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Transoral incisionless fundoplication for gastroesophageal reflux disease in an unselected patient population

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Abstract
Background EsophyX is an endolumenal approach to the treatment of gastroesophageal reflux disease (GERD). This report describes one of the earliest and largest North American experiences with this device.
Methods Prospective data were gathered on consecutive patients undergoing EsophyX fundoplication for a 1-year period between September 2007 and March 2009. During this time, the procedure evolved to the current technique. A P value less than 0.05 was considered significant.
Results The study enrolled 26 patients with a mean age of 45 years. The patients included 16 women (62%) with a mean body mass index (BMI) of 28 and an American Society Anesthesiology (ASA) classification of 2. These patients included 11 with associated small hiatal hernias, 3 with Barrett's esophagus, and 5 with esophageal dysmotility. The procedure time was 65 min (range, 29–137 min), and the length of hospital stay was 1 day (range, 0–6 days). The postoperative valve circumference was 217°, and the valve length was 2.7 cm. Two complications of postoperative bleed occurred, requiring transfusion. The mean follow-up period was 10 months. Comparison of pre- and postoperative Anvari scores (34–17; $P = 0.002$) and Velanovich scores (22–10; $P = 0.0007$) showed significant decreases. Although 68% of the patients were still taking antireflux medications, 21% had reduced their dose by half. Three patients had persistent symptoms requiring Nissen fundoplication, and there was one late death unrelated to the procedure.
Conclusion This study represents an initial single-institution experience with EsophyX. According to the findings, 53% of the patients had either discontinued their antireflux medication (32%) or had decreased their dose by half (21%). Both symptoms and health-related quality-of-life (HRQL) scores significantly improved after treatment. Further follow-up evaluation and objective testing are required.

Keywords EsophyX · Gastroesophageal reflux disease (GERD) · Transoral incisionless fundoplication

Gastroesophageal reflux disease (GERD) affects millions of Americans, significantly impairing their quality of life. According to recent surveys, the most common and debilitating symptoms are heartburn, regurgitation, and dysphagia [1]. These can be attributed to a physiologic defect in the lower esophageal sphincter, allowing acidic gastric contents to reflux into the stomach. As a chronic condition, GERD can go undiagnosed for years and may lead to other conditions such as esophagitis, Barrett's esophagus, and esophageal carcinoma [1–3].

Medical treatments in the form of antacids, H_2 blockers, and proton pump inhibitors (PPIs) are readily available over the counter and often are initiated by the patient before aid from a physician is sought. Although lifestyle modifications and medical treatment have been shown to improve patient symptoms significantly, the impaired physiology behind GERD is not addressed, and patients are

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therefore susceptible to recurrence of disease [3]. Patients seeking surgical treatment have significantly impaired quality of life and often are dependent on daily use of pharmacologic therapy. These patients seek a long-term solution to their debilitating symptoms.

The primary goal of surgical therapy is to restore the natural antireflux valve impaired in many patients with chronic GERD [4]. Laparoscopic Nissen fundoplication accomplishes this by recreating a new gastroesophageal valve (GEV) and currently is the procedure of choice for antireflux surgery. Nissen fundoplication achieves symptom relief for more than 90% of the patients studied, together with normalization of the resting lower esophageal sphincter pressure and esophageal pH [5, 6].

Endoscopic therapies for GERD attempt to decrease surgical morbidity and complications by offering a less invasive procedure. This has been the driving force for the studies investigating a host of potential endolumenal therapies for GERD. These therapies offer the potential benefit of a surgical repair for the GEV, with lower morbidity and no abdominal scars.

The most recent U.S. Food and Drug Administration (FDA)-approved endolumenal device for treatment of GERD is the EsophyX (EndoGastric Solutions, Inc., Redmond, WA, USA). This device creates a transoral incisionless fundoplication. EsophyX deploys multiple full-thickness serosa-to-serosa fasteners into the gastric wall to form an interrupted suture line at the base of the gastroesophageal (GE? junction, thus recreating the GEV mechanically. Cadière et al. [4, 7] have shown EsophyX to be safe and effective in humans at 12 months. They have demonstrated more than 50% improvement in GERD health-related quality-of-life (HRQL) scores for 73% of patients, with 85% discontinuation of PPI use [4, 7].

We first published our initial experience with EsophyX for eight patients in 2008 [8]. This current study aimed to investigate further the safety and efficacy of EsophyX in a larger patient population. The technique and the instrument continue to evolve, and this report reviews the outcomes of this novel procedure in a single-institution North American center.

