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The Impact of an Antireflux Procedure on Intestinal Metaplasia of the Cardia

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Objective

The aim of this study was to determine whether antireflux surgery is more effective in producing loss of intestinal metaplasia located only at the gastroesophageal junction than it has been in patients with intestinal metaplasia extending up into the distal esophagus.

Summary Background Data

Biopsies of a normal appearing gastroesophageal junction will demonstrate cardiac mucosa containing goblet cells—the hallmark of intestinal metaplasia—in 10% to 15% of patients who are evaluated for symptoms of gastroesophageal reflux. The incidence of adenocarcinoma of the esophagus and cardia is rising faster than any other cancer in America, and most of these cancers are found adjacent to areas of intestinal metaplasia. Antireflux surgery in patients with Barrett's esophagus may provide protection from progression to dysplasia and cancer; however, it does not reliably cause regression of the intestinal metaplasia. Less is known about the potential for intestinal metaplasia limited to the cardia (CIM) to regress.

Methods

Sixty patients with intestinal metaplasia of the esophagus or cardia had antireflux surgery. Patients in the intestinal (CIM) group (n = 15) had no endoscopically visible segment of columnar epithelium. Patients in the Barrett's group (n = 45) had columnar epithelium visible within the esophagus. Median follow-up was 25 months in each group.

Results

Postoperative biopsies showed complete loss of intestinal metaplasia in 73% of the patients with CIM compared with 4.4% of the patients with Barrett's. Low-grade dysplasia, present in 10 patients preoperatively, regressed in 7 patients (70%). No patient progressed to high-grade dysplasia or cancer.

Conclusions

Loss of intestinal metaplasia after antireflux surgery is rare in patients with Barrett's, but occurred in most patients with CIM. This suggests that cardiac epithelium is dynamic and that microscopic areas of intestinal metaplasia are able to regress much more frequently than longer, visible segments of intestinal metaplasia.

The esophagogastric junction is that area where the acid sensitive squamous mucosa of the esophagus meets the glandular, acid resistant mucosa of the stomach. Despite its importance, this area remains somewhat of an enigma. We recently have demonstrated the presence of cardiac mucosa juxtaposed between esophageal squamous and gastric fundic mucosa in most patients evaluated for symptoms of gastroesophageal reflux disease[1]. When present, the cardiac epithelium almost always had histologic evidence of inflammation unrelated to either *H. pylori* infection or mucosal pathology elsewhere in the stomach. Furthermore, the presence of inflamed cardiac mucosa, or carditis, correlated closely with objective markers of gastroesophageal reflux disease including an incompetent lower esophageal sphincter and increased esophageal acid exposure on 24-hour pH monitoring. We suggested that carditis may represent the earliest manifestation of reflux disease and that with con-

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tinued reflux there might be a creeping columnarization of the squamous epithelium within the lower esophageal sphincter, a progressive loss of sphincter competency, and ultimately explosion of the disease into the body of the esophagus.

Recently, it has been recognized that endoscopic biopsy of a normal appearing gastroesophageal junction will demonstrate the presence of intestinal metaplasia within cardiac mucosa in 10% to 15% of patients being evaluated for symptoms of gastroesophageal reflux.[1,2] In contrast to endoscopically visible segments of columnar epithelium containing intestinal metaplasia (Barrett's esophagus), for which there is a known increased risk of cancer, the natural history and premalignant nature of intestinal metaplasia limited to the cardia (CIM) is not well characterized. Of concern though is the rapidly rising incidence of adenocarcinoma in both the distal esophagus and cardia, and the frequent finding of cancers adjacent to short and even microscopic lengths of intestinal metaplasia.[3] Antireflux surgery in the setting of Barrett's esophagus may provide protection from progression to dysplasia and cancer; however, it does not reliably or predictably cause regression of the intestinal metaplasia or a reduction in the length of columnar mucosa.[4,5,6] The aim of this study was to determine whether the prevention of reflux with antireflux surgery is more effective in producing regression of intestinal metaplasia located only at the gastroesophageal junction than it has been in patients with intestinal metaplasia extending up into the distal esophagus.

