

Esophagectomy with gastropasty in advanced megaesophagus: late results of omeprazole use

Esofagectomia com gastropastia no megaesôfago avançado: análise tardia da importância do uso do omeprazol

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A B S T R A C T

Objective: To analyze the late results of advanced Chagasic megaesophagus treatment by esophagectomy associated with the use of proton pump inhibitor (omeprazole) as for the incidence of esophagitis and Barrett's esophagus in the remaining stump.

Methods: We studied patients with advanced megaesophagus undergoing esophagectomy and transmediastinal esophagogastroplasty. Patients were divided into three groups: A (20) with esophageal replacement by full stomach, without the use of omeprazole; B (20) with esophageal replacement by full stomach, with omeprazole 40 mg/day introduced after the first postoperative endoscopy and maintained for six years; and C (30) with esophageal replacement by gastric tube with use of omeprazole. Dysphagia, weight loss and BMI were clinical parameters we analyzed. Upper gastrointestinal endoscopy was performed in all patients, and determined the height of the anastomosis, the aspect of the mucosa, with special attention to possible injuries arising from gastroesophageal reflux, and the patency of the esophagogastric anastomosis. **Results:** We studied 50 patients, 28 males (56%) and 22 (44%) females. All underwent endoscopy every year. In the first endoscopy, erosive esophagitis was present in nine patients (18%) and Barrett's esophagus, in four (8%); in the last endoscopy, erosive esophagitis was present in five patients (8%) and Barrett's esophagus in one (2%). When comparing groups B and C, there was no evidence that the manufacturing of a gastric tube reduced esophagitis and Barrett's esophagus. However, when comparing groups A and C, omeprazole use was correlated with reduction of reflux complications such as esophagitis and Barrett's esophagus ($p < 0.005$).

Conclusion: The use of omeprazole (40 mg/day) reduced the onset of erosive esophagitis and Barrett's esophagus during the late postoperative period.

Key words: Chagas Disease. Esophagitis. Barrett Esophagus. Esophagectomy. Omeprazole.

INTRODUCTION

The esophagus is the organ most commonly affected by Chagas disease in the digestive tract. The resulting condition is the megaesophagus, characterized by dilation and lengthening of the organ body, progressive, functional dysphagia, the pathological substrate being the damage to the intermuscular plexus by the *Trypanosoma cruzi*^{1,2}.

Chagas is one of the most common parasitic diseases in Latin America, with a commitment of 670,000 lives / year and annual cost of morbidity and death estimated at more than eight billion dollars in 2000. Chagas disease affects eight million people in America Latin^{3,4}. The first proposal for the surgical treatment of achalasia was made by Gottstein, which indicated cardiomyotomy⁵. However, it was Heller who consecrated the procedure, with section of the muscles in the anterior and posterior aspects of the

esophagus⁶. Later, others came to perform it only in the anterior aspect⁷. However, achalasia in its most advanced stage (grade IV), requires a larger surgical procedure, the treatment of choice being the removal of the diseased organ, ie, esophagectomy⁸⁻¹¹.

In Brazil, around 1960, Câmara Lopes and Ferreira Santos successfully performed the first subtotal esophagectomy by right thoracotomy, followed by gastroplasty in two and one times, respectively^{12,13}.

From the 1970s on, the cervico-abdomino-mediastinal route gained preference in the treatment of Chagas megaesophagus. Eugenio Ferreira et al. spread the technique in our country, 28 patients underwent subtotal esophagectomy through esophagus extraction¹⁴. Subsequently, Pinotti et al. advocated section of the diaphragm from the hiatal ring to the xiphoid process, providing more security and improving the procedure results¹⁵⁻¹⁸.

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Aquino *et al.* caused surprised by performing esophagectomy through esophageal mucosal resection (removal only of the mucosal cylinder), with low complications rate¹⁹⁻²¹.

Although not appreciated by many surgeons, Rocha *et al.*, following 48 patients undergoing esophagectomy and gastropasty with cervical anastomosis, found severe chronic gastritis, as well as the presence of a "bile lake" in the gastric antrum, with endoscopic appearance similar to alkaline reflux gastritis²². Four years later, studying 48 patients who underwent subtotal esophagectomy with esophagogastropasty, they found Barrett's esophagus in four patients, the latest one at 18 months after the operation²³.

The reflux of gastric juice and bile fluid are important factors in the genesis of Barrett's esophagus, there being a direct correlation between the metaplastic segment and the time the esophagus is exposed to pH < 4²⁴.

Rocha *et al.* Studied 101 patients who underwent transmediastinal esophagectomy with gastropasty, having found 70% erosive esophagitis and 57% columnar epithelialization, besides two cases of cancer in the remaining esophageal stump²⁵.

