# Effect of Gastric Bypass on Barrett's Esophagus and Intestinal Metaplasia of the Cardia in Patients With Morbid Obesity

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Gastric bypass in patients with morbid obesity should be an excellent antireflux procedure, because no acid is produced at the small gastric pouch and no duodenal reflux is present, due to the long Roux-en-Y limb. Five hundred fifty-seven patients with morbid obesity submitted to resectional gastric bypass, and routine preoperative upper endoscopy with biopsy samples demonstrated 12 patients with Barrett's esophagus (2.1%) and three patients with intestinal metaplasia of the cardia (CIM). An endoscopic procedure was repeated twice after surgery, producing seven patients with short-segment Barrett's esophagus (BE) and five patients with long-segment BE. Body mass index (BMI) decreased significantly, from 43.2 $kg/m^2$ to 29.4 $kg/m^2$ 2 years after surgery. Symptoms of reflux esophagitis, which were present in 14 of the 15 patients, disappeared in all patients 1 year after surgery. Preoperative erosive esophagitis and peptic ulcer of the esophagus healed in all patients. There was regression from intestinal metaplasia to cardiac mucosa in four patients (57%) with short-segment BE, and in one patient (20%) with long-segment BE. Two (67%) of three cases with CIM had regression to cardiac mucosa. There was no progression to low- or high-grade dysplasia. Gastric bypass in patients with Barrett's esophagus and morbid obesity is an excellent antireflux operation, proved by the disappearance of symptoms and the healing of endoscopic esophagitis or peptic ulcer in all patients, which is followed by an important regression to cardiac mucosa that is length-dependent and time-dependent.

KEY WORDS: Gastric bypass, Barrett's esophagus, cardia intestinal metaplasia

Barrett's esophagus is an acquired condition, secondary to chronic duodeno-gastroesophageal reflux, in which the distal esophageal mucosa is replaced by columnar mucosa with intestinal metaplasia.[1–4] The main importance of this metaplastic change at the distal esophagus is that there is a significant increase in the risk of developing adenocarcinoma.[1–3,5] On the other hand, patients with morbid obesity have an increased incidence and severity of gastroesophageal reflux.[6–9] Gastric bypass is the "gold standard" operation for patients with morbid obesity.[10–14] In this operation, no acid is produced when a small gastric pouch is created with a total capacity less than 20 ml, and the presence of a long Roux-en-Y limb presents duodenal and intestinal content from refluxing into the gastric pouch and into the esophagus. Therefore, it seems an "ideal operation" for the treatment of chronic reflux in patients with Barrett's esophagus.

The purpose of the present prospective study was to determine the behavior of intestinal metaplasia at the distal esophagus (Barrett's esophagus) or at the cardia (intestinal metaplasia of the cardia) after gastric bypass in morbidly obese patients.

## MATERIAL AND METHODS

### Patients Studied

This prospective study started in August 1999 and ended on October 23, 2004, and included 557

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patients with morbid obesity who were submitted to open resectional gastric bypass. The details of the whole group and the surgical technique have been published extensively elsewhere.[15,16] All patients were submitted to preoperative endoscopy and biopsy studies. From this group, 15 patients had intestinal metaplasia at the distal esophagus or cardia and were divided in two groups: (a) 12 (2.1%) patients with Barrett's esophagus with a mean of 47.4 years (range, 33–62), consisting of five men and seven women with a mean body mass index (BMI) of 43.9 kg/m$^2$ (range, 35–61; there was no exclusion in this group); and (b) three (0.5%) patients with intestinal metaplasia of the cardia (CIM) with a mean age of 48.6 years (range, 43–56), consisting of all women with a mean BMI of 37.8 kg/m$^2$ (range, 35–39).

All patients with a BMI below 40 kg/m$^2$ had an associated comorbidity such as diabetes or arterial hypertension.