METHODS

Study Population

Between July 1991 and April 1997, 79 patients with intestinal metaplasia of the cardia or esophagus underwent an antireflux procedure in our department. Nineteen patients were excluded: 15 without postoperative endoscopy and 4 with endoscopy but without biopsies of the gastroesophageal junction. The remaining 60 patients were divided into two groups. Patients in the CIM group (n = 15) had no endoscopically visible segment of columnar epithelium, but routine biopsies of the gastroesophageal junction showed intestinal metaplasia within the cardiac mucosa. Patients assigned to the Barrett's group (n = 45) had intestinal metaplasia within any length of endoscopically visible columnar epithelium. Characteristics of each group are shown in Table 1. Standard preoperative evaluation included video esophagram, upper endoscopy with biopsies, esophageal motility, and ambulatory 24-hour pH monitoring. Additionally, 62% of patients had 24-hour esophageal bilirubin monitoring using the Bilitec 2000 probe (Synectics, Shoreview, MN). Detailed descriptions of our technique for each of these procedures have been previously published.[1,7] Median follow-up in each group was 25 months, and the time of the latest postoperative endoscopy for each patient is shown in Figure 1.

Table 1. DEMOGRAPHICS AND CLINICAL HISTORY

	CIM	Barrett's
n	15	45
Male/Female	11/4	35/10
Age (years)	55 (21–76)	53 (31–80)
Follow-up (months)	25 (8–63)	25 (7–63)
Primary symptom typical*	14 (93%)	44 (98%)
PPI > 1 year†	8 (53%)	26 (58%)
H. Pylori positive	3 (20%)	6 (13%)
Prior antireflux surgery	1 (7%)	3 (7%)

* Typical symptom = heartburn, regurgitation, or dysphagia.
† PPI = Proton pump

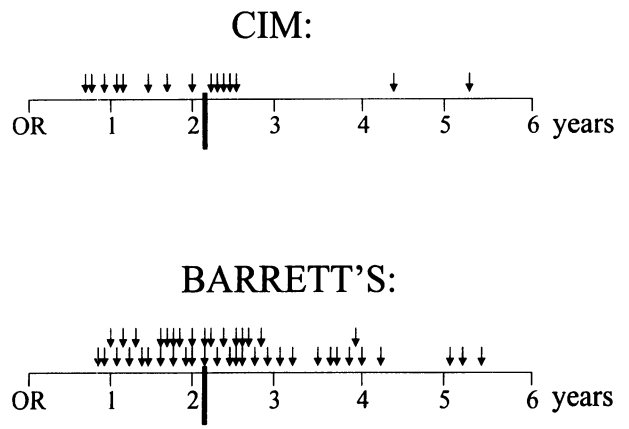

Figure 1. Time of latest follow-up endoscopy for patients in the CIM and Barrett's groups. Median follow-up is indicated for each group by the heavy vertical line and was 25 months in each. Two or more postoperative endoscopies were performed in 9/15 CIM patients, and in 22/45 Barrett's patients.

Endoscopic Definitions

The endoscopic gastroesophageal junction was defined as the point where the tubular esophagus joined the most proximal gastric rugal folds. The squamocolumnar junction was defined as the site where the pale white esophageal mucosa met the pink columnar mucosa of the cardia or Barrett's segment. A difference between the gastroesophageal and squamocolumnar junctions, and tongues of pink mucosa extending into the white squamous esophageal mucosa, were interpreted as endoscopic evidence of columnar epithelium. The length of columnar epithelium was measured from the esophagogastric junction to the squamocolumnar junction or to the top of any tongues extending into the esophagus. A hiatal hernia was diagnosed when the gastroesophageal junction was located 2 or more centimeters proximal to the crural impression. Esophagitis was identified by the presence of linear erosions or interlocking erosions giving the appearance of a cobblestone esophagus.

Biopsy Protocol

Preoperative endoscopy included routine biopsies taken from the antrum, body of the stomach, gastroesophageal junction, squamocolumnar junction, squamous epithelium above the squamocolumnar junction, and from four-quadrants every 2 cm between the gastroesophageal and squamocolumnar junctions in patients with Barrett's. A mean of six biopsies per patient were obtained from the gastroesophageal junction using both the retroflexed and antegrade endoscopic positions. This extensive biopsy protocol led to our diagnosis of CIM in all 15 patients in this study, despite one or more endoscopies having been performed in most patients before referral to our unit. Postoperatively, a similar systematic biopsy protocol was used, although our ability to obtain retroflex biopsies was hindered in some patients by the fundoplication. Typically, though, the short fundoplication we make did not interfere with taking biopsies of the gastroesophageal junction, particularly in the antegrade direction.

