Endoluminal gastroplication for gastro-oesophageal reflux disease

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Assessment report

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The Medical Services Advisory Committee is an independent committee which has been established to provide advice to the Commonwealth Minister for Health and Ageing on the strength of evidence available on new and existing medical technologies and procedures in terms of their safety, effectiveness and cost-effectiveness. This advice will help to inform Government decisions about which medical services should attract funding under Medicare.

This report was prepared by the Medical Services Advisory Committee with the assistance of Sally Wortley and Kirsten Howard from the NHMRC Clinical Trials Centre and the MSAC Supporting Committee on Endoluminal Gastroplication. The report was endorsed by the Commonwealth Minister for Health and Ageing on 26 June 2002.

Publication approval number: 3077

MSAC recommendations do not necessarily reflect the views of all individuals who participated in the MSAC evaluation.

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Endoluminal (endoscopic) gastroplication (ELGP) is a minimally invasive treatment for gastro-oesophageal reflux disease (GORD). The procedure is done using a standard endoscope and an endoscopic sewing device such as the Bard® EndoCinch™ suturing device.

Medical Services Advisory Committee—role and approach

The Medical Services Advisory Committee (MSAC) is a key element of a measure taken by the Commonwealth Government to strengthen the role of evidence in health financing decisions in Australia. The MSAC advises the Commonwealth Minister for Health and Ageing on the evidence relating to the safety, effectiveness and cost-effectiveness of new and existing medical technologies and procedures, and under what circumstances public funding should be supported.

A rigorous assessment of the available evidence is thus the basis of decision making when funding is sought under Medicare. A team from the NHMRC Clinical Trials Centre was engaged to conduct a systematic review of literature on endoluminal gastroplication for gastro-oesophageal reflux disease. A supporting committee with expertise in this area then evaluated the evidence and provided advice to the MSAC.

MSAC's assessment of endoluminal gastroplication for gastro-oesophageal reflux disease

ELGP is a minimally invasive treatment for GORD. The procedure is done using a standard endoscope and an endoscopic sewing device such as the Bard® EndoCinch™ [1] Suturing System (BESS). The procedure works by creating plications, or pleats, at the lower oesophageal sphincter (LOS) and decreasing the reflux of stomach acid into the oesophagus. There are three main steps involved in the ELGP technique: suturing, knot tying and cutting. The procedure requires two video endoscopes and nine endoscope insertions to create a plication, with each patient typically undergoing two or three plications.

Clinical need

GORD is a common condition and one that can have a significant impact on the quality of life of individuals (Revicki et al 1998a). It is estimated that 15 to 20 per cent of adults in Australia experience heartburn once a week (Gastroenterological Society of Australia 2001).

[1] Bard® is a registered trademark and EndoCinch ™ is a trademark of Bard Australia Pty Ltd, or an affiliate.

In a report published by the Australian Institute of Health and Welfare (AIHW), the prevalence of upper gastrointestinal conditions in Australian general practice was estimated at 30.8 per cent of attendances, with reflux accounting for 12.5 per cent of these problems in 1998–1999 (Sayer et al 2000).

However, as prevalence data are based on symptomatology and reflux symptoms occur along a continuum of severity, prevalence figures vary substantially and should be considered in the context of additional information such as pharmacotherapy costs and services.

Data from the Australian Pharmaceutical Benefits Scheme (PBS) and the Repatriation Pharmaceuticals Benefits Scheme (RPBS) indicates that the costs of prokinetics, histamine receptor antagonists and proton pump inhibitors was $251 million in 1995-1996, increasing to $336 million in 2000–2001. This equates to more than 8 million services.

Safety

Limited evidence was available to assess the safety of endoluminal gastroplication in patients with gastro-oesophageal reflux disease. From the data provided in the one case-series paper it would appear that a minority of patients suffered adverse events six months after the procedure. Some of the adverse events may be explained by the limited experience of surgeons in performing the procedure. However, more data are needed before a decision can be made regarding the safety of the procedure in patients with gastro-oesophageal reflux disease.

Effectiveness

Data at six months follow-up, from the one case-series paper, indicate that endoluminal gastroplication may reduce some symptoms of GORD. However, the paucity of good quality data limits the ability to draw any conclusions regarding the efficacy of this procedure. Further research focusing on randomised trials is needed in this area.

Cost-effectiveness

There is a paucity of data on the effectiveness of ELGP beyond six months of follow up. While it appears that medication use at six months is reduced, the duration of this effect is unknown due to the limited amount of data available on this procedure. A comprehensive economic evaluation should be conducted on ELGP when there are sufficient data available to do so.

Recommendation

Since there is currently insufficient evidence pertaining to endoluminal gastroplication for gastro-oesophageal reflux disease, public funding should not be supported at this time for this procedure.

The Minister for Health and Ageing accepted this recommendation on 26 June 2002.

Introduction

The Medical Services Advisory Committee (MSAC) has reviewed the use of endoluminal gastroplication, an intervention for gastro-oesophageal reflux disease. The MSAC evaluates new and existing health technologies and procedures for which funding is sought under the Medicare Benefits Scheme in terms of their safety, effectiveness and cost-effectiveness, while taking into account other issues such as access and equity. The MSAC adopts an evidence-based approach to its assessments, based on reviews of the scientific literature and other information sources, including clinical expertise.

The MSAC's terms of reference and membership are at Appendix A. The MSAC is a multidisciplinary expert body, comprising members drawn from such disciplines as diagnostic imaging, pathology, surgery, internal medicine and general practice, clinical epidemiology, health economics, consumer health and health administration.