Oberg proved that despite truncal vagotomy, there was no long-term suppression of acid reflux. Corroborating this statement, Rocha *et al.* described erosive esophagitis and Barrett's esophagus in patients undergoing esophagectomy with gastropasty. They suggested that long-term treatment with proton pump inhibitor could avoid such complications²⁶.

Prophylactic treatment done with the restoration of transit through a gastric tube with proton pump inhibitor (PPI) and annual endoscopic follow-up has been the guidance of experts to reduce reflux complications²⁶⁻²⁸.

This research aims to analyze the late results of advanced Chagasic megaesophagus treatment by esophagectomy associated with PPIs (omeprazole), targeted at the incidences of esophagitis and Barrett's esophagus in the remaining stump.

METHODS

We studied 50 patients with megaesophagus treated at the clinic of the Esophagus Group of the Departamento de Cirurgia da Faculdade de Ciências Médicas da Santa Casa de São Paulo, in the period from April 26, 1990 to January 08, 2011. They were 22 (44%) women and 28 (56%) men. The age ranged from 24 to 79 years, the average being 49.

The diagnosis was made clinically, by serological test for Chagas disease, by radiological examinations and by esophageal eletromanometry. Barium swallow was performed with Philips-Challenge N 800 HF apparatus after the ingestion of 100 ml of barium sulphate diluted in 200ml

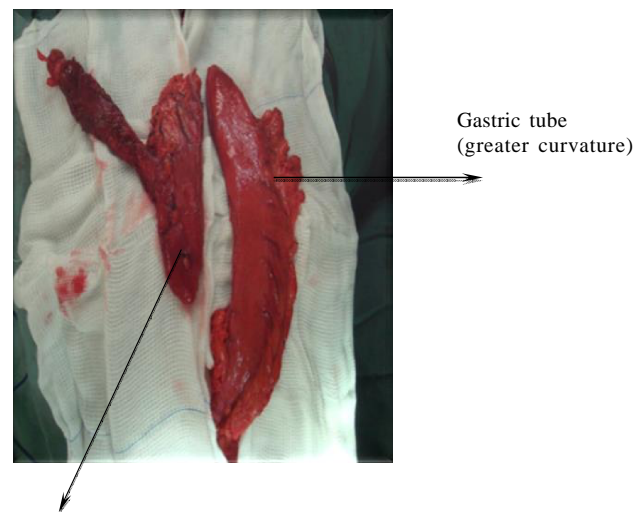
of water at three positions 180 cm distant from the bulb with films at ten seconds, five minutes and 30 minutes. The eletromanometry was made with a six channel computerized polygraph (Synectics – Sweden), EMC-R catheter under pneumo-hydraulic capillary infusion, with flow of 0.6 ml/min/channel. Patients with impaired esophageal body contraction were characterized as having megaesophagus.

Patients underwent Machado-Guerreiro complement fixation test and indirect hemagglutination or immunoenzymatic reaction (ELISA) for the confirmation of Chagas disease²⁹⁻³¹.

We included patients with achalasia with organ dilation largest than 10cm (grade IV) at the esophagus radiological contrast examination; patients with achalasia with eletromanometry revealing absence of lower esophageal sphincter relaxation and synchronous contractions of low amplitude of the esophageal body (< 15 mmHg).

We have carried out two types of operations: resection of the esophagus by esophageal extraction and resection by trans-hiatal dissection. The restoration of the transit was made with the full stomach in 20 patients and with a gastric tube of greater curvature in 30 patients (Figures 1 and 2). The cervical esophagogastric anastomosis was manual, by left lateral cervicotomy positioned at the level of the sternal notch, about 15 cm from the upper dental arch or 4 cm from the cricopharyngeal muscle (pharyngo-esophageal transition). Truncal vagotomy and pyloroplasty were performed in all patients.

Dysphagia, weight loss and body mass index were clinical parameters analyzed. Upper gastrointestinal endoscopy was performed in all patients. We determined the height of the anastomosis, the aspect of the mucosa, with special attention to possible injuries arising from



Resected distal esophagus and gastric lesser curvature.

Figure 1 - Gastric tube with resection of lesser curvature.



Figure 2 - Reconstitution of transit post-esophagectomy. Total stomach.

gastroesophageal reflux, and the patency of the esophagogastric anastomosis.

We harvested three fragments from the esophagus and three from the stomach two cm above and two below the anastomosis, after prior staining with methylene blue. The fragments were fixed in 3.7% formalin and stained with hematoxylin-eosin for subsequent histological analysis.