Histologic Analysis

Biopsy specimens were fixed in 10% buffered formaldehyde solution and embedded in paraffin, sectioned, and mounted using standard techniques. Slides were stained routinely with hematoxylin and eosin. Fundic mucosa was identified by the presence of a pitted surface lined by mucus-secreting columnar cells and a deeper glandular layer containing pepsinogen producing chief and acid producing parietal cells. Cardiac mucosa was differentiated histologically from fundic mucosa based on the absence of chief and parietal cells in the underlying glands. Carditis was characterized by the presence of eosinophil or plasma cell infiltration of the lamina propria and foveolar hyperplasia. Intestinal metaplasia was defined by the presence of goblet cells on routine sections and confirmed in the less obvious cases by positive staining with Alcian blue at pH 2.5. The presence of *Helicobacter pylori* infection was assessed in all biopsy specimens. In patients with a visible segment of columnar mucosa, the endoscopically measured length was compared with the histology at each biopsy location to confirm that what appeared to be columnar mucosa was not esophagitis within squamous mucosa.

Definition of Regression and Progression

Regression was considered to have occurred in patients within the CIM group only under the following circumstances: (a) multiple endoscopic biopsies demonstrated cardiac mucosa without intestinal metaplasia (*loss of intestinal metaplasia*), (b) there was histologic evidence of fundic mucosa adjacent to squamous epithelium on biopsies from two or more endoscopies (*loss of intestinal metaplasia and cardiac mucosa*), or (c) dysplasia was no longer present within the intestinal metaplasia (*loss of low-grade dysplasia*). Patients with CIM were considered to have progressed if an endoscopically visible segment of columnar epithelium developed that on biopsy was proven to contain intestinal metaplasia. Progression also included the development of dysplasia or cancer.

Regression in patients with Barrett's esophagus was defined as the occurrence of any of the following: (a) histologic disappearance of intestinal metaplasia, (b) loss of dysplasia, or (c) at least a 4 cm decrease in the length of intestinal metaplasia endoscopically and histologically. Four centimeters were selected because in most patients biopsies were taken 2 cm apart, thus to be confident that similar regions of the esophagus were being sampled on separate endoscopies, we required a change at two biopsy locations. The development of squamous islands within the columnar segment, no matter how many, was not considered to be regression. Progression in patients with Barrett's consisted of at least a 4 cm increase in the endoscopic and histologic length of intestinal metaplasia, or the development of dysplasia, or cancer.

Postoperative Outcome

A physician other than the responsible surgeon assessed the outcome. Using a standard questionnaire form, all patients were interviewed in person or by telephone. Outcome was considered excellent if the patient was cured of their primary symptom and had no other gastrointestinal complaints, good if their primary symptom was relieved but minor gastrointestinal complaints such as bloating or flatulence were present, fair if their primary symptom was improved but additional medications were necessary for complete relief, and poor if their primary symptom was not improved or made worse.

Statistical Analysis

Chi-square and Fisher's exact test were used to compare proportions between groups. Statistical significance was considered at $p \leq 0.05$. Values are reported as median and range unless otherwise stated.

RESULTS

As shown in Table 1, both CIM and Barrett's occurred more commonly in men. The median age in each group was similar. All but one patient in each group had typical reflux symptoms of heartburn, regurgitation, and/or dysphagia. More than half of the patients in each group had used proton pump inhibitors for at least 1 year before antireflux surgery. Endoscopic findings and the results of physiologic studies are illustrated in Figure 2. In patients with Barrett's, the mean length of intestinal metaplasia was 3 cm (range 1 cm –13 cm).

All patients underwent antireflux surgery (Table 2).

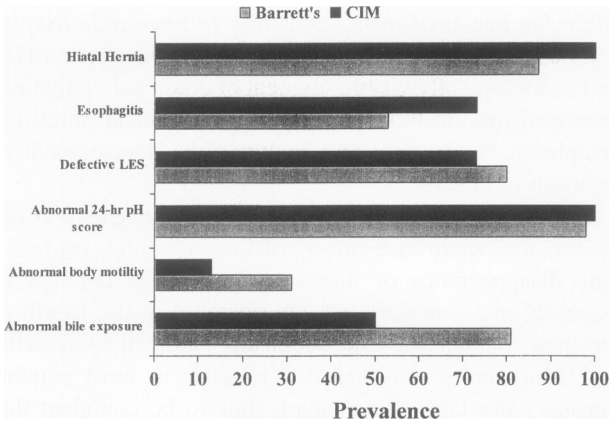

Figure 2. The prevalence of manifestations of gastroesophageal reflux in patients with CIM and Barrett's esophagus who underwent antireflux operations. Abnormal 24-hour pH was defined as a composite score more than 14.7. Abnormal esophageal motility was defined as amplitude of contractions less than 30 mm Hg, or the presence of more than 20% simultaneous contractions in the distal 3/5ths of the esophagus. Abnormal bile exposure was defined as bilirubin absorbance above 0.2 for more than 1.7% of the total time.

