Late Results of the Surgical Treatment of 125 Patients With Short-Segment Barrett Esophagus

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Hypothesis: The results of surgical treatment of patients with long-segment Barrett esophagus (BE) have been extensively reported. However, few publications refer to the results of surgery 5 years after the fact among patients with short-segment BE. This study aimed to determine the late results of 3 surgical procedures in patients with short-segment BE by subjective and objective measurements.

Design: Prospective, nonrandomized study starting on March 1, 1987, and ending on December 31, 2005.

Setting: A prospective, descriptive study of a group of patients.

Patients: A total of 125 patients with short-segment BE underwent 3 operations in different periods: duodenal switch plus highly selective vagotomy and antireflux technique in 31 patients, vagotomy plus partial gastrectomy and Roux-en-Y loop with antireflux surgery in 58 patients, and laparoscopic Nissen fundoplication in 36 patients.

Main Outcome Measures: Late subjective and objective outcomes of the 3 different surgical procedures.

Results: No operative mortality and only 2 postoperative complications (1.6%) occurred. The regression from intestinal metaplasia to cardiac or oxyntocardiac mucosa occurred in 60.8% to 65.4% of the patients, at a mean time of 39 to 56 months after surgery. Visick grading showed Visick grade I or II in 86.3% to 100.0% of the patients. No progression to low- or high-grade dysplasia or adenocarcinoma occurred.

Conclusions: On the basis of these results, laparoscopic Nissen fundoplication seems to be the surgical option for patients with short-segment BE because it is less invasive, has fewer side effects, and produces good results in the long-term follow-up.

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See Invited Critique at end of article

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Barrett esophagus (BE) is a condition in which the normal squamous epithelium of the distal esophagus is replaced by an abnormal columnar epithelium that undergoes 2 metaplastic changes. The first change is in the appearance of cardiac mucosa, and the second is in the presence of specialized intestinal metaplasia.1-7 This disease is the final consequence of long-standing duodenogastroesophageal reflux, and its importance lies in its association with a risk of a 30- to 125-fold development of adenocarcinoma. Currently, BE is divided into 2 groups8: short-segment BE (if the endoscopic distance between the gastroesophageal junction and the upper limit of the columnar mucosa is less than 3 cm) and long-segment BE (if this distance is more than 3 cm).

The outcomes of the surgical treatment of patients with long-segment BE have been extensively published by many authors and summarized by some of us in several review articles.9-11 However, despite patients with short-segment BE being much more common than patients with long-segment BE, the results of surgical treatment among patients with short-segment BE have been analyzed and published by only 6 groups of authors,12-17 to our knowledge. Therefore, the purpose of the present prospective study was to determine the late subjective and objective outcomes of 3 different surgical procedures performed in different time periods as treatment of patients with short-segment BE: laparoscopic Nissen fundoplication,18 open antireflux surgery with duodenal switch,19 and open antireflux surgery with distal gastrectomy plus Roux-en-Y loop.20,21
PATIENTS

This prospective, nonrandomized study started on March 1, 1987, when a special surgical protocol was established for patients with BE, either with a short- or long-segment columnar epithelium, and ended on December 31, 2005. A total of 125 patients with short-segment BE were included; all the patients had BE secondary to chronic pathologic gastroesophageal reflux. Exclusion criteria included cardiac intestinal metaplasia, hiatal hernia without BE, scleroderma or achalasia with short-segment BE, and low- or high-grade dysplasia (these patients were described in another publication). Patients with esophageal or cardiac adenocarcinoma were also excluded.

CLINICAL QUESTIONNAIRE

A careful clinical assessment that assessed the presence of typical gastroesophageal reflux symptoms was performed in all patients before and several times after surgery. For the late clinical evaluation, a modified Visick gradation was used, as previously described.

