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Regression of intestinal metaplasia following magnetic sphincter augmentation device placement

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Abstract

Background Intestinal metaplasia represents an esophageal mucosal transformation due to uncontrolled gastroesophageal reflux disease. Fundoplication has been shown to lead to regression of disease. Magnetic sphincter augmentation is an alternative to fundoplication that effectively treats reflux disease. Initially, patients with intestinal metaplasia were not considered candidates for device placement, so outcomes in these patients are unknown.

Methods A retrospective review of all patients who underwent magnetic sphincter augmentation device placement between 2007 and 2017 was performed. All patients underwent pre-operative endoscopic evaluation and were categorized as having ultra-short segment (less than 1 cm), short-segment (1–3 cm), or long-segment (greater than or equal to 3 cm) disease. To be included in the study, pathologic examination demonstrating columnar mucosa with goblet cells was required.

Results There were 86 patients with biopsy-proven non-dysplastic intestinal metaplasia. 35 patients had ultra-short segment, 37 patients had short-segment, and 14 patients had long-segment disease. At a median follow-up of 1.2 years, 67/86 (78%) patients completed endoscopic follow-up. 48/67 (71.6%) patients had regression of intestinal metaplasia. There was no progression to dysplasia or carcinoma. Patients with abnormal post-operative DeMeester scores were less likely to have regression of disease. Regression was more likely in the ultra-short segment (82.8%) and short-segment (73.3%) groups compared to the long-segment group (25.0%).

Conclusions Magnetic sphincter augmentation is effective in achieving regression of intestinal metaplasia. Longer-term follow-up is needed to assess durability of effect and make meaningful comparisons to fundoplication.

Keywords Gastroesophageal reflux disease · Magnetic sphincter augmentation · Intestinal metaplasia · Barrett's esophagus

Intestinal metaplasia, more commonly known as Barrett's esophagus, represents a transformation of the esophageal mucosa in response to prolonged acid exposure. The presence of metaplasia is recognized as a pre-cancerous lesion given the well-established risk of progression to dysplasia and carcinoma [1]. Medical management with anti-secretory therapy is the most common treatment modality currently used for patients with symptoms of gastroesophageal reflux disease (GERD) and intestinal metaplasia. Anti-reflux surgery can further prevent acid exposure and more importantly prevent exposure to the non-acidic gastric contents which have been implicated in the pathogenesis and progression of intestinal metaplasia. Long-term studies in gastric fundoplication have demonstrated regression of intestinal metaplasia in this population [2, 3].

Magnetic sphincter augmentation (LINX Reflux Management System, Torax Medical Inc.) is a novel surgical option for the management of GERD [4]. The LINX device is a small flexible band of interlinked titanium beads with magnetic cores which is placed around the esophagus at the level of the gastroesophageal junction. It was designed to augment the natural function of the lower esophageal sphincter. The magnetic beads are designed to separate during swallowing to allow passage of the food bolus. Long-term studies have demonstrated that this device is effective in controlling subjective and objective measures of GERD [5, 6]. Initial use of the device was limited to patients with no or small hiatal

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hernia, mild esophagitis, BMI less than 35, and no evidence of Barrett's esophagus [4]. Subsequent studies have demonstrated efficacy in groups initially excluded [7–9]. Nevertheless, the effect of magnetic sphincter augmentation on the natural evolution of Barrett's esophagus is unknown. Our aim was to examine the possible progression as well as the anticipated regression rate of intestinal metaplasia following magnetic sphincter augmentation for gastroesophageal reflux disease.

Materials and methods

A retrospective review was performed of all patients who underwent placement of the magnetic sphincter augmentation device for GERD. The study period was from April 2007, when the earliest device was placed as part of the initial clinical trial, to November 2017. The first patient with intestinal metaplasia to have the device placed was in 2012.

Standard pre-operative evaluation of all patients included esophagogastroduodenoscopy (EGD). Biopsy of mucosa at the gastroesophageal junction was routinely performed. If visible segments of abnormal mucosa were present, endoscopic appearance was categorized as ultra-short segment (abnormal mucosa less than 1 cm in length), short-segment (abnormal mucosa between 1 and 3 cm in length), and long-segment (abnormal mucosa greater than or equal to 3 cm in length). Visible segments of abnormal mucosa were biopsied in accordance with the Seattle Protocol. A patient was identified as having intestinal metaplasia based on pathologic evidence of columnar mucosa with presence of goblet cells.

Post-operatively, patients were initially followed for resolution of symptoms and then completed routine endoscopy, pH testing, and a videoesophagram at 1-year post-op and then annually thereafter. Biopsies were taken even if the mucosa did not have visible segments of disease to assess for microscopic regression. Patients with symptomatic complaints prior to the 1-year follow-up underwent diagnostic testing as indicated by their clinical condition. When this included an EGD, biopsies were performed to assess for disease regression even if follow-up was less than 1 year.

This study was approved by the Institutional Review Board of the University of Southern California. Statistics were performed with SAS version 9.4 (SAS Institute Inc.).

Results

The charts of 443 patients were reviewed which identified 86 patients with biopsy-proven non-dysplastic intestinal metaplasia to include in the study. Patient demographics and the details of the surgical procedure are shown in Table 1. There were no major post-operative complications. 8 patients had persistent dysphagia requiring balloon dilatation and 2 patients developed a recurrent hiatal hernia. These 2 patients have undergone repeat hiatal hernia repair with LINX device replacement.