The use of proton pump inhibitor was done at a dose of 40 mg/day for all patients undergoing esophagectomy operated from 2006 on. Since 2006, the transit reconstitution of all patients comprised an enlarged proximal gastrectomy (gastric tube). Three groups were formed: Group A - Operated from 1990 to 2006 with full stomach esophageal replacement, without the use of omeprazole during this period, and the first postoperative endoscopy performed in 2006; Group B - operated from 1990 to 2006 with esophageal replacement through full stomach, without the use of omeprazole during that period, and after the first postoperative endoscopy in 2006, initiating omeprazole use, which lasted six years until 2011; Group C - operated between 2006 and 2011 with esophageal replacement with gastric tube (enlarged proximal gastrectomy), with use of omeprazole during this period, and the first endoscopy performed in 2006.

For the descriptive analysis, we used position measurements for continuous variables and frequency for categorical variables. For comparison groups and times of

endoscopy results we used the GEE model (Generalized Estimating Equation Model). To compare weight loss between groups we used analysis of variance (ANOVA). To compare dysphagia and heartburn between groups we used the Chi-square test and, when necessary, the Fisher's exact test. We deemed significant a p value ≤ 0.05 .

RESULTS

We found no patient with severe dysphagia; 13 (26%) patients had dysphagia (mild), of whom 92% had no aspiration or weight loss. As for the remaining 37 (74%), they did not have such complaint after esophagectomy.

The records of the current weight and height allow us to state that 39 (78%) patients were healthy (normal weight). As for the other 11: 16% were overweight and 6% were malnourished after esophagectomy. Ten patients (21%) had heartburn after the surgical procedure.

The first endoscopy was performed in 2006 and the last in 2011. In the first endoscopy erosive esophagitis was present in nine (18%) patients and Barrett's esophagus in four (8%); during the last endoscopy we observed erosive esophagitis in four (8%) patients and Barrett's esophagus in one (2%) (Table 1).

There was a statistically significant difference ($p = 0.002$) between groups A and C in relation to the results of digestive endoscopy (Table 2). There was no statistically significant difference ($p = 0.416$) between groups B and C regarding the outcome of digestive endoscopy (Table 3).

DISCUSSION

Considering our findings regarding the clinical aspects – dysphagia, heartburn, aspiration, weight loss and nutritional status –, we can say that esophagectomy in advanced megaesophagus provides good quality of life in

Table 1 - Distribution of patients according to treatment with PPI after esophagectomy.

Total Group	50 patients	
	N	%
Endoscopy (First)-2006		
Absent	37	74
Erosive Esophagitis	9	18
Barrett	4	8
Endoscopy (Last)-2011		
Absent	45	90
Erosive Esophagitis	4	8
Barrett	1	2

Source: Santa Casa de Misericórdia de São Paulo (1990 to 2011).

Table 2 - Distribution of Endoscopies' results (First and Last) after esophagectomy for groups A and C.

Group	A	C	p
Endoscopy (First)			
Absent	10	27	0.002
Erosive Esophagitis	6	3	
Barrett	4	0	
Endoscopy (Last)			
Absent	10	29	
Erosive Esophagitis	6	1	
Barrett	4	0	

Source: Santa Casa de Misericórdia de São Paulo (1990 to 2011).

Table 3 - Distribution of Endoscopies' results (First and Last) after esophagectomy for groups B and C.

Group	B	C	p
Endoscopy (First)			
Absent	16	27	0.416
Erosive Esophagitis	3	3	
Barrett	1	0	
Endoscopy (Last)			
Absent	16	29	0.143
Erosive Esophagitis	3	1	
Barrett	1	0	

Source: Santa Casa de Misericórdia de São Paulo (1990 to 2011).

the short and medium term, especially as for the nutritional aspect^{11,20,21,28,32}.

It is worth remembering that 80% of patients were asymptomatic and did not complain of heartburn. In the long-term monitoring, the presence of erosive esophagitis and Barrett's esophagus brought reflections.

It was believed that truncal vagotomy associated to pyloroplasty and the use of the entire stomach in the transit reconstitution was sufficient to reduce gastric acidity, minimizing reflux. Considering that in these patients, basal and stimulated acid secretion is lower than that found in normal subjects, and the right colon may be affected by the disease, reconstitution with the stomach initially appeared to be a great option. However, the follow-up of patients submitted to esophagectomy with this type of reconstitution and without the use of proton pump inhibitor (PPI) may show disastrous complications, such as Barrett's esophagus and esophageal stump cancer^{25,33-35}.