ENDOSCOPIC EXAMINATION

All endoscopic procedures were performed by 2 of the authors (A.C. and I.B.) using an XQ-20 endoscope (Olympus Corporation, Tokyo, Japan) and later a video endoscope manufactured by the same company. Extensive details of the procedures have been published previously. The presence of isolated or confluent erosions was carefully recorded, as well as the presence of a hiatal hernia, which was defined as a saccular structure between the diaphragmatic pinch-cock and the endoscopic gastroesophageal junction. This procedure was performed in all patients before and several times after surgery (every 1 or 2 years).

HISTOLOGIC ANALYSIS

In all patients, 4 biopsy specimens were obtained immediately below the squamous-columnar junction and 2 samples 2 cm distally. They were submerged in a 10% formalin solution and stained with hematoxylin-eosin and Alcian blue at pH 2.5 to determine the type of epithelium that lined the distal esophagus. Fundic mucosa was identified by the presence of parietal and chief cells at the deep glandular layer. Cardiac mucosa was identified by the presence of mucous-secreting columnar cells. Oxyntocardiac mucosa was defined by the presence of parietal cells and mucous-secreting columnar cells. Intestinal metaplasia was defined by the presence of well-defined goblet cells, confined by positive staining with Alcian blue. The presence of Helicobacter pylori was investigated in the gastroesophageal biopsy specimens and the antrum specimens.

ESOPHAGEAL MANOMETRIC STUDIES

Esophageal manometric studies were performed after a 12-hour fast with the patient in the supine position. The complete details have been extensively published in previous reports. Three manometric characteristics were determined at the lower esophageal sphincter (LES): total length (in millimeters), abdominal length (in millimeters), and resting pressure (in Hg of mercury), as well as the amplitude of the contraction of the distal esophageal waves (in millimeters of mercury). An amplitude of less than 30 mm Hg was considered an ineffec-

tive peristaltic contraction. The presence of a mechanically incompetent sphincter was diagnosed if at least 1 of the following parameters was present: resting pressure equal to or less than 6 mm Hg, an abdominal length equal to or less than 10 mm, and a total length equal to or less than 20 mm. This test was performed before and 1 to 2 years after surgery.

ESOPHAGEAL 24-HOUR pH MONITORING

Esophageal 24-hour pH monitoring was performed after a 12-hour fast by introducing the catheter (Digitrapper Synectics; Stockholm, Sweden) through the nose. The catheter was placed 5 cm proximal to the manometric upper limit of the LES (which is why manometric measurements are always performed before pH is studied). The details of this procedure have been published previously. Among the 6 different parameters that can be evaluated, the most practical is the total percentage of time in which the intraesophageal pH remains below 4, which is usually less than 4% in 24 hours.

ESOPHAGEAL 24-HOUR SPECTROPHOTOMETRIC BILIRUBIN MONITORING

Esophageal 24-hour spectrophotometric bilirubin monitoring was developed to determine the magnitude of duodenogastroesophageal reflux by measuring the total intraluminal concentration of bilirubin at the distal esophagus. Special dietary advice was given to the patient concerning certain foods, the consumption of which interferes with measurements. The final calculation is based on the percentage of time that bilirubin is measured in the esophagus with an absorbance greater than 0.2 (usually below 2% during 24-hour monitoring session).

DEFINITION OF REGRESSION

For the present study, regression of intestinal metaplasia was considered to be the disappearance of intestinal metaplasia into cardiac or oxyntocardiac mucosa in 2 consecutive endoscopic and biopsy studies.

STATISTICAL ANALYSIS

For statistical evaluation, the Mann-Whitney test, Fisher exact test, and χ² test were used, with P < .05 considered to be statistically significant. All values are expressed as means and standard deviations.

SURGICAL PROCEDURES

Three surgical techniques were used in these 125 patients with short-segment BE in different periods: (1) acid suppression and duodenal diversion procedure performed by laparotomy, a truncal or selective vagotomy, an antireflux procedure, partial distal gastrectomy, and a Roux-en-Y gastrojejunal anastomosis with a loop 70 cm long (this technique was used between 1987 and 1995); (2) laparotomic duodenal switch procedure, associated with highly selective vagotomy and an antireflux surgery (this operation was performed between 1992 and 1995); and (3) laparoscopic Nissen fundoplication (this procedure has been performed from 1996 to the present).

