Endoscopic Reflux Treatments

15

Jeffrey D. E. Hawel and James C. Ellsmere

Introduction

The prevalence of gastroesophageal reflux disease (GERD) in Western countries ranges from 10% to 20% of the population [1]. Of those who suffer from GERD, as many as 40% will not respond to medical treatment [2]. Furthermore, the adverse effects of long-term proton pump inhibitor (PPI) use are not insignificant. Laparoscopic fundoplication offers improvement in control of symptoms and quality of life but comes with need for general anesthesia, surgical incisions, and risks inherent to any laparoscopic procedure. Symptom recurrence postlaparoscopic fundoplication can occur. Typically this requires reintroduction of PPI or sometimes revisional surgery. There is emerging data that endoscopic solutions can provide less invasive alternative therapies to treat GERD.

Endoscopic devices developed to treat GERD have been used since 2001 [3]. Several different approaches have been employed that alter the gastroesophageal junction to decrease reflux, namely, (i) implantation of prostheses to narrow the lumen, (ii) radiofrequency (RF) energy to induce remodeling, and (iii) sutured fundoplication. Devices designed to implant prostheses at the GEJ are no longer on the market largely because of rare but serious complications. Three endoscopic devices currently have FDA approval – Stretta®, EsophyX™, and MUSE™ – and are discussed below in further detail. A summary of these devices and their predecessors is outlined in Table 15.1.

J. D. E. Hawel · J. C. Ellsmere (✉)
Department of General Surgery, Dalhousie University, Halifax, NS, Canada
e-mail: jellsmer@dal.ca

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Table 15.1 Summary of endoscopic devices for the treatment of reflux disease

Device	Company	Method of action
FDA approved		
Stretta®	Mederi Therapeutics	RF delivery to the LES to promote remodeling and hypertrophy of the muscle
EsophyX™	EndoGastric Solutions	Transoral incisionless fundoplication using full-thickness polypropylene H-fasteners
MUSE™ system	Medigus Ltd.	Transoral incisionless fundoplication using a full-thickness stapling device under EUS guidance
No longer available		
EndoCinch	Bard	Partial-thickness sutured gastroplication
Enteryx	Boston Scientific	Injectable biocompatible polymer implant at the LES
Gatekeeper	Medtronic	LES submucosal implantation of hydrogel prosthesis
NDO Plicator	NDO	Full-thickness plication of the GEJ

Stretta® (Mederi Therapeutics)

The Stretta® procedure delivers radiofrequency (RF) energy to the lower esophageal sphincter (LES). Reflux is felt to be improved as a result of subsequent remodeling and thickening of the LES, leading to a reduction in compliance and an increase in basal pressure.

Stretta® can be safely used in patients with large hiatal hernias (>3 cm), short segment Barrett's esophagus, or even prior fundoplications [4, 5]. Erosive esophagitis should be treated medically until healed prior to performing Stretta.

The procedure begins with upper endoscopy to identify the location of the gastroesophageal junction. The RF delivery catheter, composed of four nickel-titanium treatment elements distributed radially around a balloon, is then delivered and positioned 2 cm proximal to the squamocolumnar junction. After insufflation of the balloon, the treatment elements are deployed 1–2 mm into the LES muscle to deliver the thermal treatments (Fig. 15.1). Temperature and impedance are measured along each treatment element by a RF generator system, and chilled water from the catheter irrigates the esophageal mucosa to prevent injury. Additional treatment sets are performed by rotating the catheter 45° and varying its linear position. A total of 15–25 treatment sets are created in most patients [4, 5].

A systematic review and meta-analysis published in 2012 by Perry et al. showed that RF treatment resulted in statistically significant improvement in heartburn scores, quality of life as measured by GERD-health-related quality of life (HRQL) scale, and reflux and dyspepsia scores. LES average pressure increased from 16.5 mmHg to 20.2 mmHg following Stretta, while esophageal acid exposure decreased from a pre-procedure DeMeester score of 44.4–28.5 post-procedure [6].