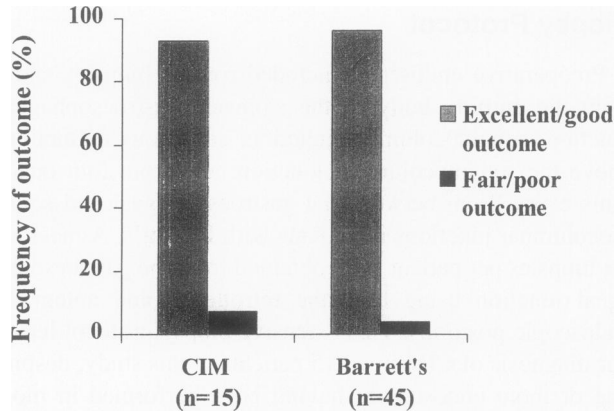

Figure 3. Postoperative outcome determined by physician survey (see text for details). Over 90% of patients in each group had relief of their primary symptom.

Laparoscopic procedures were more common in the CIM group (80%) compared with the Barrett's group (51%). Reoperations and patients with suspicion of a short esophagus underwent an open procedure. Overall, 80% of the patients underwent a Nissen fundoplication (93% in the CIM group, 75% in the Barrett's group). Although no patient in the CIM group required an esophageal lengthening procedure, 18% of the patients in the Barrett's group underwent a Collis gastroplasty for short esophagus. Postoperative clinical outcome was excellent or good in most patients in both groups (Figure 3). No patient had esophagitis on postoperative endoscopy.

Regression

The most significant finding of this study was the high frequency of loss of intestinal metaplasia after antireflux surgery in the CIM group. There was a highly significant difference between groups, as shown in Figure 4. After antireflux surgery, the inflammation within cardiac mucosa typically subsided (data not shown), and in 5 of 15 patients (33%) with CIM areas of cardiac mucosa were found with oxyntic transformation into cardiac-fundic mucosa. We believe this represents a regressive change of cardiac epithelium that can occur in the absence of continued inflammation. One of these 5 patients was found 1 year after fundoplication to have cardiac and cardiac-fundic mucosa without intestinal metaplasia on biopsies. Subsequent endoscopies in this patient have demonstrated only fundic mucosa adjacent to squamous epithelium, suggesting that there has been complete replacement of cardiac and cardiac-fundic mucosa by fundic mucosa. The other four patients continue to demonstrate both cardiac and cardiac-fundic mucosa on postoperative biopsies—three without and one with persistent intestinal metaplasia.

Regression of preoperative low-grade dysplasia and the length of Barrett's also occurred and is shown in Table 3. A total of 10 patients (1 CIM, 9 Barrett's) had preoperative low-grade dysplasia. Postoperatively, there was loss of low-grade dysplasia in 7 of the 10 patients (70%) —1 CIM and 6 Barrett's.

Table 2. TYPE OF ANTIREFLUX PROCEDURE

	CIM	Barrett's
Laparoscopic Nissen	12	22
Laparoscopic Toupet	–	1
Abdominal Nissen	1	–
Thoracic Nissen	1	12
Belsey-Mark IV	1	2
Collis-Belsey	–	8

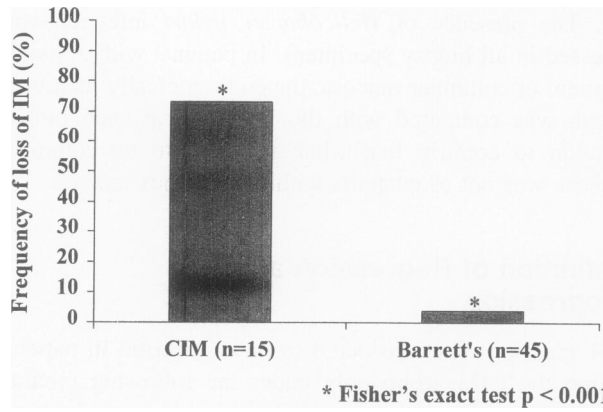

Figure 4. Frequency of complete regression (loss) of intestinal metaplasia after antireflux surgery. Both patients with complete regression in the Barrett's group had short segments (2 cm) of intestinal metaplasia. Within the CIM group one patient lost both intestinal metaplasia and cardiac mucosa postoperatively, whereas the others continued to show histologic evidence of cardiac mucosa (see text for details).