## Endoscopic Examination

One author (A.C.) performed all endoscopic procedures, employing an Olympus GIFXQ-20 endoscope (Olympus, Tokyo, Japan). After a 12-hour night fast and pharyngeal anesthesia with lydocaine, the scope was introduced through the mouth with the patient in supine left lateral position. Special care was taken to measure the exact location of the squamous-columnar junction at the beginning and at the end, avoiding the "push" and "pull" effect of the endoscope.[17] The length of the columnar-lined distal esophagus was measured as the distance between the squamous-columnar junction and the endoscopically located lower esophageal sphincter, which is the point where the proximal extent of the gastric rugal folds meet with the tubular esophagus.[17,18] The presence of erosions proximal to the squamous-columnar junction was carefully recorded. For the present study, endoscopic procedure was performed before surgery and at least two times after surgery in each patient. During this procedure, in every patient, 4-quadrant biopsy samples were taken 5 mm distal to the squamous-columnar junction. In patients with short-segment Barrett's esophagus (BE), two more samples were taken 2 cm distal. Among patients with long-segment BE, four samples were taken, each 2 cm distally according to the length of the columnar mucosa. Therefore, between 6 and 16 samples were taken in each patient during each endoscopic procedure, with a mean of 8.5 samples per patient. Also, in each patient, two samples were taken at the antrum.

Patients were divided into two groups[10]: (a) short-segment Barrett's esophagus, (length $\geqslant$ 30 mm) and (b) long-segment Barrett's esophagus, (length $\geqslant$31 mm).

## Regression of BE

We defined the regression of BE as: (1) the loss of intestinal metaplasia with the presence of only cardiac and/or fundic mucosa on two consecutive endoscopic examinations with biopsy specimens and (2) the decrease in length of columnar-lined mucosa at the distal esophagus, at least 3 cm in length.

## Histologic Analysis

All samples were submerged immediately in 10% formalin solution, sent for histologic examination, and stained with hematoxylin-eosin and Alcian blue stain at pH 2.5; fundic mucosa was identified by the presence of parietal and chief cells at the deep glandular layer, and cardiac mucosa was identified by the presence of mucous-secreting columnar cells. Intestinal metaplasia was defined by the presence of goblet cells. The presence of Helicobacter pylori was also evaluated at the columnar-lined mucosa with intestinal metaplasia.

## Monitoring of Esophageal Exposure to Acid Reflux

All examinations were performed after 12 hours of fasting. The details of this procedure have been extensively detailed in previous publications.[19–21] The results of acid reflux test were expressed as the percentage of time during which the intraesophageal pH was less than 4 (normal values less than 4%).

## Surgical Procedure

In all patients, a resectional open gastric bypass was performed as previously described.[15,16] A small gastric pouch with a total capacity less than 20 ml was constructed with the use of linear staplers (Tyco Healthcare, Norwalk, CT). The gastrojejunal anastomosis was performed with a circular Stapler 25 (Tyco Healthcare). The length of the Roux-en-Y loop varied between 125 and 150 cm.

## Statistical Analysis

The chi-square test and the variance analysis test were employed, with $P < 0.05$ as significant.

### Follow-up

All patients with intestinal metaplasia of the distal esophagus or cardia were carefully followed and there was no loss of patients. Endoscopic control was performed at 12 to 14 months after surgery.

## RESULTS

After operation, all patients had an uneventful recovery, and no postoperative complications were observed in any patient. Eleven patients out of 12 with BE (91.7%) had symptoms of chronic gastroesophageal reflux of more than 2 years duration, whereas all three patients with CIM had gastroesophageal (GE) reflux symptoms. Upper endoscopy before operation was normal in all patients with CIM, whereas among patients with BE, seven (58.3%) had erosive esophagitis and two of them also had a peptic ulcer of the esophagus (16.7%). Hiatal hernia was present in three patients (25%). Patients with BE were divided in two groups: (a) short-segment BE with seven patients (58.3%) and (b) long-segment BE with 5 patients (41.7%).

The 24-hour pH study performed on four patients with BE had a mean percent time with pH $< 4$ of 40.2% (range, 19–75), whereas resting lower esophageal sphincter pressure, performed in five patients, showed a mean pressure of 10.2 mmHg (range, 3–17).

Table 1 shows the endoscopic and histologic findings before and several times after surgery in all patients included in the present study. The mean follow-up for patients with BE was 24 months; patients with CIM had a mean follow-up of 29 months. The BMI, before and at 24 months after surgery, is also included.

The mean BMI among patients with BE decreased significantly, from 43.2 kg/m$^2$ to 29.4 kg/m$^2$ ($P < 0.0001$). The same occurred among patients with CIM. The results of antral biopsies showed no intestinal metaplasia in any patients. H pylori was present in three patients with BE (25%) and in one CIM patient (33%) at the antrum.