This report summarises the assessment of current evidence on endoluminal gastroplication for gastro-oesophageal reflux disease.

Background

Endoluminal gastroplication for gastro-oesophageal reflux disease

The procedure

Endoluminal (endoscopic) gastroplication (ELGP) is a minimally invasive treatment for gastro-oesophageal reflux disease (GORD). The procedure is done using a standard endoscope and an endoscopic sewing device such as the Bard® EndoCinch™ Suturing device System (BESS). The procedure works by creating plications, or pleats, at the lower oesophageal sphincter (LOS) and decreasing the reflux of stomach acid into the oesophagus. There are three main steps involved in the ELGP technique: suturing, knot tying and cutting. The procedure requires two video endoscopes and nine endoscope insertions to create a plication, with each patient typically undergoing two to three plications. The figures below are of the Bard® EndoCinch™ suturing device and demonstrate the gastroplication procedure.

The first step in the procedure is to insert one of the endoscopes into the oesophagus to confirm prior endoscopic findings. An oesophageal overtube is then placed over an oesophageal dilator with the dilator then removed and the overtube left in place (Figure 1).

The sewing machine device is then inserted into the mouth and through the overtube to just beyond the squamocolumnar junction (Figure 2). A fold of tissue is sucked into the cavity of the sewing capsule and a hollow needle is pushed through the sucked fold of tissue to create a 'tilt' stitch (Figure 3). The suction is then released, allowing the tissue through which the stitch has been placed to fall out of the device. Good suction is needed or it is possible that the machine may fail to place a full thickness suture. The device is then withdrawn, which pulls the running stitch through the gastric fold.

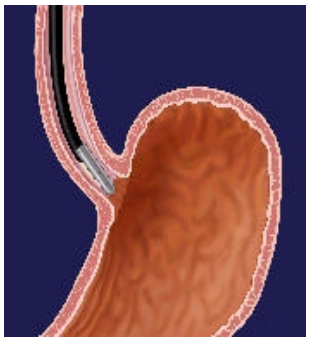

Figure 1

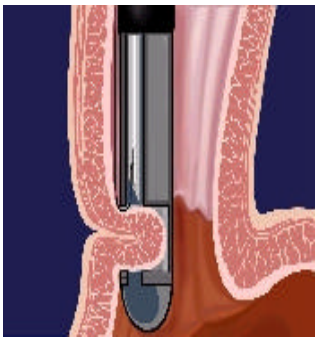

Figure 2

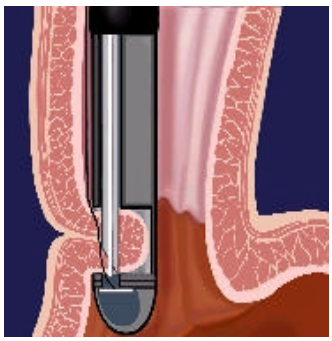

Figure 3

The device is then reloaded. A second stitch is placed at a location adjacent to the first. The same procedure is followed, which results in a suture that runs through two tissue bites and out of the oesophagus (Figure 4). Both ends of the running suture should be exiting from the patient's mouth. Half-hitches are tied extracorporeally outside the mouth.

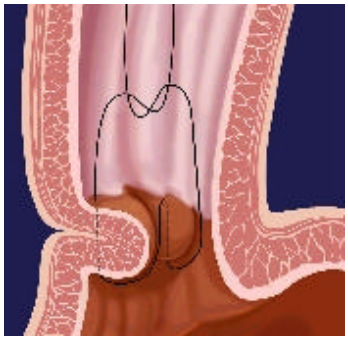

Figure 4

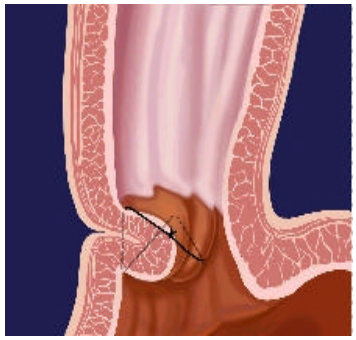

Figure 5

It is at this point that the second endoscope is introduced transorally with a knot pushing device to tie the knots. This device pushes the half-hitch throw in the suture down to the stitch location. The process of creating an extracorporeal half-hitch throw which is pushed down to the stitch location, is then repeated (Figure 5) until six alternating half-hitches have been delivered to the location and a plication has been created. Each plication takes at least eight passes (Raju 2001). The endoscope is removed and a suture cutter is inserted into the endoscope's biopsy channel. The endoscope is reinserted into the plication and excess suture is removed with the suture cutter.

The above steps are repeated, the number of times depending on how many plications are needed. After all plications are completed, the system and overtube are removed. The endoscope is reinserted to evaluate post-procedure LOS tone. The patient is then returned to the recovery area. It is estimated that the procedure time is approximately 90 minutes, with pre- and post-procedure times being typically about 45 minutes each.

C.R. Bard Inc are also working on a more advanced form of the suturing device (EndoCinch™ 2) that ties, cuts and fixes stitches in one movement, thus negating the need for a separate knot pushing and cutting device. Consequently, fewer insertions should be required to perform the operation, leading to a decrease in procedure time.

Intended purpose

ELGP is a procedure in which plications are created for the treatment of symptomatic GORD.