Table 3. TYPE OF REGRESSION

	CIM	Barrett's
n	15	45
Decrease length of Intestinal Metaplasia (≥4 cm)	–	2 (4.4%)
Loss of Intestinal Metaplasia	11 (73%)*	2 (4.4%)*†
Loss of dysplasia/number with preoperative low-grade dysplasia	1/1	6/9
TOTAL	12 (80%)‡	10 (22%)‡

*Fisher's exact test $p < 0.001$.
†Both patients had less than 3 cm of intestinal metaplasia.
‡Chi-square test $p < 0.001$.

Progression

There was a total of 130 patient-years of follow-up. No patient in either group had progression to high-grade dysplasia or cancer. No patient in the CIM group developed low-grade dysplasia postoperatively. Within the Barrett's group 4 of the 36 patients (11%) without preoperative low-grade dysplasia developed low-grade dysplasia postoperatively. No other form of progression occurred in the Barrett's group.

DISCUSSION

A problem with any discussion about the gastroesophageal junction is that "normal" is not clearly and unequivocally defined. An attractive theory about this region was introduced into the scientific literature in 1961 by Hayward, who without any supporting data suggested that the cardia, or distal 1 cm to 2 cm of the esophagus, is normally lined by a mucus-secreting columnar epithelium that has the ability to resist acid-pepsin digestion.[8] There are several problems with this theory. First, autopsy data suggest that in most people younger than 20 years, esophageal squamous mucosa directly abuts gastric fundic mucosa, and there is no transitional epithelium.[9] Columnar cardiac mucosa was frequently found in patients older than 20, but it is not clear that this represents the normal state. Second, cardiac mucosa is not acid-resistant, but instead, when present, nearly always shows histologic evidence of inflammation and injury. Furthermore, the presence of carditis is commonly associated with objective evidence of gastroesophageal reflux disease, including increased esophageal acid exposure on 24-hour pH monitoring, a structurally defective lower esophageal sphincter, and erosive esophagitis.[1] Lastly, there is evidence that cardiac epithelium replaces squamous epithelium exposed to chronic irritation and injury by refluxed gastric juice. Clear evidence for this comes from follow-up of patients that have undergone partial esophagogastrectomy with intrathoracic anastomosis of the esophagus to the fundus of the stomach. This arrangement leads to significant reflux, and despite a vagotomy, the stomach continues to make acid. Over time, columnar epithelium histologically identical to cardiac mucosa has developed proximal to the anastomosis in what was unquestionably the esophagus and in what unquestionably had been squamous epithelium.[10,11] Further substantiation of this concept comes from Csendes et al.[12], who have shown that as the severity of gastroesophageal reflux disease progresses, the length of columnar lining above the anatomic gastroesophageal junction increases. Of note, if one accepts the theory that cardiac epithelium does not normally exist at the gastroesophageal junction, then the replacement of squamous epithelium by cardiac mucosa is not really a metaplastic process, because there is no place in the body where cardiac mucosa is normally found. Instead, this process represents an injury-induced replacement of the normal esophageal squamous epithelium by a histologically distinct type of columnar epithelium that has come to be called cardiac mucosa.

If cardiac epithelium replaces squamous epithelium in response to the chronic injury of refluxed gastric juice, what is intestinal metaplasia of the cardia, and what is its significance? The hallmark of intestinal metaplasia is the presence of goblet cells within columnar epithelium. Goblet cells are not normally found in the stomach or esophagus. Therefore, the presence of goblet cells within cardiac mucosa represents a metaplastic process that is always abnormal. There is general agreement that as the length of columnar epithelium increases within the esophagus, the likelihood of finding intestinal metaplasia increases. Spechler et al.[13] reported that intestinal metaplasia was present in 93% of patients with columnar segments more than 3 cm in length and in 36% of patients with columnar segments 1 cm to 2 cm in length. It follows quite nicely that intestinal metaplasia within the cardia is seen in 10% to 15% of patients. This suggests that CIM and Barrett's are related through the common denominator cardiac mucosa. As the length of cardiac epithelium increases, the likelihood of a second insult, necessary to induce a metaplastic change within the cardiac epithelium, also increases. Although the pathogenesis of this process is unknown, it may occur by induction of mucosal cell gene expression and the production of a phenotypic rather than a mutational change. Current theories implicate the role of noxious luminal contents, in particular gastroduodenal juice, which when refluxed chronically over 5 to 7 years causes the metaplastic transformation from columnar mucosa to intestinalized columnar mucosa.