After surgery, symptoms of GE reflux disappeared in all patients; the endoscopic study at 1 and 2 years after surgery showed esophageal mucosa was normal in all patients. At 12 months after surgery, erosive esophagitis or peptic ulcer of the esophagus had healed in all. The careful histological analysis of the columnar-lined mucosa revealed that among seven patients with short-segment BE, four (57%) patients showed regression of IM to cardiac mucosa at a mean time of 25 months after surgery. Among five patients with long-segment BE, one (20%) patient showed regression to oxyntic cardiac mucosa. There was no progression to low- or high-grade dysplasia. Of two patients with low-grade dysplasia and short-segment BE, one patient regressed to cardiac mucosa, whereas the other patient showed disappearance of low-grade dysplasia with persistence of intestinal metaplasia after surgery. The evaluation of the presence of H pylori at the columnar-lined mucosa revealed that before surgery, it was present in two patients, and after surgery, it was absent in both of them; however, it appeared in two patients, one with cardiac and one with oxyntic cardiac mucosa.

Among the three patients with CIM, two (67%) patients showed regression to cardiac mucosa at a mean of 14 months after surgery. H pylori was present in one patient before surgery and disappeared after surgery; however, it appeared in one other patient after surgery.

## DISCUSSION

The results of the present study suggest that gastric bypass, in patients with morbid obesity and the presence of Barrett's esophagus or intestinal metaplasia of the cardia, is an excellent antireflux operation, resulting in regression of IM to cardiac mucosa in a significant number of patients.

We have reviewed a large number of publications concerning obesity and GE reflux, the effect of bariatric surgery on GE symptoms, and functional studies. However, very few mention the specific study of patients with BE before operation, and there is no publication concerning the effect of bariatric surgery on BE or CIM. There is only one study from Balsiger et al.[22] from the Mayo Clinic, which mentions that the endoscopic control in seven patients with BE and gastric bypass has shown no progression to severe dysplasia, but makes no mention of any regression. Several years ago, we published a study concerning the incidence of obesity in control subjects, patients with reflux esophagitis and patients with BE.[23] We noticed that 25% of patients with BE were obese, compared to 5% of control or reflux esophagitis patients. Later Ovrebo et al.[24] found no BE in any of 38 patients with morbid obesity who were submitted to surgery. Furthermore, Balsiger et al.[22] reported that of 25 patients submitted to conversion from vertical banded gastroplasty to Roux-en-Y gastric bypass, 29% showed histologic changes of BE at the distal esophagus. Finally, Surter et al.[25] reporting on the endoscopic findings among 344 patients with morbid obesity, found BE in four patients (1.2%).

**Table 1.** Endoscopic and histologic findings at the distal esophagus before and after gastric bypass for morbid obesity in patients with Barrett's esophagus or intestinal metaplasia of the cardia

| Sex | Age | BMI before surgery | BMI after surgery (24 mo) | Length BE (mm) | Endoscopy | | Histological findings | | | | H pylori at columnar mucosa | | Time for regression (mo) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Before surgery | After surgery | Before surgery | I Control (mo)* | II Control (mo)* | III Control (mo)* | Before surgery | After surgery | |
| Barrett's esophagus | | | | | | | | | | | | | |
| Woman | 46 | 37 | 29 | 20 | Esophagitis | Normal | IM | Carditis (14) | Carditis (28) | | (−) | (−) | 14 |
| Man | 33 | 61 | 42 | 20 | Esophagitis | Normal | IM | IM (26) | | | (+) | (−) | No |
| Woman | 52 | 35 | 22 | 20 | Normal | Normal | IM + LGD | IM + LGD (24) | IM (36) | Carditis (48) | (−) | (−) | 48 |
| Woman | 60 | 38 | 26 | 30 | Esophagitis | Normal | IM | Carditis (24) | Carditis (36) | | (−) | (−) | 24 |
| Woman | 54 | 39 | 27 | 20 | Normal | Normal | IM | IM (12) | IM (24) | | (−) | (−) | No |
| Man | 38 | 48 | 31 | 20 | Normal | Normal | IM | Carditis (14) | Carditis (28) | | (+) | (+) | 14 |
| Man | 46 | 51 | 28 | 20 | Normal | Normal | IM + LGD | IM + LGD (12) | IM + LGD (24) | IM (48) | (−) | (−) | No |
| Man | 39 | 45 | 27 | 40 | Normal | Normal | IM | IM (28) | IM (40) | | (−) | (−) | No |
| Woman | 56 | 36 | 31 | 40 | Peptic ulcer | Normal | IM | Funditis (24) + Carditis | Funditis (36) + Carditis | | (−) | (+) | 24 |
| Woman | 44 | 40 | 29 | 60 | Esophagitis | Normal | IM | IM (18) | IM (28) | | (−) | (−) | No |
| Man | 39 | 45 | 32 | 80 | Esophagitis | Normal | IM | IM (33) | IM (72) | | (−) | (−) | No |
| Woman | 62 | 44 | 29 | 120 | 2 Peptic ulcer | Normal | IM | IM (12) | IM (24) | | (−) | (−) | No |
| | | Mean 43.2 | 29.4 | | | | | | | | | | |
| Intestinal metaplasia of the cardia | | | | | | | | | | | | | |
| Woman | 43 | 36 | 22 | — | Normal | Normal | IM | Carditis (14) | Carditis (28) | | (−) | (−) | 14 |
| Woman | 56 | 39 | 25 | — | Normal | Normal | IM | IM (12) | IM (24) | | (−) | (+) | No |
| Woman | 47 | 38 | 23 | — | Normal | Normal | IM | Carditis (14) | Carditis (34) | | (+) | (−) | 14 |
| | | Mean 37.7 | 23.3 | | | | | | | | | | |