In line with these findings, the Stretta® procedure received strong recommendation in guidelines from SAGES, who considered it "appropriate therapy for patients being treated for GERD who are 18 years of age or older, who have had symptoms of heartburn, regurgitation, or both for 6 months or more, who have been partially or completely responsive to antisecretory pharmacologic therapy, and who have declined laparoscopic fundoplication" [7].

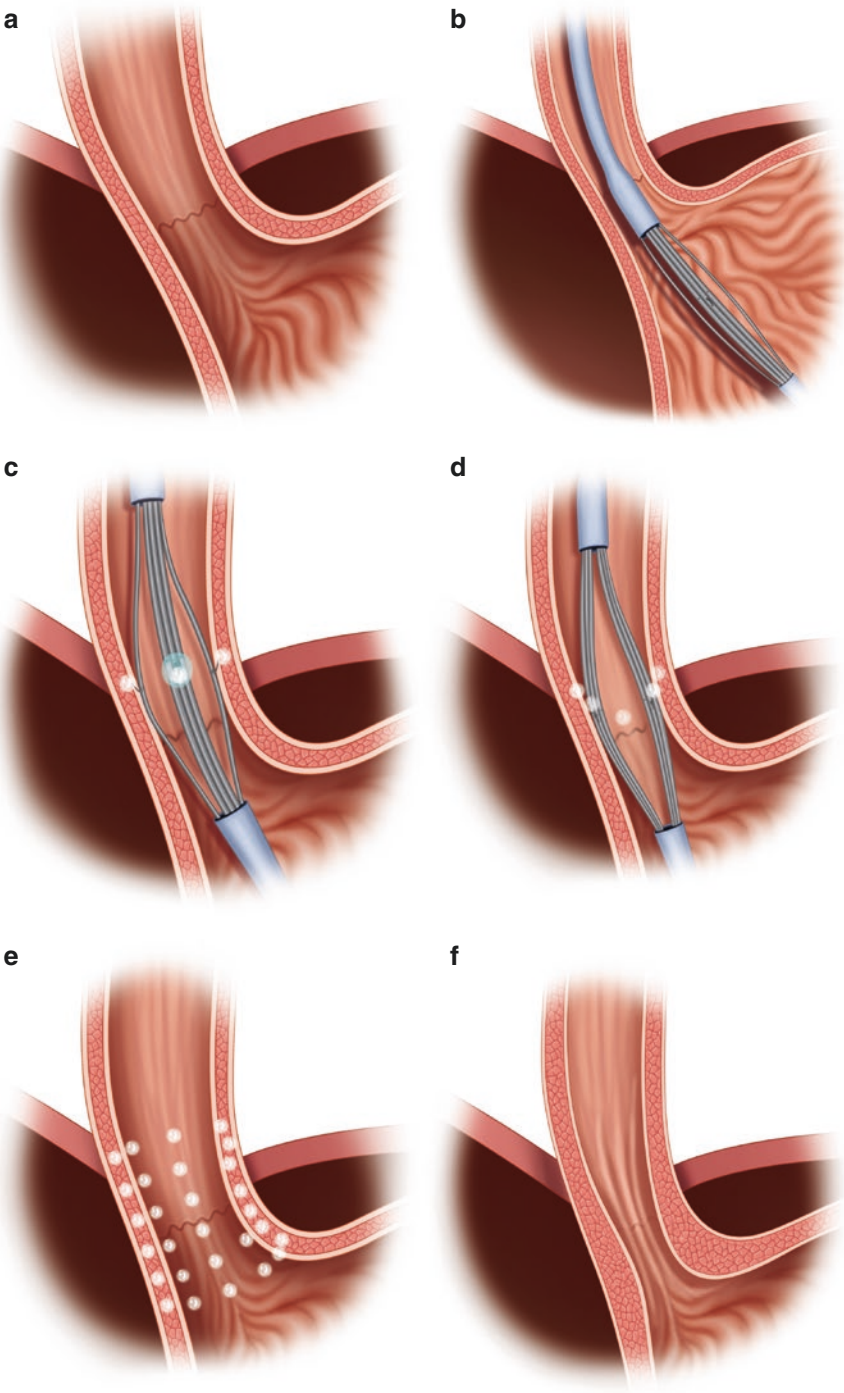

Fig. 15.1 Stretta® radiofrequency modulation of the GEJ. (**a**) Lower esophageal sphincter (LES) zone pretreatment. (**b**) Catheter insertion. (**c**) Initial axial burn. (**d**) Second axial burn; 45 °C burn. (**e**) Completion of RF treatments (eight per axial level) above/below gastroesophageal junction (GEJ). (**f**) LES zone posttreatment

However, the conclusions drawn by prior reviews were criticized for methodological error. This led to a subsequent rigorous systematic review and meta-analysis by Lipka et al. [8]. In this study, the outcomes assessed included: time the pH < 4 over 24 hours, lower esophageal sphincter pressure, ability to stop PPIs and HRQL. The pooled results of this study showed no difference when comparing Stretta to either sham or management with PPIs in patients with GERD.

An important consideration in reflux treatments, and indeed where many endoscopic therapies lack evidence, is long-term outcomes. Noar et al. recently published their 10-year data on 99 patients. Included in the trial were patients with previous fundoplication or large (>3 cm) hiatal hernias. Stretta showed durability and safety, with 72% of patients achieving normalization of GERD-HRQL scores. At 10 years, 23% of patients eliminated medical treatment entirely, and 41% of patients were off PPIs and taking no regular medical therapy. There were no major complications. Patients who initially partially respond are able to safely undergo repeat procedures to achieve maximal response, as was seen in 11 patients in the study [5].