The significance of CIM has to be assessed in light of the above conclusions. If cardiac mucosa replaces injured esophageal squamous mucosa, and CIM occurs within cardiac mucosa, it follows that CIM represents intestinal metaplasia within the esophagus, but is limited to the immediate area of the gastroesophageal junction. It is well established that most cases of esophageal adenocarcinoma arise from the intestinal metaplasia of Barrett's esophagus.[14,15] Retrospectively, intestinal metaplasia has been found in associa-

tion with 79% to 100% of esophageal adenocarcinomas and in 42% to 73% of adenocarcinomas at the gastroesophageal junction.[2,16,17] In addition, short and even microscopic segments of intestinal metaplasia have been correlated with the development of adenocarcinoma.[3,17–19] Of importance, the intestinal metaplasia of CIM is histologically identical to the intestinal metaplasia of Barrett's esophagus, and both can become dysplastic. Indeed, 1 of our 15 CIM patients had low-grade dysplasia preoperatively. Although the natural history and malignant potential of CIM is not characterized completely, one has to suspect that CIM is linked to the rapidly rising rate of adenocarcinoma of the cardia. If the risk of developing dysplasia and cancer correlates with the area of intestinal metaplasia at risk, then any one patient with CIM is probably at a much lower risk for cancer than a patient with 7 cm of intestinal metaplasia. However, given the much greater prevalence of CIM compared with long segments of intestinal metaplasia, if CIM is premalignant, even at a low rate, then the population as a whole is at significant risk for adenocarcinoma of the cardia. This concern seems to be born out by the fact that the incidence of adenocarcinoma of the cardia is seven times that of adenocarcinoma of the esophagus.[20]

Given that intestinal metaplasia of the cardia is abnormal, and potentially associated with adenocarcinoma of the cardia, the next question is can anything be done to make it go away. The important finding in this study was the high rate of regression of intestinal metaplasia in the CIM group. As opposed to regression of the length of columnar mucosa, it is the loss of the mucosa potentially at risk for malignant degeneration that is the critical issue in protection against malignancy. In the current study, 73% of patients with CIM who underwent an antireflux procedure had complete regression of their intestinal metaplasia, compared with only 4.4% in the Barrett's group. This finding suggests that cardiac mucosa is dynamic and that microscopic and perhaps short segments of intestinal metaplasia are not as fixed as the longer segments seen in traditional Barrett's esophagus. Further support for the dynamic nature of cardiac epithelium is the finding that with control of reflux and reduction of inflammation, cardiac mucosa can change into a more fundic type mucosa called cardiac-fundic mucosa, and in some cases on to mature fundic mucosa (9). In five patients with CIM (33%) we noted this process. Further follow-up will be necessary to determine whether the loss of intestinal metaplasia and regressive changes found frequently in the CIM group are permanent, or whether with potential loosening of the fundoplication over time intestinal metaplasia will redevelop in some patients. In addition, years of careful follow-up will be necessary to determine the malignant risk of CIM and the impact of a fundoplication on this risk.

In contrast to the frequent loss of intestinal metaplasia found in the CIM group, complete regression of intestinal metaplasia rarely occurred in patients with endoscopically visible segments of columnar epithelium. This finding is similar to what has previously been reported in the literature after both antireflux surgery and medical therapy.[5,6,21,22] The two patients in the Barrett's group with complete loss of intestinal metaplasia after fundoplication had columnar segments less than 3 cm in length. No patient with a segment of columnar epithelium 3 cm or longer had complete loss of intestinal metaplasia. Perhaps those patients with long, visible segments of Barrett's, particularly when associated with persistent postoperative low-grade dysplasia, should be considered for mucosal ablation therapy. Salo et al.[23] have recently demonstrated regeneration of squamous mucosa in a group of patients that underwent antireflux surgery followed by ablation of their columnar mucosa.