ANTIREFLUX SURGERY

Two types of antireflux technique were used in these patients. The first technique was Nissen fundoplication, either open or laparoscopic, whose surgical steps were described in detail in...
Table 1. Clinical and Endoscopic Features of 125 Patients With Short-Segment Barrett Esophagus

<table>
<thead>
<tr>
<th>Feature</th>
<th>Duodenal Switch (n=31)</th>
<th>Acid Suppression—Duodenal Diversion (n=58)</th>
<th>Laparoscopic Nissen Fundoplication (n=36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean, y</td>
<td>52</td>
<td>53.7</td>
<td>51.9</td>
</tr>
<tr>
<td>Reflux symptoms, No. (%)</td>
<td>31 (100)</td>
<td>58 (100)</td>
<td>36 (100)</td>
</tr>
<tr>
<td>Barrett esophagus length, mm</td>
<td>23.5</td>
<td>24.5</td>
<td>22.3</td>
</tr>
<tr>
<td>Erosive esophagitis, No. (%)</td>
<td>17 (55)</td>
<td>24 (41)</td>
<td>11 (31)</td>
</tr>
<tr>
<td>Hiatal hernia, No. (%)</td>
<td>12 (39)</td>
<td>17 (29)</td>
<td>14 (39)</td>
</tr>
<tr>
<td>Intestinal metaplasia, No. (%)</td>
<td>31 (100)</td>
<td>58 (100)</td>
<td>36 (100)</td>
</tr>
<tr>
<td>No. of postoperative endoscopies per patient</td>
<td>4.2</td>
<td>3.1</td>
<td>3.0</td>
</tr>
<tr>
<td>Length of hospital stay, mean (SD), d</td>
<td>6.2 (1)</td>
<td>5.9 (1.2)</td>
<td>3.0 (0.5)</td>
</tr>
</tbody>
</table>

a P values are > .90 for duodenal switch vs acid suppression duodenal diversion, < .001 for duodenal switch vs laparoscopic Nissen fundoplication, and < .001 for laparoscopic Nissen fundoplication vs acid suppression duodenal diversion.

The main clinical and endoscopic features of the 125 patients with short-segment BE are given in Table 1. No significant differences were found among the 3 groups in any parameter evaluated. Among the 31 patients who underwent the laparotomic duodenal switch procedure, the antireflux technique was a posterior gastropexy with cardial calibration in 20 patients and a Nissen fundoplication in 11. Among the 58 patients who underwent the acid suppression and duodenal diversion procedure, posterior gastropexy with cardial calibration was performed in 31 patients and a Nissen fundoplication in 27 patients. Among patients who underwent the laparoscopic procedure, Nissen fundoplication was performed in 33 patients and calibration of the cardia in 3 patients. Therefore, Nissen fundoplication was used in 71 patients and posterior gastropexy with calibration of the cardia in 54 patients. No operative mortality was observed. The postoperative course was uneventful in all patients who underwent laparoscopic Nissen fundoplication. One patient who underwent the duodenal switch procedure developed gastric stasis after surgery, which required endoscopic dilatation, with unevenful posterior evolution. After vagotomy and partial gastrectomy, 1 patient developed a gastric fistula, which required subsequent operation and drainage, with an excellent postoperative course. The only significant difference among these operations was observed in the length of the hospital stay, which was significantly shorter for laparoscopic fundoplication compared with the other 2 techniques.

Table 2 gives the manometric features before and after the antireflux procedure in the 3 groups. Because this test only measures the effect of antireflux technique on the LES and the amplitude of distal esophageal waves, the changes after surgery were similar. There was an increase in LES pressure compared with preoperative values, which was statistically significant in all groups. There was an increase in the abdominal length of the LES compared with preoperative values, which was highly statistically significant in all 3 groups. There was a statistically significant increase in the total length of the LES in all groups. There was a statistically significant decrease in the presence of an incompetent LES. There was a similar increase in the amplitude of the distal esophageal waves after surgery but without statistical significance. The comparison of each parameter in the 3 groups, eg, of values before and after surgery, showed no statistically significant difference.