At the time of this review only one study on ELGP that met the eligibility criteria had been published. This study included patients with three or more heartburn episodes per week while off medication, dependency on antisecretory medication (H_2 receptor antagonists or proton pump inhibitors (PPIs)), documented acid reflux by pH monitoring (pH <4 for more than 4 per cent of a 24-hour monitoring period) and non-erosive reflux oesophagitis or grade 1–2 oesophagitis on the modified Savary-Miller scale (Los Angeles grade A or B, see Appendix E).

Expert advice from the Supporting Committee indicated that these criteria were perhaps too restrictive and that a more appropriate patient group for the ELGP procedure would consist of those patients with clinically proven GORD who are dependent on antisecretory medication and who are LA grade A or B (Lundell et al 1999) (see Appendix E). It was also noted that owing to the size of the overtube through which the procedure is performed, ELGP is currently only suitable for adults.

Clinical need and burden of disease

Epidemiology and clinical presentation

GORD is a common condition that can have a significant impact on the quality of life of individuals (Revicki et al 1998a). Several factors alone or in combination can lead to the development of GORD, such as impaired oesophageal clearance, hiatal hernia and delayed gastric emptying (Bittinger, Barnert, & Wienbeck 1997; Lee & Omorain, 1998). While it has also been suggested that there may be a relationship between *Helicobacter pylori* and GORD, debate is ongoing as to whether this relationship is protective or harmful or whether these entities are in fact independent (Malfertheiner & Gerards 2000).

GORD can be primarily attributed to the failure of the LOS and the crural diaphragm. As a result of this failure the oesophageal mucosa is exposed to refluxed gastric contents including acid and pepsin, which in turn places the person at risk of tissue damage and impairment of wellbeing.

In general, symptoms of GORD can be broadly grouped into those directly related to reflux episodes such as heartburn, regurgitation and waterbrash, and those symptoms caused by complications of reflux disease, including respiratory symptoms, dysphagia and odynophagia (painful swallowing). Impairment of wellbeing (quality of life) is considered clinically significant when symptoms occur on two or more days a week (Gastroenterological Society of Australia 2001).

It is estimated that 15 to 20 per cent of adults in Australia experience heartburn once a week (Gastroenterological Society of Australia 2001). In a report published by the Australian Institute of Health and Welfare (AIHW), the prevalence of upper gastrointestinal conditions in patients attending Australian general practice was estimated at 30.8 per cent, with reflux accounting for 12.5 per cent of these problems in 1998–1999 (Sayer et al 2000). However, as prevalence data are based on symptoms and reflux symptoms occur along a continuum of severity, prevalence figures vary substantially and should be considered in the context of additional information such as pharmacotherapy costs and services.

In 1995–1996 the costs of prokinetics, histamine receptor antagonists (H_2RAs) and PPIs through the Pharmaceutical Benefits Scheme (PBS) and the Repatriation Pharmaceutical Benefits Scheme (RPBS) was $251 million, increasing to $336 million in 2000–2001, which equates to more than 8 million services (Table 1). In the 1999–2000 financial year 60,939 hospital separations were attributable to GORD (Australian Institute of Health and Welfare 2000; Australian Institute of Health and Welfare 2001) (Table 2).

Table 1 Pharmaceutical Benefits Scheme (PBS) and Repatriation Pharmaceutical Benefits Scheme (RPBS) costs and services for pharmacotherapy used to treat gastro-oesophageal reflux disease (GORD)

		PBS and RPBS 1995–1996		PBS and RPBS 1999–2000		PBS and RPBS 2000–2001	
Drug class	Drug	$	No. services	$	No. services	$	No. services
Prokinetics	cisapride[a]	13,815,928	542,181	20,799,049	703,266	11,608,238	370,300
Subtotal		**13,815,928**	**542,181**	**20,799,049**	**703,266**	**11,608,238**	**370,300**
Histamine receptor blockers	cimetidine	14,111,148	506,753	4,131,669	173,809	3,078,935	141,081
	famotidine	38,867,590	1,436,132	17,359,396	958,139	15,344,066	815,382
	nizatidine	5,233,558	182,331	7,185,078	402,776	5,944,667	341,674
	ranitidine hydrochloride	90,922,016	3,241,234	62,327,006	3,461,252	62,394,235	3,405,776
Subtotal		**149,134,312**	**5,366,450**	**91,003,149**	**4,995,976**	**86,761,903**	**4,703,913**
Proton pump inhibitors	lansoprazole	7,317,964	81,947	38,076,715	517,964	39,050,432	627,564
	omeprazole	80,703,254	863,626	162,152,193	2,300,883	175,663,713	2,718,040
	pantoprazole	489,463	5,803	16,735,128	226,399	22,954,620	400,455
	rabeprazole sodium	-		-		56,349	1,028
Subtotal		**88,510,681**	**951,376**	**216,964,036**	**3,045,246**	**237,725,114**	**3,747,087**
TOTAL		**251,460,921**	**6,860,007**	**328,766,234**	**8,744,488**	**336,095,255**	**8,821,300**

a) Cisapride is now generally not used to treat gastro-oesophageal reflux disease
These figures may be an overestimate because of the other indications for the same drugs
Note: The years covered ie 1999-2000 are financial years

Table 2 Statistics for gastro-oesophageal reflux disease, Australia 1998–99 and 1999–00

	Separations		% same-day separations		Patient days per 10,000 population		Average length of stay (days)	
Principal diagnosis ICD-10	1998–99	1999–00	1998–99	1999–00	1998–99	1999–00	1998–99	1999–00
K21 gastro-oesophageal reflux disease: public hospital	27,703	26,247	79.6	-[a]	22.8	21.1	1.6	1.5
K21 gastro-oesophageal reflux disease: private hospital	32,361	34,692	93.1	-	21.3	22.2	1.2	1.2

a) Percentage same day separations were not reported in 1999-2000
Source: Australian Institute of Health and Welfare 2000 and Australian Institute of Health and Welfare 2001.

