Endoscope-based Treatments for Gastroesophageal Reflux Disease

Summary

- Endoscope-based products for the treatment of more severe forms of gastroesophageal reflux disease provide an alternative to the use of drugs or surgery.
- Results from case series have shown that selected patients benefit through relief of symptoms and reduction of medication. Reported adverse effects appear to be minor.
- Efficacy has been mostly assessed over short periods and there is little information on comparison with other treatments.
- Procedural skills and appropriate training in their use are required.
- These technologies are promising, but their place in health care is not established.

The Technologies

Gastroesophageal reflux disease (GERD) is a common, chronic condition that occurs when the lower esophageal sphincter is relaxed, allowing the contents of the stomach to flow back into the esophagus. Possible complications of chronic GERD include esophagitis, Barrett’s esophagus and esophageal adenocarcinoma. Patients with severe GERD are treated with drugs or by surgery. Alternative technologies delivered via an endoscope have become available for the treatment of GERD (Table 1). These are intended for use in a hospital or clinic setting as outpatient procedures.

Table 1: Recent endoscope-based technologies for treatment of GERD

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Principle of Operation</th>
</tr>
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<tbody>
<tr>
<td>EndoCinch™</td>
<td>C.R. Bard, Inc.,</td>
<td>Suturing system used to create pleat near lower esophageal sphincter (process known as gastroplication)</td>
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<tr>
<td></td>
<td>Billerica MA US</td>
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<tr>
<td>Stretta™</td>
<td>Curon Medical Inc.,</td>
<td>Delivery of radio frequency energy to smooth muscle of gastroesophageal junction</td>
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<td></td>
<td>Sunnyvale CA US</td>
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</tr>
<tr>
<td>Enteryx™</td>
<td>Boston Scientific, Inc., Natick MA US</td>
<td>Solution of ethylene-vinyl alcohol copolymer injected into wall of lower esophagus, under fluoroscopic visualization; copolymer solidifies into spongy material as solvent separates</td>
</tr>
<tr>
<td>Gatekeeper™</td>
<td>Medtronic, Inc.,</td>
<td>Placement of prostheses made from polyacrylonitrile-based hydrogel in distal esophagus; prostheses are dry when inserted and expand upon contact with moisture</td>
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<tr>
<td></td>
<td>Minneapolis MN US</td>
<td></td>
</tr>
<tr>
<td>Plicator™</td>
<td>NDO Surgical Inc.,</td>
<td>Full-thickness plication device secures tissue at gastroesophageal junction</td>
</tr>
<tr>
<td></td>
<td>Mansfield MA US</td>
<td></td>
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</tbody>
</table>

Regulatory Status

The EndoCinch™ Suturing System received licensing approval from Health Canada in 2001 and marketing approval from the US Food and Drug Administration (FDA) in March 2000. The Stretta System received approval for US marketing from the FDA in April 2000. Enteryx was approved by the FDA in April 2003 for use in patients with GERD symptoms who require and respond to certain medications. Use of the Medtronic Gatekeeper has been limited to selected centres in Europe (Vern Dale-Johnson, Medtronic of Canada, Mississauga, ON: personal communication, 2003 June 16). The Plicator system received FDA approval in April 2003.
Patient Group

The endoscope-based technologies have been used for selected patients with chronic heartburn or regurgitation who regularly require antisecretory drug therapy. In studies undertaken to date, non-eligible patients have included those with a hiatus hernia larger than 2 cm; dysphagia; active grade III or IV esophagitis; Barrett’s esophagus; esophageal stricture or varices; high grade dysplasia or cancer; or previous gastric-thoracic surgery.

Current Practice

Moderate to severe forms of GERD may be treated with drugs, most commonly proton pump inhibitors (PPIs). In cases where the symptoms are refractory to PPIs or where the patient does not wish to continue with drug treatment, an accepted alternative is laparoscopic or open fundoplication.

The Evidence

Most studies on the safety and efficacy of the technologies have come from prospective case series, with outcomes being compared to health and quality of life measures obtained before the intervention, while the patients were off PPIs.

EndoCinch: In a series of 22 patients, at 12 months after the procedure, mean symptom, regurgitation and normalized quality of life (QOLRAD) scores had improved from those at baseline. All patients were initially on PPIs; the proportion decreased to 33% at six months and was 40% at 12 months. There was, however, no significant change at 12 months in the esophageal acid exposure time (the proportion of time with pH<4). Plications were undone at three months in five patients. The corresponding value at 12 months is not reported. A case-control study (n=27 in each group) found that 78% of persons who had endoscopic gastroplasty and 96% who had laparoscopic fundoplication were satisfied with their symptomatic outcomes at six weeks post-procedure. There was no significant difference (NSD) in median symptom scores.