This study had two primary objectives: (1) to demonstrate the feasibility and safety of EsophyX in an unselected patient population and (2) to evaluate symptom severity using the Anvari scale, improvement in HRQL using the Velanovich scale, and cessation of medication use.

Materials and methods

Patient selection

Patients referred for surgical management of GERD were given the option of undergoing endolumenal fundoplication. The risks, benefits, and alternatives of the procedure were explained to the patient. The patient who then chose endolumenal fundoplication was entered into a prospective database. The research protocol was approved by the Ohio State University Institutional Review Board (IRB #2007H0292). When necessary, supplemental retrospective chart review was performed.

The inclusion criteria for endolumenal fundoplication specified patients 18–80 years old with documented GERD who had received PPI treatment for more than 6 months with normal or reduced manometry. The exclusion criteria specified a body mass index (BMI) greater than 40, grade D esophagitis, pregnancy, or moderate to large hiatal hernias (>3 cm). All the patients underwent a routine antireflux surgery workup including endoscopy, pH studies, and a video esophagram. Esophageal manometry was performed when indicated by symptoms or an abnormal video barium esophagram.

Technique

Our technique, modeled after that of Cadière et al. [9], has been described elsewhere [8]. Briefly, the patient is placed in the left lateral decubitus position after undergoing nasotracheal intubation. After an initial upper endoscopy has been performed, the EsophyX device is passed over a standard gastroscope into the stomach. A helical retractor is screwed into the gastric wall distal to the gastroesophageal junction and then retracted into the device. Next, the device is withdrawn slightly, and polypropylene fasteners are fired, creating a full-thickness apposition of the gastric wall above the GE junction. The device is rotated over an axis of 200°–300° to create a new GE junction valve over a length of 2–3 cm. Patients were routinely admitted overnight and discharged the next day.

Data collection and analysis

During the fundoplication, procedural findings and results were recorded. Patients were seen in the clinic for follow-up assessment after 2–4 weeks. A history, physical examination, and review of symptoms and medication use were performed. Data are expressed as mean ± standard deviation. A P value less than 0.05 was considered significant. Data analysis was performed with SPSS 11 (SPSS, Chicago, IL, USA).

The primary outcome measurement was self-reported symptom severity using the Anvari scale [10] and HRQL using the Velanovich score [11]. These scores were derived preoperatively and 3 months postoperatively. Medication use and overall patient satisfaction also were recorded. Follow-up phone calls were performed every 3 months to reevaluate medication use and patient satisfaction.

Results

The study enrolled 26 consecutive patients. Three of these patients were lost to follow-up evaluation, and one patient withdrew from the study (had a complication). Follow-up data were complete for the remaining 22 patients (84%). The mean follow-up period was 10 months.

Patient demographics and procedural data are shown in Table 1. Among the patients, 11 had associated small hiatal hernias, 3 had biopsy-proven Barrett's esophagus, 5 had esophageal dysmotility, and 1 had an esophageal stricture dilated preoperatively.

One patient died of a drug overdose unrelated to the procedure a few months after the operation. Procedural complications occurred for two patients. The one was an 18-year-old woman with cystic fibrosis had undergone remote Nissen fundoplication at the age of 6 months, and the other was a 43-year-old woman. Both were noted to be tachycardic the evening after their procedure. Both were transfused and underwent upper endoscopy. Their hospital lengths of stay were respectively 3 and 6 days.

Three symptomatic failures occurred in this group. One patient had early postoperative vomiting and then a recurrence of his heartburn. Upper endoscopy showed more than a 50% loss of his fasteners and a loss of postprocedure valve geometry. This patient underwent Nissen fundoplication 6 months after his initial procedure. Another patient had persistent symptoms at the 1-month follow-up assessment. This patient underwent Nissen fundoplication 6 months after endolumenal fundoplication. Laparoscopic examination demonstrated a portion of the fundus tacked to the GE junction, but the wrap was less than 180°. The final patient had excellent results for 2 weeks, then had a sudden reappearance of his symptoms. Upper endoscopy showed that the fasteners had broken through the fundoplication. The patient subsequently underwent Nissen fundoplication at an outside institution.