The reported severity of symptoms, however, does not correlate with the degree of oesophageal damage (Lee et al 1998). Typically people who have had an endoscopy can be divided into two categories: those who have a negative result (endoscopically negative reflux disease - ENRD) and those with oesophagitis. Most patients have normal endoscopic findings and up to 50 per cent of patients have no visible signs of oesophagitis (Spechler 1992).

GORD is, however, a chronic disease, with most patients having a relapse of symptoms despite initial healing. In patients with more severe disease, the risk of relapse is greater, with around 50 per cent of patients experiencing recurrence over a five year period (Monnier et al 1995; Muller-Lissner 1997). Up to 20 per cent of patients with severe disease will also develop complications such as oesophageal stricture and Barrett's oesophagus (Lee et al 1998). Barrett's oesophagus is a recognised risk factor for

oesophageal cancer, with an annual incidence of one per cent in those with the condition (Drewitz, Sampliner & Garewal 1997).

Treatment

The main objectives in the treatment and management of GORD include symptom relief, restoring quality of life, healing of oesophagitis, if present, and reduction of the risk of complications or recurrence. However, for most patients with GORD, the main goal of treatment is relief of symptoms.

GORD may be managed through a combination of lifestyle modifications, antacid-antirefluxant drugs, prokinetic drugs and/or acid-suppressant agents (for example H_2RAs, PPIs) or surgery. Mild symptomatic GORD can usually be managed by the former options, whereas for patients with more severe symptoms or oesophagitis, intensive pharmacological therapy or anti-reflux surgery may be needed. For most patients, pharmacological therapy will be the mainstay of treatment.

Typically treatment is divided into two stages: acute and maintenance treatment. Acute treatment is focused on promoting healing and reducing symptoms associated with GORD. Two main treatment strategies are advocated at this acute stage, these being the 'step-up' approach and the 'step-down' approach. In the 'step-up' approach, management starts with lifestyle modifications and moves through the other pharmacological treatments depending on the response of the patient. In contrast, the 'step-down' approach begins with patients being given PPIs and titrating these down to the lower doses or an acid suppressor or prokinetic. This approach will often be the most appropriate for patients with more severe symptoms and advanced endoscopic findings (Lee et al 1998). However, there is little evidence available comparing the efficacy and cost-effectiveness of each of these approaches. While a considerable proportion of patients achieve symptom relief after initial acute treatment, a significant minority will develop complications as a result of GORD. Maintenance therapy is thus an important issue and aims at the prevention of oesophagitis and risk management of complications. The therapeutic options include on-demand drug treatment, maintenance treatment (usually with PPIs) or anti-reflux surgery (Galmiche, Letessier & Scarpignato 1998). However, there is still debate as to what constitutes the best treatment option.

Existing procedures

Lifestyle changes

A common first-line recommendation given to patients who present with GORD symptoms is to modify their diet or lifestyle. Changes can include elevation of the head during sleeping, weight reduction, eating a low fat diet, avoiding large, late night meals and foods that reduce the oesophageal sphincter tone (for example chocolate, alcohol, caffeine and peppermint).

These recommendations are primarily based on data from pathophysiological studies. Well controlled clinical trial data that demonstrate the effectiveness of these measures are lacking. However, as lifestyle and dietary changes are not thought to be harmful and in

some cases may have other health benefits (Galmiche, Letessier, & Scarpignato 1998), these changes are often recommended.

Pharmacological therapy

For most patients with GORD, pharmacological therapy is the mainstay of treatment. As already mentioned, there are two main drug classes (not including prokinetics) used in the treatment and management of GORD (Table 3), and all are listed on the schedule of pharmaceutical benefits and/or the RPBS.

Table 3 Drugs that are used to treat gastro-oesophageal reflux disease

Drug and class	Generic name	Indication
Prokinetic agents	cisapride	Treatment of gastroparesis where the diagnosis has been made or confirmed by a consultant physician.
		Note: Cisapride used to be prescribed for GORD but its use has been discontinued owing to concern over the effect of cisapride on cardiac function (Wysowski & Bacsanyi 1996)
H_2 receptor antagonists	cimetidine	Restricted to and/ or authority:
		maintenance therapy for peptic ulcer in patients who are negative for *Helicobacter pylori*; reflux oesophagitis; scleroderma oesophagus; Zollinger-Ellison syndrome.
	famotidine	Restricted to and/or authority
		maintenance treatment of duodenal ulcer in patients who are negative for *H. pylori* or in whom there has been a failure of *H. pylori* eradication therapy; reflux oesophagitis; scleroderma oesophagus; Zollinger-Ellison syndrome.
	nizatidine	Restricted to:
		maintenance treatment of duodenal ulcer in patients who are negative for *H. pylori* or in whom there has been a failure of *H. pylori* eradication therapy; reflux oesophagitis
	ranitidine	Restricted and authority:
		maintenance for peptic ulcer in patients who are negative for *H. pylori*; reflux oesophagitis; scleroderma oesophagus; Zollinger-Ellison syndrome.
Proton pump inhibitors	lansoprazole	Restricted to:
		gastro-oesophageal reflux disease, scleroderma oesophagus
	omeprazole	Restricted to:
		gastro-oesophageal reflux disease, scleroderma oesophagus, Zollinger-Ellison syndrome
	pantoprazole	Restricted to:
		gastro-oesophageal reflux disease
	rabeprazole sodium	Restricted to:
		gastro-oesophageal reflux disease, scleroderma oesophagus

Antacids and alginic acid

Antacids and alginic acid are typically available over the counter and are popular with people who are after immediate relief from symptoms. Alginates seem to be more useful than antacids in controlling symptoms but no placebo-controlled study has shown healing of oesophagitis with either of these drug classes. In general, antacids and alginic acid should only be used in the short term.