Stretta: A sham-controlled randomized controlled trial (RCT) found that active treatment statistically significantly (SS) improved patients’ symptoms and quality of life. The effects persisted 12 months after treatment. At six months, however, there was no NSD between the groups in their daily medication use or in esophageal acid exposure time.

Twelve-month follow-up data for 94 of 118 patients enrolled in an open-label trial showed improvements from baseline values for median heartburn score and GERD scores, satisfaction, mental and physical subscales for the SF-36 instrument and esophageal acid exposure (p=0.0001 for all differences). In a series of 20 patients, there was a change in esophageal acid exposure from 10.6% at baseline to 6.8% at six months and 6.3% at 12 months.

Several groups have reported reductions in the proportion of patients taking PPIs. Values ranged from 88% to 100% at baseline, 16% to 35% at six months and 30% to 35% at 12 months.

Enteryx: In a series of 81 patients followed to 12 months after treatment, PPI use was eliminated in 70% and reduced by >50% in another 10% Quality of life scores using the GERD-HRQL survey and the SF-36 were comparable to those obtained during PPI use before implantation. Esophageal acid exposure time was SS reduced, although endoscopically assessed esophagitis grades were unchanged. Nineteen patients underwent repeat implantation because of inadequate therapeutic response. Similar results for reduction in PPI use were reported by Costamagna et al.

Gatekeeper: For 40 patients enrolled in an uncontrolled multicentre study, heartburn and regurgitation scores were SS improved at one month (n=35). This was maintained at six months (n=14).

Plicator: In a multi-centre study, 64 patients, 59 of whom needed daily PPI treatment, underwent endoscopic plication. Results for 41 of the patients at six months post-procedure showed improvement in mean off-medication GERD-
HRQL scores, which were superior to baseline on-medication HRQL scores. Thirty-four of the 41 patients remained off daily PPI therapy at six months.

**Adverse Effects**

In the multi-centre study of EndoCinch, most adverse effects were procedural rather than device-related. Of the 26 patients in the study by Mahmood et al., two had significant bleeds, requiring overnight observation and one had a mucosal tear.

In an open-label study on Stretta, the complications that occurred in 10 of 118 patients were all acute and self-limiting.

No serious adverse effects with Enteryx were reported. There were two serious adverse events in the first 490 humans treated with Gatekeeper (pharyngeal perforation and post-prandial nausea). The design of the delivery system has since been changed.

In the study on the Plicator system, the most common adverse event was pharyngitis (41%), which spontaneously resolved within several days post-procedure.

**Cost**

The US price per procedure of Stretta, including pre-treatment testing, is estimated by the manufacturer as US$3,000 to US$4,000. Advice to a health care organization indicated that the capital cost of the Stretta system in the US was US$24,200. The manufacturer estimates the cost per procedure in the US with the EndoCinch system is approximately US$3,000. No cost information is yet available for the other products covered in this bulletin.

**Rate of Technology Diffusion**

There has been increasing use of EndoCinch and Stretta, particularly at major centres in the US, but evidence on their effectiveness is still limited. The rate of diffusion of endoscope-based treatments will be influenced by longer term evidence of safety and benefit, their applicability to patients with severe complications or co-morbidities and developments in alternative technologies.

**Concurrent Developments**

Other endoscopic technologies for GERD have been tested in pilot studies. A further endoscopic sewing system, The Sew-Right Device, has been developed, but it does not have FDA approval for use in an anti-reflux application. Partial fundoplications are as effective as complete fundoplications and have fewer complications. An endoscopic fundoplication approach, using a flexible video gastroscope combined with a stapler mechanism, is under development.

**Implementation Issues**

There is still little information on these products in comparison with other treatments and no studies that compare different endoscope-based technologies. Efficacy and safety have been mostly assessed over short periods. The promotion of the widespread introduction of such techniques in the absence of controlled studies and of long-term follow-up has been criticized. Most trials have excluded patients with esophagitis and other conditions. Reduced PPI use in a high proportion of patients is an important benefit, though acid exposure returns to normal in only half of those treated. Cost-effectiveness is not yet established. Any implementation of these technologies would need to take account of the required learning curve and make use of available training programs.

The use of these technologies may be most appropriate in tertiary care hospitals until they have been accepted as routine treatments.

**References**


12. Johnson DA, Ganz R, Aisenberg J, Cohen LB,

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