78% (67/86) of patients completed post-operative endoscopic follow-up. At a median follow-up of 1.2 years, 48 patients had no pathologic evidence of intestinal metaplasia corresponding to an overall regression rate of 71.6%. In addition, there was no progression to dysplasia or cancer. 47 patients completed post-operative pH testing. The median DeMeester score improved from 35.3 pre-operatively to 9.2 post-operatively. 70.2% (33/47) of patients had a DeMeester score < 14.72. Patients with normal

Table 1 Demographic and surgical characteristics

	N = 86
Age (years)[a]	58 (17–80)
BMI (kg/m^2)[a]	27.3 (17.8–44.3)
Sex	
Female	30
Male	56
Duration of symptoms	
Less than 1 year	5
1–5 years	17
6–9 years	14
More than 10 years	45
Esophagitis	
None	59
Grade A	13
Grade B	8
Grade C	6
Hiatal hernia size	
None	18
Less than 3 cm	21
3–5 cm	36
Greater than 5 cm	11
Barrett's esophagus length	
Ultra-short segment	35
Short segment	37
Long segment	14
Operative time (minutes)[a]	66 (22–153)
Length of stay (days)[a]	0.5 (0.1–2.2)
Size of device placed	
12	2
13	14
14	21
15	18
16	24
17	7

[a]Mean (range)

Table 2 Comparison of regression of intestinal metaplasia by normalization of esophageal acid exposure

	Intestinal metaplasia on post-operative endoscopy	
	Present (%)	Not present (%)
DeMeester score < 14.72	7 (21.2)	26 (78.8)
DeMeester score > 14.72	5 (35.7)	9 (64.3)

Table 3 Regression of intestinal metaplasia by segment length

Segment length	Post-operative endoscopy completed	Barrett's esophagus present	Barrett's esophagus not present	Regression rate (%)
Ultra-short	29	5	24	82.8
Short	30	8	22	73.3
Long	8	6	2	25.0

DeMeester scores were more likely to have regression of intestinal metaplasia (Table 2).

Regression rates were examined by segment length group (Table 3). Patients with ultra-short segment disease were most likely to have disease regression followed by short segment. Long-segment disease was unlikely to regress. The 2 patients in the long-segment group that did have regression both had segment lengths of 3 cm.

To assess the possibility of sampling error, an additional subset analysis was performed by including only patients with more than 1 post-operative endoscopy. 34 patients had more than 1 post-operative endoscopy (17 patients with 2 endoscopies, 13 with 3 endoscopies, and 4 with 4 or more). The regression rate remained constant at 73.5%.

Discussion

The importance of understanding the effect of the LINX device on intestinal metaplasia has increased given its increasing prevalence and the emergence of reports of adenocarcinoma developing in patients that have had the device implanted [10]. Our study demonstrates that the regression rate of Barrett's esophagus in patients who have undergone magnetic sphincter augmentation with the LINX device is 72% at 1 year after surgery. Additionally, the regression rates of patients with ultra-short segment, short-segment, and long-segment disease are 85.7, 73.3, and 25.0% respectively.

Achieving regression of intestinal metaplasia is directly related to successfully decreasing acid exposure. In a study examining the feasibility of eradicating Barrett's esophagus with endoscopic therapies, over 200 patients were treated with a protocol involving radiofrequency ablation (RFA) and a standardized acid control program [11]. In an analysis performed on patients that did not achieve disease regression, those patients were more likely to have persistently abnormal pH testing (79.1% versus 6.3%). Our study corroborates this finding but follows magnetic sphincter augmentation. Patients who had normal post-operative DeMeester scores were more likely to have regression of disease. This is an important factor during post-operative surveillance as patients without adequate acid control are unlikely to have improvement of their disease. Re-initiation of medical therapy and investigation into possible surgical failure should be considered more aggressively.

The segment length of intestinal metaplasia has increasingly been accepted as representative of differing severity of reflux with long-segment Barrett's esophagus being associated with higher levels of acid and bile exposure [1]. Nevertheless, the risk of malignant transformation has been shown to be similar between the two groups [12]. In this study, patients with long-segment Barrett's esophagus were significantly less likely to have regression of disease. This is consistent with reports of outcomes following other forms of anti-reflux therapy [13, 14]. This not only has importance in patient counseling and establishing patient expectations, but should also influence the consideration for ablative therapies earlier on in the disease course.

This is the first study to demonstrate the efficacy of the LINX device in achieving regression of Barrett's esophagus. Previous studies in patients having undergone fundoplication have demonstrated regression of metaplasia, especially in patients with short-segment disease [2]. In a recent study examining the long-term effects of anti-reflux surgery, Knight et al. reported on the outcomes of 50 patients with 12 years of follow-up [3]. While most patients continued to have significant symptomatic improvement, 41% of patients had regression of their Barrett's esophagus. Longer-term studies are needed to make meaningful comparisons between the traditional fundoplication and the relatively novel LINX device. Perhaps most importantly, longer follow-up in patients treated with the LINX device will investigate its ability to prevent the progression to dysplasia and carcinoma, which has been established following fundoplication [15].

Compliance with ethical standards

Disclousres Nikolai Bildzukewicz and John C. Lipham—consultant for Torax Medical, Inc. Evan T. Alicuben, James M. Tatum, Kamran Samakar, Jamil S. Samaan, Einav N. Silverstein, Kulmeet Sandhu, and Caitlin C. Houghton have no conflict of interest or financial ties to disclose.

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