Table 3 gives the results of the functional studies before and after surgery in each group. The 24-hour pH monitoring before surgery and the Bilitec studies before surgery showed similar results in all 3 groups (P > .5). After the antireflux procedure, a significant reduction was seen in acid reflux in all groups compared with preoperative values. However, this reduction was not uniform: after duodenal switch, 80.7% of the patients had acid reflux with normal or below-normal values; an entirely similar value (82.8%) of reduction of acid reflux was observed among patients with acid suppression who underwent the duodenal diversion procedure. However, after Nissen fundoplication only 75.0% of the patients showed absence of abnormal acid reflux. The results of the 24-hour bile monitoring were evaluated before and after surgery mainly in the open procedures: they showed an abolition of duodenoesophageal reflux of 83% to 100% compared with preoperative values. This monitoring was not performed after Nissen fundoplication.
Table 4 gives the histologic changes at the short-segment columnar mucosa in its comparison of patients before and several times after surgery. In each group at least 3 endoscopic and biopsy procedures were performed after surgery. Some patients were lost to follow-up, and all evaluations were performed only after 12 months of the operation. Mean follow-up varied from 54 to 106 months. Persistence of intestinal metaplasia after at least 3 endoscopic and histologic analyses was observed in a similar proportion of patients in each group (35%-39%), a finding that was not statistically significant (*P* < 0.01). Regression to cardiac or oxyntocardiac mucosa occurred in 61% to 65% of the patients comparing all groups, without statistical significance (*P* < 0.01). The time to regression varied from 39 to 56 months after surgery, without statistical significance (*P* < 0.01).

Table 5 gives the Visick gradation months after surgery. We considered Visick grades I and II to be good postoperative results, although Visick grade II corresponded to patients who had to start taking proton pump inhibitors again to remain asymptomatic. These grades were registered in 86% of patients after duodenal switch, in 94% of patients after acid suppression and the duodenal diversion procedure, and in 100% of patients after laparoscopic fundoplication. Visick grades III and IV corresponded to patients with persistence of esophagitis or with dumping syndrome. None of the patients showed progression to low- or high-grade dysplasia or adenocarcinoma.

**COMMENT**

The results of the present prospective, nonrandomized study suggest that in patients with short-segment BE who undergo surgical treatment, laparoscopic Nissen fundoplication is the procedure of choice compared with the other 2 more aggressive surgical procedures. In these patients with short-segment BE, regression from intestinal metaplasia to cardiac or oxyntocardiac mucosa oc-
 occurred in nearly 60% of the patients, at a mean time of 50 months after the procedure. In addition, no progression to low- or high-grade dysplasia occurred.

For most surgeons dedicated to the care of patients with BE, the surgical treatment is focused on the reestablishment of the competence of the LES. Careful review of all publications concerning this topic shows that final results are usually shown in a mixed fashion. To our knowledge, only 6 publications have focused their results exclusively on patients with short-segment BE (Table 6).