Described serious adverse events associated with Stretta® in the US FDA maintained database are rare but include pneumonia, gastroparesis, esophageal perforation, cardiac arrest, and death [8]. Up to 50% of patients, however, have minor transient side effects following the procedure, the most common of which are chest discomfort and dyspepsia.

EsophyX™ (EndoGastric Solutions)

The EsophyX™ device was designed to create a full-thickness gastroesophageal valve, via transoral incisionless fundoplication (TIF). The initial TIF 1.0 technique created a 270°, 3 cm gastro-gastric plication centrally on the greater curvature at the squamocolumnar junction of the esophagus and the fundus. The TIF 2.0 creates a physiological valve via esophagogastric plication on the far posterior and anterior sides of the lesser curvature.

The technique is performed under general anesthesia with the patient in the left lateral decubitus position and can be completed in under an hour. Two endoscopists are required – one operates the device, while the other operates the endoscope to ensure proper exposure and continuous visualization throughout the entire procedure. The EsophyX™ device fits over a standard endoscope and is passed through the esophagus into the stomach. A helical screw is deployed and anchored into the fundus and used to draw gastric tissue into the device. Proprietary polypropylene H-fasteners are then delivered across the esophagus and gastric fundus to augment the valve (Fig. 15.2). Following completion of the procedure, the device is withdrawn, and endoscopy is repeated to evaluate the length and circumference of the newly created valve. Patients are usually admitted overnight for monitoring and discharged the following day [9].