Histamine receptor antagonists

Four H_2receptor antagonists, (H_2RAs) are currently marketed in Australia. These agents work by inhibiting the secretion of gastric acid by competitively blocking the H_2 receptor located on the gastric parietal cells. While these drugs reduce acid secretion they do not stop production.

Proton pump inhibitors

The proton pump inhibitors (PPIs), specifically work to inhibit the enzyme H+, K+-ATPase, which regulates the final common pathway for acid secretion. This process reduces acid secretion from that cell until new pumps are formed and recruited. Currently a single daily dose of the PPIs can inhibit gastric acid secretion for 10 to 16 hours per day. Reversible acid pump inhibitors are currently in development.

Prokinetic/motility agents

These are no longer in general use for the treatment of patients with GORD.

Evidence

A number of systematic reviews and meta-analyses have been undertaken to compare the different drug classes available for patients with GORD. These reviews, however, generally include prokinetics, which are no longer prescribed in Australia for GORD, and lack data on PPIs, which are becoming more common as a treatment option for patients with the disease. The following information should be interpreted in this context.

Iskedjian and Einarson (1998) undertook a meta-analysis of cisapride, omeprazole and ranitidine in the treatment of GORD. It was found that omeprazole appeared to be the most effective agent for severe GORD and cisapride the treatment of choice for mild GORD. The authors also concluded that either of these two treatments seemed to be superior to ranitidine for the prevention of relapse (Iskedjian & Einarson 1998). The meta-analysis, however, covered only the period 1984–1995, and the authors note that the analysis did suffer from certain limitations, such as the inclusion of only a small number of studies on some drug classes. The conclusions reported by Iskedjian and Einarson (1998) are similar to those found in the report by the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) (Perras & Otten 1996). However, this report only included results from trials in adults with oesophagitis grades II-IV. It was concluded that in the treatment of acute oesophagitis, omeprazole results in better healing rates than ranitidine or cisapride and that cisapride and ranitidine result in comparable disease-free periods when used in maintenance strategies. In another meta-analysis comparing prokinetics, H_2RAs and PPIs in patients with grade II-IV GORD, Chiba et al (1997) found that PPIs healed oesophagitis in the most patients when compared with all other drug classes, irrespective of the dose of medication and duration of treatment. Again limitations were noted in the analysis because of the paucity of information on some treatments and differences in measurement of symptom data. In the most recent review of pharmacological therapy for patients with GORD, van Pinxteren et al (2001) reviewed short term treatment in patients with endoscopically negative reflux disease and those for whom endoscopy was not used to allocate treatment. The review concluded that in these patients for whom there was a high probability of GORD, PPIs were superior to both H_2RAs and prokinetics in achieving heartburn remissions. van Pinxteren et al (2001) also noted that H_2RAs were effective in promoting symptom relief, although the evidence for prokinetics was less convincing.

Anti-reflux surgery

There are three main indications for anti-reflux surgery in the treatment of GORD: 1) failure to respond satisfactorily to medical therapy; 2) intolerable side-effects or failure of compliance; and 3) a desire to be free of long term medication for GORD (Lee et al 1998). All procedures adhere to the same basic principles: restoration of the LOS to an intra-abdominal position, extrinsic bolstering of the LOS pressure and repair of the patulous hiatus (Galmiche, Letessier & Scarpignato 1998).

In the last decade the number of anti-reflux surgical procedures performed for GORD has considerably increased. This increase, according to a number of authors, can be attributed largely to the trend towards more minimally invasive procedures using either endoscopic or laparoscopic technology (Klingler et al 1999). Nissen fundoplication, however, remains the most commonly performed operation for the treatment of GORD.

Rudolf Nissen first described fundoplication in 1956 following the discovery that a fundal patch used to reinforce an oesophageal suture line could also aid gastro-oesophageal reflux. This procedure became known as a Nissen fundoplication and involves the patient having an incision in the abdomen where the fundus of the stomach is completely wrapped (360°) around the oesophagus and sutured to the front wall of the oesophagus. Despite the reported success of the operation, significant morbidity was noted with this procedure with patients experiencing side effects such as dysphagia, chronic gas retention and gas bloat stomach. It was found that shortening the wrap and ensuring a loose and floppy fundoplication, with division of the short gastric vessels and a crural repair, markedly lessened the post-operative sequelae. The 'floppy' Nissen fundoplication as it became known, and a number of variants such as the Toupet and Rossetti fundoplication (Table 4), have all been advocated for treatment of GORD (Watson & Jamieson 1998).