Table 1 Patient demographics and procedural data

Demographics	
n	26
Age (years)	45 ± 15
BMI	28 ± 5
ASA	2 ± 1
Females	16 ± 62
Procedural data	
Time (min)	65 ± 27
Length of stay: days (range)	1 (0–6)
Valve circumference (°)	217 ± 31
Valve length (cm)	2.7 ± 0.6

Data displayed as mean ± standard deviation unless otherwise indicated

BMI body mass index, *ASA* American Society of Anesthesiology

Table 2 Preoperative versus postoperative changes

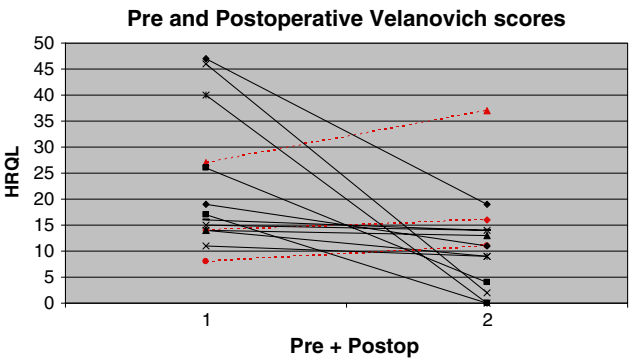
	Preoperative	Postoperative	*P* value
HRQL (Velanovich, 0–50)	22 ± 13	10 ± 7	0.0007
Symptom score (Anvari, 0–72)	34 ± 14	17 ± 15	0.002
Medication use (%)	100	68	

Data displayed as mean ± standard deviation unless otherwise indicated.

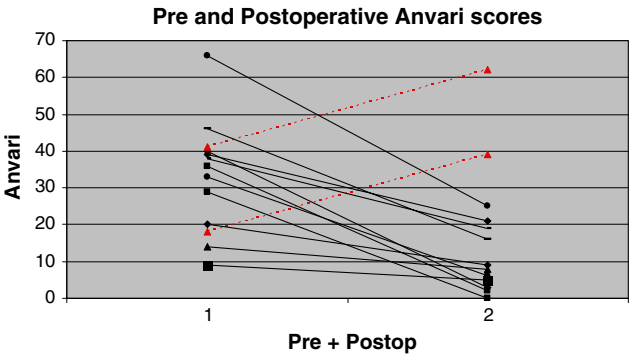
Note: lower scores indicate improved symptom scores

HRQL health-related quality of life

The mean HRQL and symptom severity scores were significantly improved at the 3-month follow-up assessment (Table 2). However, only 45% of the patients had more than a 50% improvement in HRQL. Graphs 1 and 2 demonstrate individual pre- and postprocedure HRQL and Anvari scores. Follow-up telephone interviews showed that 68% of the patients still were taking PPIs (Table 2). Of the patients still taking PPIs, 31% had decreased the dose by half. At a mean of 10 months after EsophyX, 45% of the patients were satisfied with the procedure, 25% were neutral, and 30% were dissatisfied.



Graph 1 Pre- and postoperative Velanovich scores



Graph 2 Pre- and postoperative Anvari scores

Many of the patients reported a sore throat and left shoulder pain on postoperative day 1, which resolved within the first postoperative week. Two patients also reported sharp chest pain the first week after the procedure, prompting a cardiac workup, which was normal in both cases. One other patient was readmitted on postoperative day 3 with nausea and vomiting. Diagnostic test results were normal, and the patient was rehydrated then discharged.

Discussion

Patients, endoscopists, and surgeons have been excited by the prospect of an outpatient antireflux procedure. An incisionless procedure with less morbidity than a surgical technique would have numerous patient and physician benefits. Many purported endolumenal antireflux devices have been developed over the past 15 years. Unfortunately, most of these devices have not demonstrated clinical effectiveness, or the companies have not demonstrated financial viability [12].

Endolumenal therapies for GERD include radiofrequency energy delivered to the lower esophageal sphincter (Stretta; Curon Medical Inc, Fremont, CA, USA), plication techniques using such devices as the Endocinch (Endocinch; C.R. Bard, Inc., Murray Hill, NJ, USA) and the NDO Plicator (NDO Surgical, Mansfield, MA, USA), and injectable prosthetics such as Gatekeeper (Endonetics, San Diego, CA, USA) and Enteryx (Boston Scientific, Boston, MA, USA) [3, 7].

Most of these devices have poor long-term data, and none are currently marketed. Investigation of the Endocinch device, an internal mucosa-to-mucosa plication, showed poor overall results [13]. The short-term results for the NDO Plicator, a serosa-to-serosa plication, were similarly disappointing [14, 15]. The Stretta procedure resulted in improved quality-of-life scores but did not decrease esophageal acid exposure or medication use at 6 months compared with a sham group [16]. Curon Medical has since filed for bankruptcy and ceased operations. Both the Gatekeeper and Enteryx manufacturers also have ceased operations and filed for bankruptcy.