We recognize the concern that a fundoplication may have hampered our ability to biopsy the gastroesophageal junction and that the high frequency of loss of intestinal metaplasia in the CIM group merely represents sampling error. We believe, however, that this possibility is unlikely. First, we found that postoperatively in the patients in the CIM group, the squamocolumnar junction was near the top of our short Nissen fundoplications, and there was no particular difficulty obtaining cardiac mucosa on nearly every biopsy specimen, with the exception of retroflex biopsies in some cases. Secondly, we used the same systematic biopsy protocol postoperatively that allowed us to detect the presence of CIM preoperatively. We believe that with a mean of five biopsies directed at the gastroesophageal junction in each patient, sampling error was minimized. Furthermore, for the difference we observed in the frequency of loss of intestinal metaplasia between the CIM and Barrett's groups to become statistically nonsignificant, 8 the 11 patients in the CIM group with regression would have to be found to have intestinal metaplasia. Additional support for our findings comes from other studies suggesting that short segments of intestinal metaplasia are able to regress completely. Weston et al.[24] have described complete regression of less than 2 cm lengths of intestinal metaplasia in 32% of patients treated for 18 months with acid suppression medication. Interestingly, we found that many of our patients had used proton pump inhibitors for more than a year preoperatively, and despite medical therapy, intestinal metaplasia developed or persisted. Lastly, we also noted loss of intestinal metaplasia in two patients in the Barrett's group, both with 2 cm lengths of intestinal metaplasia. Sampling error here was particularly unlikely given that both of these patients had endoscopically visible short segment Barrett's before regression.

Another important finding in this study was the high rate of regression of low-grade dysplasia in both the CIM and Barrett's groups. Overall, 70% of patients with preoperative low-grade dysplasia reverted to no dysplasia postoperatively. Furthermore, despite 130 patient-years of follow up, no patient developed high-grade dysplasia or cancer. The expected frequency of cancer in patients with Barrett's esophagus is 1 per 100 patient-years of follow-up. However, the expected incidence of cancer in patients with CIM is not

known, and thus, long-term follow-up of large numbers of patients will be required to determine the natural history of CIM and whether antireflux surgery protects against progression to dysplasia and cancer in these patients. In contrast to our findings with antireflux surgery, Sharma et al.[19] followed 32 patients with short segment Barrett's (mean length = 1.5 cm) who were treated medically for a mean of 36.9 months and found a 5.7% annual incidence of progression to dysplasia. During the 98 patient-years of follow-up in their series, two patients developed high-grade dysplasia, and one of these patients progressed to cancer. All patients were treated with omeprazole, ranitidine, and/or promotility agents. They commented that most patients developed dysplasia while on acid suppression medication, and they concluded that medical treatment does not prevent the development of dysplasia.

In conclusion, we found that in our series of 60 patients who underwent antireflux surgery and had intestinal metaplasia of the esophagus or cardia, most were men in their 60s. Most patients in the CIM and Barrett's groups had typical reflux symptoms and objective evidence of increased gastroesophageal reflux. There was a trend toward increased bile exposure and an increased prevalence of poor esophageal body motility in patients with Barrett's, and it is possible that these two factors contribute to the development of Barrett's. Importantly, the indication for operation in all patients was abnormal gastroesophageal reflux, not the presence of intestinal metaplasia per se. This is particularly true in the CIM group, where in addition to symptoms, all patients had increased esophageal acid exposure on 24-hour pH monitoring, and most had other stigmata of reflux disease including esophagitis, hiatal hernia, and a mechanically defective lower esophageal sphincter. In this group, it was these standard indications for antireflux surgery that drove the operation and not the presence of CIM. After antireflux surgery, we found that loss of intestinal metaplasia in patients with Barrett's was rare. In contrast, 73% of patients with CIM had loss of intestinal metaplasia after fundoplication. This suggests that cardiac mucosa is dynamic and that as opposed to intestinal metaplasia extending several centimeters into the esophagus, intestinal metaplasia of the cardia is much more readily reversed. Antireflux surgery also was associated with regression of dysplasia in 70% of patients with preoperative low-grade dysplasia and protection against the development of high-grade dysplasia and cancer in both the CIM and Barrett's groups. However, long-term follow-up of large numbers of patients will be necessary to determine the natural history of CIM and the ultimate impact of antireflux surgery on this disease.

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