Table 4 Types of anti-reflux surgery

Type of fundoplication	Description
Total fundoplication Floppy Nissen	Involves full mobilisation of the gastro-oesophageal junction and posterior fundus with division of the upper short gastric vessels and a crural repair
Rosetti	A modification of the original Nissen procedure, using the anterior wall of the gastric fundus to build the wrap, thus obviating the extensive mobilisation and division of the short gastric vessels.
Partial fundoplication Toupet	The features of the partial fundoplication are full mobilisation of the gastro-oesophageal junction, posterior fundus crural repair and fixation of the partial wrap to both crural limbs and to the anterolateral walls of the oesophagus on either side of the anterior vagal trunk. The extent of the oesophageal wrap varies from 180° to 240°. The toupet fundoplication is a 270 degrees posterior wrap in which the stomach is wrapped around two thirds of the lower oesophagus.
Dor	Limited mobilisation of the fundus which is sutured to the anterior aspects of the gastro-oesophageal junction and to the left crus.
Lind	Involves a 300° partial oesophageal wrap. This operation is rarely performed.
Besley Mark IV	In this operation an anterior 270° partial fundoplication is fixed to the undersurface of the diaphragm and is performed through the left chest.
Watson	Consists of full mobilisation of the lower oesophagus and gastro-oesophageal junction as well as crural repair, fixation of the oesophagus to the cura and anterior 180° Dor-type fundoplication.
Cardiopexies Hill posterior gastropexy	Used rarely, this procedure, like most, aims to return the hiatal hernia to the abdomen and help create a new gastro-oesophageal valve mechanism.
Tres cardiopexy	Involves dissection of the round ligaments (ligamentum teres), which are then rerouted around the mobilised gastro-oesophageal junction and attached to the anterior wall of the stomach. The apex of the fundus is then sutured to the oesophagus.
Angelchik (not fundoplication)	A c-shaped ring of silicone is placed around the gastro-oesophageal junction to prevent reflux.

The era of laparoscopic anti-reflux surgery began in the 1990s when the first laparoscopic Nissen fundoplication was performed successfully. While most anti-reflux procedures have now been performed laparoscopically, the two most common procedures to be performed laparoscopically are the Nissen fundoplication and the Toupet partial fundoplication. The laparoscopic Nissen fundoplication is performed essentially to the same principles as the open procedure except that instead of using a large incision, this newer method of surgery uses a lighted tube inserted through tiny ports, typically five, in the abdomen. Randomised controlled trials have looked at the efficacy and safety of laparoscopic fundoplication compared with the open procedure (Bais et al 2000; Heikkinen et al 1999; Heikkinen et al 2000; Laine et al 1997; Luostarinen et al 2001; Nilsson 2000; Wenner et al 2001). While four out of five of these trials concluded that laparoscopic fundoplication is as effective in controlling the symptoms of GORD as open fundoplication, most of the trials reported on a small number of patients and had only short term follow-up (Table 5). Different measures have been used to assess outcomes and it appears that few outcomes were assessed blinded. Several papers also made reference to the learning curve experienced by surgeons undertaking laparocopic procedures. The learning curve relates to the time taken to master a particular skill. During the learning curve there may be higher rates of intraoperative and postoperative complications as well as a greater likelihood of conversion from laparoscopic to open surgery (Watson, Baigrie & Jamieson 1996). Despite this, laparoscopic fundoplication is considered the method of choice (Watson and Jamieson

1998), with this decision primarily based on retrospective data, cohort studies and randomised controlled trials on small numbers of patients.

Table 5 Open versus laparoscopic surgery

Study	No of patients b		Follow-up (months)	Gastro-oesophageal reflux symptoms (n)								Conversions	
				Dysphagia		Heartburn		Regurgitation		Bloating			
	Op	Lap		Op	Lap	Op	Lap	Op	Lap	Op	Lap	Op	Lap
Bais et al 2000	46 (69)	57 (79)	3	0% (0)	12% (7)	-	-	-	-	-	-	-	9% (5)
Heikkinen et al 1999; Heikkinen et al 2000	19 (20)	19 (22)	24	-	-	42% (8)	21% (4)	5% (1)	5% (1)	-		-	4.5% (1)
Laine et al 1997	49 (55)	45 (55)	3[a]	16% (8)	18% (8)	4% (2)	0% (0)	-	-	22% (11)	22% (10)	-	9% (5)
Luostarinen et al 2001	15	13	12	40% (6)	31% (4)	-	-	-	-	-	-	-	7.7% (2)
Nilsson 2000; Wenner et al 2001	29 (30)	25 (30)	6	7% (2)	8% (2)	3.5% (1)	0% (0)	0% (0)	3% (1)	-	-	-	17% (5)

a) Data for follow-up at 12 months were also reported in the paper. However this information was not included in the table as it reported on only 18 pts in the laparoscopic group and 30 in the open group.
Op=open; Lap=laparoscopic
Numbers in brackets represent number of patients originally enrolled in the study

As noted earlier, there are also variants of the Nissen fundoplication. In a review comparing the results of different surgical techniques, 23 randomised studies were included. It was found that a few techniques had poorer results than others: simple closure of the His angle, the Hill operation, the Besley Mark IV technique and the Angelchik prosthesis. In most studies, results of partial fundoplication on reflux were as good as those of total Nissen fundoplication and fewer patients had postoperative dysphagia (Huguier, Barrier, & Houry 2001).

Pharmacotherapy and surgery

Studies directly comparing the efficacy and safety of pharmacotherapy and surgery for GORD are uncommon. In a recent review, six randomised trials and three cohort studies looking at medical or surgical treatment for chronic GORD were analysed (Allgood & Bachmann 2000).