EsophyX is a novel endolumenal device that attempts to mimic antireflux surgery by constructing a fundoplication at the gastroesophageal junction. The goal is to reduce any small hiatal hernia and restore the angle of His. This device differs from other endolumenal therapies by offering a mechanical fundoplication that uses multiple full-thickness fasteners. The fundoplication is a partial anterior fundoplication, usually ranging from 200° to 300° over a length of 2–3 cm. This device was demonstrated to be safe in an initial feasibility study of 17 patients [17]. The most common side effects were left shoulder pain, sore throat, abdominal pain, and nausea. These resolved within the first 2 weeks.

The initial efficacy of the device then was demonstrated in a European multicenter trial of 84 patients [7]. This study showed that 67% of the patients were not using any PPI medication at the 12-month follow-up assessment. A clinically significant improvement in GERD-HRQL was achieved for 73% of the patients, but 20% were dissatisfied with their health condition. Acid exposure was reduced for 61% of the patients but normalized for only 37%. Serious adverse events consisted of two esophageal perforations during device insertion and one case of postprocedure bleeding requiring blood transfusion and endoscopy.

The 2-year follow-up data on 14 patients from this study have recently been published [17]. Of the 17 patients who were more than 2 years post-EsophyX, 2 had undergone retreatment (Nissen, repeated EsophyX) and 1 patient had been lost to follow-up evaluation. Of the remaining 14 patients, 71% were not taking any PPI medication, and 59% had improvement compared with their baseline GERD-HRQL values. Esophagitis was eliminated for 55% of the patients. Global assessment showed a cure for 29% of the patients and remission for 50% of the patients 2 years after EsophyX.

Clinical effectiveness in this current study was demonstrated by the fact that HRQL and symptom severity scores were significantly improved with EsophyX. However, a large percentage of patients (68%) still were taking PPI medication. Of these patients, 31% had halved their dose, whereas the remaining 69% were back to their preoperative PPI dose. Three treatment failures occurred, ultimately leading to Nissen fundoplications. These failures occurred in the first half of our experience for patients 8, 9, and 14. Early postoperative vomiting may dislodge the fasteners and result in treatment failure.

These data differ from those in the Cadière et al. [7] study, which demonstrated that only 33% of patients were taking PPI medication after their procedure. The superior results of Cadière et al. [7] may be due to this group's larger experience with the device and stricter patient selection criteria. The current study was undertaken with a relatively unselected patient population that included patients with esophageal dysmotility ($n = 5$), esophageal stricture ($n = 1$), and atypical symptoms. Our population also included a patient who had cystic fibrosis and previous Nissen fundoplication. The patient population studied by Cadière et al. [7] had a lower BMI (mean BMI, 25 vs 28) and a lower percentage of female patients (34 vs 62%). The results from the current study may demonstrate results more generalizable to the average patient population seeking surgical treatment for GERD. Further analysis of our data (including age, BMI, presence of hiatal hernia,

presence of Barrett's esophabus, dysmotility, and preoperative pH score) did not show any other predictors of failure.

The second objective of this study was to evaluate device safety. We experienced two significant postoperative bleeds requiring transfusion and endoscopic therapy. Neither of these complications was recognized at the time of the procedure. We did not experience any esophageal perforations as reported by Cadière et al. [7]. The possibility of bleeding or perforation is not insignificant, as demonstrated by these findings. We recommend caution with device insertion, especially in small or thin patients, and removal of the device should always be performed under endoscopic visualization.

A major limitation of this study was the lack of postoperative pH testing for the patients. There has been much criticism of endoscopic therapies for GERD, and direct comparisons with Nissen fundoplication have not been undertaken. Furthermore, most studies have not made comparisons with a sham control population, which is critical because GERD is associated with a placebo response of 25–50% [12, 18]. Routine postoperative pH studies and endoscopy would allow for better assessment of clinical effectiveness. Furthermore, complete follow-up data were lacking for four patients (16%).

In conclusion, this early report describes one of the largest North American single-institution experiences with EsophyX. The patient population was referred to surgical practice, and the data represent outcomes for patients with poor control of symptoms. Although this is in contrast to many other studies of GERD patients, it represents a more realistic sampling of patients who desire surgical management of their GERD. Although HRQL and symptom severity scores show significant improvement, few patients are cured, as demonstrated by the high proportion of patients still requiring PPI medication. Further study with pH testing and endoscopic evaluation of the neovalve are required. Increased experience will help to identify the patient population most likely to benefit from transoral incisionless fundoplication compared with other treatments.

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