BMI = body mass index (Kg/M2); BE = Barrett's esophagus; IM = intestinal metaplasia; LGD = low-grade dysplasia.
*Endoscopy performed after surgery (mo).

There is no mention in any publication concerning patients with CIM or the effect of surgery on BE among patients submitted to gastric bypass or any other bariatric procedure. We have performed routine endoscopic and histologic assessment in 557 patients with morbid obesity and have found 2.1% of patients with BE and 0.5% of patients with CIM. This seems a low figure, which probably is due, in part, to the young age of patients with morbid obesity, but the importance of treating BE supports the need for endoscopic and histologic surveillance.

The most important point of our study refers to the postoperative findings concerning the behavior of the metaplastic epithelium after gastric bypass in patients with morbid obesity. The pathophysiological effect of this type of surgery is very similar to what we have used for patients with Barrett's esophagus.[20,26] In this operation, acid secretion is abolished after bilateral vagotomy plus partial distal gastrectomy, and duodenal content is diverted by the addition of a Roux-en-Y loop of 60 to 70 cm long. We have published the results concerning the decrease in acid secretion,[20] the significant decrease in acid reflux into the esophagus,[19,20,26–28] and the complete and permanent abolition of reflux of duodenal content into the esophagus.[20,27] Gastric bypass completely reproduces the following pathophysiological consequences: (a) gastric acid secretion is reduced to a minimal output because there is a large reduction in parietal cell mass with the creation of the gastric pouch[29,30] and (b) the long Roux-en-Y limb (125 to 150 cm) produces a permanent and complete abolition of reflux of duodenal or intestinal content into the esophagus. Therefore, if both types of surgical procedures produce similar pathophysiological effects, the behavior of intestinal metaplasia at the distal esophagus should be similar. In another study,[31] we have examined the effect of acid suppression and duodenal diversion in 78 patients with BE, all surveyed more than 5 years after the primary operation. Thirty-one patients had short-segment BE and 47 patients had long-segment BE. Among them, the regression of intestinal metaplasia to cardiac or fundic mucosa occurred in 66% and 60%, respectively. The mean time for regression was about 44 months after surgery.

In the present study, the regression of IM to cardiac mucosa occurred in 57% of patients with short-segment BE, at a mean of 25 months after surgery. Among patients with long-segment BE, there was regression in 20%. The present report may have a possibility of sampling error, which is present in any study of this kind. Although we tried to obtain at least eight samples during every endoscopic procedure, the possibility of sampling error cannot be excluded. A much longer follow-up (more than 5 years) than the present study (24 months) is needed to reach definitive conclusions. However, the importance of the present study is that if the refluxate material is eliminated (which is harmful to the distal esophagus, i.e., acid and duodenal content, even without performing any antireflux procedure to improve the function of the lower esophageal sphincter), intestinal metaplasia, and therefore the eventual risk of developing adenocarcinoma, can regress to cardiac or oxyntic cardiac mucosa, which is length-dependent (inversely related to the length of BE) and time-dependent (it is directly related to the length of follow-up). We have not found any previous reference to the behavior of intestinal metaplasia of the cardia after gastric bypass, and therefore we cannot compare our results with other reports. We challenge other surgical groups performing gastric bypass to determine an objective surveillance and to conduct several endoscopic and histologic studies among patients with BE and morbid obesity.

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