The overall conclusion of the review was that in patients with chronic or severe GORD, surgery is more effective than medical treatment for reducing symptoms. However, at the time of publication only three randomised controlled trials included patients on PPIs, with the information from two of these trials available only in abstract form. This is a significant limitation considering that PPIs have become a common treatment option for patients with chronic or severe GORD. The review also has the problem of including trials comparing different types of anti-reflux surgery such as open fundoplication and posterior gastropexy, with medication. In addition there are few trials included that have a laparoscopic fundoplication arm despite this procedure becoming increasingly more

common than the open procedure in patients with GORD. As a result, possibly the only conclusion that can be drawn from the review is that open surgery is superior to H_2RAs in patients with chronic or severe GORD.

Since this systematic review was published, one of the trials has published its results (Lundell 2000; Lundell et al 2001; Myrvold et al 2001). In this trial 310 patients with erosive oesophagitis were randomised to receive either continuous omeprazole therapy (n = 155) or open anti-reflux surgery (n =155). It was found that at five years, open anti-reflux surgery resulted in fewer treatment failures than did use of omeprazole (Lundell et al 2001). However, when the dose was adjusted with respect to symptom relapse, few differences were observed between the two groups.

Spechler et al (2001) have also published the long-term results of their study comparing medical therapy (antacids and ranitidine) and open Nissen fundoplication. Mean follow-up was 10.6 years for medical patients and 9.1 years for surgical patients. The authors state that it should not be expected that those patients undergoing anti-reflux surgery would no longer need to take antisecretory medication. Their findings were that 92 per cent of patients in the medical treatment group and 62 per cent of those in the surgical treatment group had reported that they had used anti-reflux medications regularly since completion of the original study (P<0.001).

Other procedures

ELGP is not the only new intervention to enter the arena of GORD management. The increasing emphasis on minimally invasive procedures has seen new methods, such as the Wilson Cook system and the Stretta procedure, trialled on patients with GORD (Raju 2001).

Comparator

There are two appropriate comparators for the ELGP procedure. The first is pharmacotherapy or continuing anti-secretary medication, and the second is surgery. The latter comparator is considered appropriate for patients who do not respond, or do not wish to be on a pharmacotherapy regime, and are considering fundoplication.

Marketing status of the device

Accessories needed for the Bard® EndoCinch™ suturing device are listed on the Australian Register of Therapeutic Goods (ARTG) as follows:

AUSTL 75102 Suture Tag

AUSTL 75103 Suturing Kit

AUSTL 75110 Suturing Handle

Current reimbursement arrangement

ELGP for the treatment of GORD is not currently funded through Medicare.

Approach to assessment

Review of literature

The medical literature was searched to identify relevant studies and reviews. Searches were conducted in the following databases from their commencement to December 2001.

- Medline/Pre-Medline
- EBM Reviews – Best Evidence
- EMBASE
- Current Contents
- the Cochrane Library
- International Pharmaceutical Abstracts
- ISTAHC online database (International Society for Technology Assessment in Health Care)
- NHS Centre for Reviews and Dissemination databases
  - DARE (Database of Abstracts and Reviews of Effectiveness)
  - EED (Economic Evaluation Database)
  - HTA (Health Technology Assessment Database)

The search strategy shown in Table 6 was used to identify papers on endoluminal gastroplication (ELGP) in Medline, CINAHL and Best Evidence. The same search strategy was used for EMBASE, with the MeSH terms replaced with EMTREE terms.

Table 6 Search strategy

1.	exp esophageal motility disorders/ or exp gastroesophageal reflux/
2.	(gastro$ adj reflux$).mp
3.	(GORD or GERD).mp.
4.	reflux.mp.
5.	dysphagia.mp.
6.	or/1-5
7.	gastroplicat$.mp.
8.	endoluminal.mp.
9.	(plication adj6 proced$).mp.
10.	(plication$ adj4 esophag$).mp.
11.	(plication$ adj4 oesophag$).mp.
12.	exp suture techniques/
13.	exp GASTROPLASTY/
14.	sewing.mp.
15.	or/7-15
16.	16 and 6
17.	limit 17 to english language
18.	Animal/
19.	Human/
20.	18 not (18 and 19)
21.	17 not 20

The search retrieved 293 articles relating to ELGP. Two hundred and fifty-nine (89%) were considered irrelevant to the topic. Thirty-three studies were considered relevant to the indication of interest, although 32 of 33 were review or background papers. The applicant also provided abstracts relating to the procedure. Included studies and abstracts are listed in Appendix C and Appendix D respectively.

From the literature search, one full-text paper that evaluated ELGP using an endoscopic sewing machine in humans was identified.

Electronic searching also included the internet sites of the health technology assessment groups and information sources listed in Table 7.