The first report followed up 22 patients with short-segment BE for 5 years, including another 9 patients who underwent mucosal thermal ablation. There was a loss of intestinal metaplasia to cardiac or cardiac-fundic mucosa in 59% of the patients. No mention of the time to regression was given. The main problems with this report are that the investigators performed only 1 postoperative endoscopy plus biopsy in most patients and no functional studies are reported. From the whole group (66 patients), including both patients with short-segment and long-segment BE, moderate to severe gastroesophageal reflux disease symptoms were present in 35%, antisecretory medications were used in 27%, and an additional operation was performed in 7 patients (11%). The second report includes 33 patients with short-segment BE who mainly underwent laparoscopic Nissen fundoplication. At least 2 postoperative endoscopies and biopsies were performed. Regression from intestinal metaplasia to cardiac mucosa or oxyntocardiac mucosa, and rarely to cardiac fundiplication. At least 2 postoperative endoscopies and biopsies were performed. Regression from intestinal metaplasia to cardiac or oxyntocardiac mucosa occurred in 33% of the patients, after a follow-up of 50 months. No functional studies were reported. The third report was probably the most complete study; it included manometric and 24-hour pH monitoring evaluations before and after surgery. The problems with this study were mainly the short endoscopic follow-up period (30 months after surgery) and the fact that only 1 postoperative endoscopy was reported in most patients. There was a loss of intestinal metaplasia in 56% of the patients at a period of 30 months after surgery. The fourth report described 9 patients with short-segment BE who underwent Nissen-Rossetti fundoplication, with a 67% regression from intestinal metaplasia to squamous epithelium at a mean follow-up of 45 months. This finding is intriguing because the regression of intestinal metaplasia is to cardiac or oxyntocardiac mucosa and rarely to complete disappearance of the columnar mucosa and its replacement by squamous epithelium. The strength of this study is the performance of complete functional studies, which found that 42% of patients with BE had an abnormal acid reflux test result late after surgery. This study showed again what we have pointed out several times: control of symptoms does not happen parallel to the abolishment of acid reflux. The fifth report described 11 patients who underwent laparoscopic Nissen fundoplication. The follow-up is short (28 months after surgery), and no functional studies were reported. In 6 patients (55%) regression to cardiac mucosa occurred. The sixth publication followed up 59 patients with short-segment BE who underwent laparoscopic Nissen fundoplication. The criterion of the authors for regression was a decrease or disappearance of the columnar lined distal esophagus, but no mention is made of loss of intestinal metaplasia. No functional studies were reported.

In our study, we started to perform an acid suppression and duodenal diversion procedure for patients with BE in 1987 based on the fact that the harmful refluxate material in the esophagus is composed mainly of gastric and duodenal juice. Later, we included another type of duodenal diversion for patients with BE, which included, besides the Roux-en-Y loop as part of the duodenal switch, an antireflux procedure plus highly selective vagotomy. In 1995, we gradually incorporated laparoscopic Nissen fundoplication as the only surgical

| Table 4. Histologic Changes at the Columnar Mucosa in Patients With Short-Segment Barrett Esophagus |
|--------------------------------------------------------|----------------|----------------|----------------|-----------|
| Histologic Change | Duodenal Switch (n=31) | Acid Suppression—Duodenal Diversion (n=52) | Laparoscopic Nissen Fundoplication (n=36) | P Value |
| Mean follow-up, mo | 106 (36) | 76.3 (35) | 54.3 (39) | <.70 |
| Persistence of intestinal metaplasia, No. (%) | 8 (27) | 18 (35) | 9 (26) | <.80 |
| Regression to cardiac mucosa or oxyntocardiac mucosa, No. (%) | 14 (64) | 34 (65) | 14 (61) | <.11 |
| Time to regression, mo | 55.7 | 39.2 | 48.8 | | |

| Table 5. Visick Grading Months After Surgery in Patients With Short-Segment Barrett Esophagus |
|--------------------------------------------------------|----------------|----------------|----------------|----------------|
| Follow-up, mo | Duodenal Switch (n=22) | Acid Suppression—Duodenal Diversion (n=52) | Laparoscopic Nissen Fundoplication (n=36) | P Value |
| No. (%) of patients | 106 - 76.3 | 54.3 | | |
| Visick grade I | 15 (68.2) | 46 (88.4) | 17 (73.9) | |
| Visick grade II | 4 (18.2) | 3 (5.8) | 6 (26.1) | |
| Visick grades III-IV | 3 (13.6) | 3 (5.8) | NA | |
technique for these patients\textsuperscript{18} because it is much less aggressive than the other 2 techniques and we had conquered the learning curve for the laparoscopic antireflux procedure. Besides, in a prospective, randomized trial that compared the results of laparoscopic Nissen fundoplication with calibration of the cardia with posterior gastroscopy, we demonstrated similar late results at 10 years of follow-up,\textsuperscript{23} which is why we adopted Nissen fundoplication as the antireflux procedure of choice. The careful follow-up of all 125 patients who underwent these 3 procedures that assessed subjective and objective variables showed that the results are similar comparing the 3 techniques, measured with symptomatic evaluations (Visick grading), functional studies (manometric tests, 24-hour pH monitoring, and 24-hour bile monitoring), and histologic evaluations expressing the percentage of loss of intestinal metaplasia to cardiac or oxytocardiac mucosa.