The initial description of EsophyX™ (TIF 1.0) was published in 2008 by Cadiere et al. [9], and subsequent studies were small and observational in nature. However,

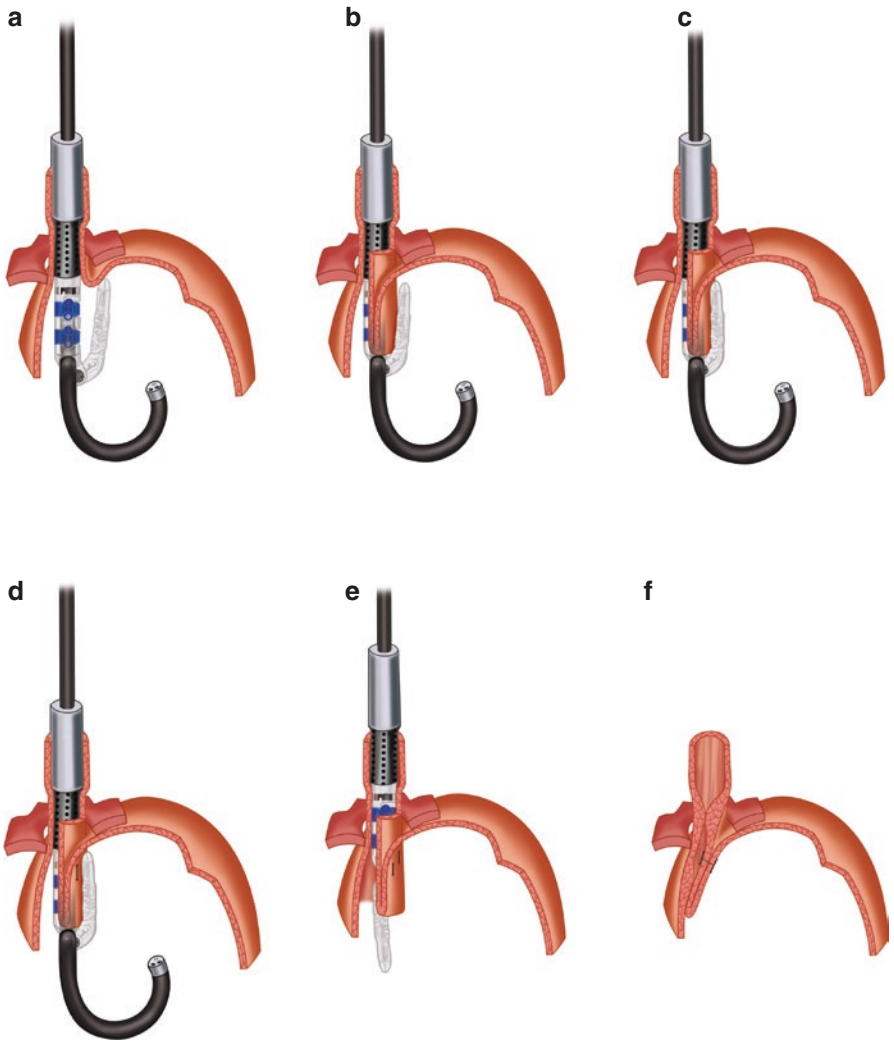

Fig. 15.2 EsophyX™ device for the creation of a transoral incisionless fundoplication. (**a**) Helix retractor engages fundus. (**b**) Fundus retracted. (**c**) Valve molded. (**d**) H-fasteners deployed. (**e**) Device retrieval. (**f**) Valve with serosa-to-serosa approximation below Z-line

five randomized control trials (RCTs) were published between 2014 and 2015, all of which studied the TIF 2.0 device. In 2016, Huang et al. summarized the available literature for EsophyX™ in their systematic review and meta-analysis. In their analysis of available RCTs, TIF was comparable with PPI therapy and showed improvement over sham groups with respect to esophageal acid exposure time. A significant reduction in total number of reflux episodes was seen following TIF in comparison

to groups who did not undergo fundoplication. There was no significant difference in the incidence of acid reflux episodes compared to patients taking PPIs. In the observational studies, most patients eventually resumed PPIs in long-term follow-up; however, dosages generally were reduced. Weighted average rate of satisfaction with the procedure was 69.15% [10].