From the first year after surgery, the pepsinogen levels and acid secretion, both at baseline and under stimulus, increase despite truncal vagotomy and pyloroplasty. As a consequence, there has been found up

to 20% esophagitis in the cervical esophageal stump during the first year after surgery, and approximately 70% in the seventh year, and the presence of Barrett's esophagus in the cervical stump in up to 27.7% of cases, which is more serious^{26,34}. Of course, the destruction of reflux containment mechanisms (loss of inferior esophageal sphincter mechanism, cardia and pylorus), promote mixed reflux (acid and bile), extremely harmful to the esophageal mucosa^{36,37}.

In an attempt to reduce acid reflux, an option has been made for the resection of the lesser curvature of the stomach, reducing the population of acid-producing parietal cells, and manufacturing of a gastric tube^{25,28}. Results have not improved, though.

When more specifically considering complications arising from the duodenogastric reflux (esophagitis and Barrett's esophagus), we found no statistically significant correlation ($p = 0.143$) between groups B and C. We remember that both received PPIs (omeprazole) at the same dosage, but differed in that Group B had the reconstitution with full stomach and Group C had the gastric tube. Thus, we cannot say with certainty that the enlarged proximal gastrectomy contributed to the reduction of esophagitis and Barrett in our patients. Other authors also found the occurrence of esophagitis and Barrett's esophagus in the esophageal stump of patients with gastric tube, since its vertical position is maintained, facilitating rapid gastric emptying, as well as duodenogastric reflux^{34,35,38,39}.

We conducted esophagectomy with enlarged proximal gastrectomy (gastric tube) and yearly endoscopy, as experts recommend. We noted that Group A, which was devoid of PPI, showed a greater number of complications due to acid and bile reflux^{25,27,28,40}. In addition, our statistical calculations emphasize the use of omeprazole (Group C) as the most significant independent variable correlated with reduced complications of mixed reflux (erosive esophagitis and Barrett's esophagus – Group A) in the univariate analysis, showing a statistically significant difference (Table 2).

We understand that the use of PPIs in continuous monitoring of patients submitted to esophagectomy is essential, and that a dosage of 40 mg/day can reduce the appearance of erosive esophagitis and Barrett in the remaining stump.

We stress the utmost importance of the clinical follow-up and annual endoscopic exam of patients undergoing esophagogastroplasty, combined with the continued use of proton pump inhibitors, beginning in the early postoperative period in an attempt to decrease tumor development in the remaining esophageal stump^{26,33,35,40-43}.

The results obtained in this study, with 50 Chagas megaesophagus patients, support the conclusion that the use of omeprazole (40 mg/day) reduced the onset of erosive esophagitis and Barrett's esophagus during the late postoperative period.

R E S U M O

Objetivo: analisar os resultados tardios do tratamento do megaesôfago chagásico avançado através da esofagectomia associada ao IBP (omeprazol), com vistas à incidência de esofagite e esôfago de Barrett do coto esofágico remanescente. **Métodos:** foram estudados pacientes com megaesôfago avançado submetidos à esofagectomia e à esofagogastroplastia transmediastinal posterior. Os pacientes foram distribuídos em três grupos: A (20) com substituição esofágica por meio do estômago total, sem o uso do omeprazol; B (20) com substituição esofágica por meio do estômago total, sem o uso do omeprazol durante este período; após a primeira endoscopia, realizada no pós-operatório, foi introduzido IBP (omeprazol 40mg/dia) e mantido por seis anos; e C (30) com substituição esofágica por meio do tubo gástrico com uso do omeprazol. A disfagia, a perda ponderal e o IMC foram os parâmetros clínicos analisados. A endoscopia digestiva alta foi realizada em todos os pacientes. Foi determinada a altura da anastomose, a aparência do aspecto da mucosa, com especial atenção para possíveis lesões oriundas de refluxo gastroesofágico, a patência da anastomose esofagogástrica. **Resultados:** na primeira endoscopia, a esofagite erosiva esteve presente em nove pacientes (18%) e o esôfago Barrett, em quatro (8%); na última endoscopia, a esofagite erosiva esteve presente em quatro pacientes (8%) e o esôfago de Barrett em um (2%). Comparando-se os grupos B e C, não houve redução da esofagite e do esôfago de Barrett. Porém, comparando-se os grupos A e C, houve redução de complicações do refluxo, como esofagite e o esôfago de Barrett ($p < 0,005$). **Conclusão:** os resultados obtidos permitem concluir que o uso de omeprazol (40mg/dia) reduziu o aparecimento de esofagite erosiva e esôfago de Barrett no decorrer do pós-operatório tardio.

Descritores: Doença de Chagas. Esofagite. Esôfago de Barrett. Esofagectomia. Omeprazol.

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