Finally, the less aggressive surgical approach has shown that laparoscopic Nissen fundoplication is the treatment of choice when dealing with the surgical treatment of patients with short-segment BE. Patients with low-grade dysplasia were not included in this study and have been described elsewhere.\textsuperscript{21} As described recently for patients with long-segment BE,\textsuperscript{24} none of our patients who underwent the duodenal diversion procedure has developed high-grade dysplasia or adenocarcinoma, even after 120 months of follow-up. Although the follow-up after Nissen fundoplication is shorter (54 months), we have not seen any progression among these patients. We need a longer follow-up to determine the real effect of this technique. We ask other authors to report their results with a much longer follow-up (no studies have more than 5 years, and 2 studies have only 2½ years of follow-up) and to perform at least 3 postoperative endoscopies in each patient and incorporate functional studies in their evaluations to determine by several objective parameters the real long-term effect of Nissen fundoplication. We do not believe that a follow-up by telephone or written questionnaire is an adequate way to determine the late results of a particular surgical procedure, especially when dealing with patients with BE.

In conclusion, after we compared 3 different operations for patients with short-segment BE, we found that laparoscopic Nissen fundoplication is the procedure of choice because it is less invasive, has fewer side effects, and produces good results in long-term follow-up, results that are similar to those found with other more aggressive surgical techniques.

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Author Contributions: Study concept and design: Csendes and Braghetto. Acquisition of data: Braghetto, Smok, and Henriquez. Analysis and interpretation of data: Csendes, Braghetto, Burdiles, and Burgos. Drafting of the manuscript: Henriquez and Burgos. Critical revision of the manuscript for important intellectual content: Csendes, Burdiles, and Smok. Statistical analysis: Burgos. Administrative, technical, and material support: Smok and Henriquez. Study supervision: Burdiles.

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REFERENCES
Questions Regarding Surgery to Correct Short-Segment BE

Barrett esophagus develops as a consequence of long-standing reflux of gastric juice into the esophagus, and it is likely that continued reflux drives the progression of BE to dysplasia and adenocarcinoma. Both acid and bile have been implicated in the development of BE, and increasingly there is evidence that the relative proportions of each and the resultant pH of the refluxed gastric juice may be important in this process. In many patients, BE, once it develops, never progresses. However, an important and unresolved issue is whether medical or surgical intervention can alter the natural history of BE such that progression does not occur in those in whom BE otherwise would have progressed. Regression or loss of intestinal metaplasia certainly suggests an alteration in the natural history, and Csendes and colleagues report in this issue of the Archives of Surgery that there was loss of intestinal metaplasia in approximately 60% of patients with short-segment BE after surgical correction of reflux. However, a number of important issues remain unanswered:

1. Is intestinal metaplasia, once lost, gone forever?
2. When, if ever, can surveillance endoscopy be terminated in patients who lost their intestinal metaplasia?

3. Does loss of intestinal metaplasia eliminate the risk of esophageal adenocarcinoma?
4. What is different about the intestinal metaplasia in the patients who lost it after surgery, and are these the patients in whom BE would never have progressed anyway (in other words, is persistence of intestinal metaplasia a marker for a subtype of intestinal metaplasia that is more likely to progress)?
5. Does the degree of reduction of reflux correlate with the likelihood of regression?
6. How often does regression happen with incomplete control of reflux?
7. Is control of acid, bile, or both the most important factor in regression of intestinal metaplasia?

It is hoped that the answers to these and other questions will come from continued clinical and laboratory studies on this fascinating condition.

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