In this same systematic review, severe adverse events were seen in 2.4% of patients – 19 events in a total of 781 patients who underwent TIF. Severe adverse events included seven perforations, five cases of post-TIF bleeding, four cases of pneumothorax, one requiring intravenous antibiotics, and one involving severe epigastric pain. One death was reported 20 months after TIF [10].

MUSE™ System (Medigus Ltd.)

The Medigus Ultrasonic Surgical Endostapler (MUSE™) system combines a flexible video gastroscope with ultrasonography and a stapler mechanism. Similar to EsophyX™, it aims to create an endoscopic fundoplication, although a few key differences are present. First, ultrasound visualization ensures proper alignment of the anvil at the tip of the stapler cartridge on the shaft before firing. Second, staples are utilized rather than sutures, with the idea of creating a more permanent, true fundoplication.

The operator inserts the endoscope and retroflexes in the stomach. The top of the fundus is engaged with the tip of the endoscope and brought against the shaft of the endoscope, where the stapler cartridge is located (Fig. 15.3). The anvil and cartridge are aligned and locked by means of two pins that penetrate across the walls of the stomach and esophagus. A series of five staples arranged horizontally are fired. The staples are the same as those used for surgical gastrointestinal anastomoses. The scope is then rotated and the procedure repeated, thus creating a fundoplication of the anterior wall of the stomach [11].

Long-term clinical outcomes of 37 patients who underwent endoscopic fundoplication with the MUSE™ device were analyzed at baseline, 6 months, and 4 years post-procedure. At 6 months post-procedure, 83.8% remained off of PPIs. This dropped to 69.4% at 4 years. GERD-HRQL scores (off PPI) were significantly decreased. Significant reductions in the PPI dose required for patients who had resumed PPIs were also noted and were preserved at 4 years. Larger studies with sham control groups are awaited [12].

The most common adverse events reported were chest pain in 22% and sore throat in 21% of patients in the series from Zacherl et al. There were two severe adverse events in the series. The first presented with empyema and pneumothorax 3 days post-procedure and was managed with chest tube and antibiotic therapy. The second patient presented with an upper gastrointestinal hemorrhage 8 days post-procedure, requiring two-unit blood transfusion. Endoscopy did not reveal the source of the bleeding [13].

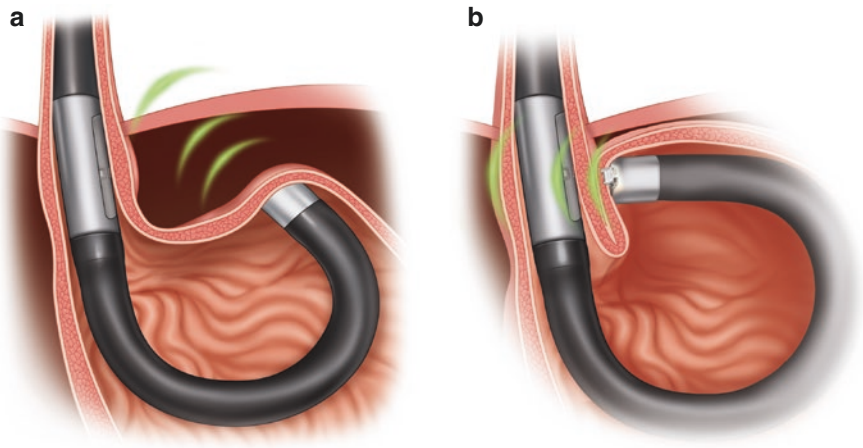

Fig. 15.3 MUSE™ System for the creation of an ultrasound-guided stapled fundoplication

Summary

Endoscopic therapies for GERD continue to evolve to meet patient needs. The goal is an effective mechanical solution that can be delivered with minimal morbidity and excellent long-term durability. There has been much progress over the last decade. Currently available devices – Stretta®, EsophyX™, and MUSE™ – have been shown to be safe and effective in improving symptom control and quality of life and offer a well-established alternative to laparoscopic interventions.

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