dysphagia, only 3 had an endoscopically confirmed stenosis. The remainder patients had reflux esophagitis or a normal esophagus, suggesting in the latter the presence of esophageal motor disorders.

The major limit of our study was, as mentioned, the small number of patients who presented for evaluation. This did not allow solid conclusions regarding the incidence of reflux esophagitis after total gastrectomy with esojejunostomy. However, the group of patients was large enough as compared to other published series (Table VI) for analyzing the relation between symptoms and lesions and the interval after surgery when those developed.

Conclusions

Although Roux en Y esojejunostomy is considered to be a reconstructive method of the alimentary tract which can prevent the reflux, an important percentage of operated patients presented alkaline reflux esophagitis. In most cases, alkaline reflux esophagitis was moderate or severe. Reflux esophagitis complications, such as benign stenosis and Barrett's esophagus occurred after a relatively long period of time. More than half of the patients with alkaline esophagitis, and especially those with LA grade C esophagitis, had reflux symptoms.

Conflicts of interest

None to declare.

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