Table 7 Health technology assessment organisations

Organisation	Website
International Society for Technology Assessment in Health Care (ISTAHC)	www.istahc.org
International Network of Agencies for Health Technology Assessment (INAHTA)	www.inahta.org
British Columbia Office of Health Technology Assessment (Canada)	www.chspr.ubc.edu.ca/bcohta
Swedish Council on Technology Assessment in Healthcare (Sweden)	www.sbu.se
Oregon Health Resources Commission (US)	www.ohppr.state.or.us/ohrc
Minnesota Department of Health (US)	www.health.state.mn.us
ECRI (US) (formerly the Emergency Care Research Institute)	www.ecri.org
Canadian Coordinating Office for Health Technology Assessment (CCOHTA)	www.ccohta.ca
Alberta Heritage Foundation for Medical Research (Canada)	www.ahfmr.ca
Veterans' Affairs Research and Development Technology Assessment Program (US)	www.va.gov/resdev
National Library of Medicine Health Service (US)	http://text.nlm.nih.gov
NHS Health Technology Assessment (UK)	www.hta.nhsweb.nhs.uk
Office of Health Technology Assessment Archive (US)	www.wws.princeton.edu/~ota
Institute for Clinical Evaluative Science (Canada)	www.ices.on.ca
Conseil d'Evaluation des Technologies de la Sante du Quebec (Canada)	www.cets.gouv.qc.ca
National Information Centre of Health Services Research and Health Care Technology (US)	http://www.nlm.nih.gov/nichsr/nichsr.html
Finnish Office for Health Technology Assessment (FinOHTA) (Finland)	http://www.stakes.fi/finohta/linkit/
Institute Medical Technology Assessment (Netherlands)	http://www.bmg.eur.nl/imta/
Agencia Evaluacion Tecnologias Sanitarias (AETS) (Spain)	http://www.isciii.es/unidad/aet/cdoc.htm
Agence Nationale d'Accreditation et d'Evaluation en Sante (France)	www.anaes.fr

The evidence presented in the selected studies was assessed and classified using the dimensions of evidence defined by the National Health and Medical Research Council (NHMRC, 2000).

These dimensions (Table 8) consider important aspects of the evidence supporting a particular intervention and include three main domains: strength of the evidence, size of the effect and relevance of the evidence. The first domain is derived directly from the literature whilethe last two require expert clinical input as part of its determination.

Table 8 Evidence dimensions

Type of evidence	Definition
Strength of the evidence	
Level	The study design used, as an indicator of the degree to which bias has been eliminated by design.[a]
Quality	The methods used by investigators to minimise bias within a study design.
Statistical precision	The *P* value or alternatively the precision of the estimate of the effect. It reflects the degree of certainty about the existence of a true effect.
Size of effect	The distance of the study estimate from the 'null' value and the inclusion of clinically important effects only in the confidence interval.
Relevance of evidence	The usefulness of the evidence in clinical practice, particularly the appropriateness of the outcome measures used.

a) See Table 9

The three sub-domains (level, quality and statistical precision) are collectively a measure of the strength of the evidence. The designations of the levels of evidence are shown in Table 9.

Table 9 Designations of levels of evidence

Level of evidence	Study design
I	Evidence obtained from a systematic review of all relevant randomised controlled trials.
II	Evidence obtained from at least one properly-designed randomised controlled trial.
III-1	Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).
III-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group.
III-3	Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group.
IV	Evidence obtained from case series, either post-test or pre-test/post-test.

Eligibility criteria

The non-duplicate citations were then evaluated to determine whether they met the following eligibility criteria.

- Patients must have symptomatic GORD and have had ELGP by a sewing or suturing device to treat GORD.
- Papers must have more than 10 patients with the condition of interest.
  - The exception for this may be in the situation where there are no publications reporting more than 10 patients. Rather than excluding all papers for a clinical indication on the basis of this criterion, available information will be reported, and limitations noted.
- Case series will be excluded.
- Review only, editorial and technical papers will be excluded.
- Papers with duplicate information on the same group of patients will be excluded.
- Data available in abstract form only will be excluded.
- Papers that report no clinical results will be excluded.
- All non-English papers will be excluded.
- Animal studies and laboratory studies will be excluded
- Where these criteria could not be evaluated from the abstract, full papers were to be examined.

Existing reviews

The Alberta Heritage Foundation for Medical Research listed a Techscan report on the Bard® EndoCinch™ suturing system. This is not a health technology assessment (HTA) but a brief (one page) horizon scanning document on the purpose and potential implications of the emerging technology.

Expert advice

A supporting committee with expertise in gastroenterology, gastric surgery and consumer health was established to evaluate the evidence and provide advice to the MSAC from a clinical perspective. In selecting members for supporting committees, the MSAC's practice is to approach the appropriate medical colleges, specialist societies and associations and consumer bodies for nominees. Membership of the supporting committee is provided at Appendix B.

Results of assessment

The evidence for the efficacy and safety of the endoscopic sewing machine is based on one small published study with no control group (level IV evidence) (Filipi et al 2001). While one other study (Shafer et al 2001) that reported on patients undergoing ELGP was also identified, only six patients were included and the article was published in German (Table 10).

Five abstracts detailing surgeons' experience with ELGP were also identified. These are listed in Appendix D. The information provided in these abstracts is not included in the discussion below, given that abstracts generally contain insufficient information to allow adequate assessment of methodology and results. Given the paucity of information on ELGP, however, the results of these abstracts are reported in Appendix D to give some additional indication as to patient outcomes after ELGP. To date (including abstracts), fewer than 350 patients have been reported in the literature as having undergone ELGP (Rosen & Ponsky 2001).

Table 10 ELGP full-text publications

Author(s)	Title	Publication	Year	NHMRC evidence level
Filipi et al 2001	Transoral endoscopic suturing for gastro-oesophageal reflux disease: a multicenter trial.	*Gastrointestinal Endoscopy*	2000	IV
Shafer et al 2001	Endoluminal gastric plication for the treatment of gastroesophageal reflux disease: a pilot study.	*Viszeralchirurgie*	2001	IV

An important factor to also take into consideration when reviewing an emerging technology is the issue of bias: both pipeline and publication bias. For example, positive studies (ie ones that find statistically significant treatment effects) are more likely to be published in peer-reviewed journals than negative studies (that find no treatment effects). This is especially true for an emerging technology as early data tend to be biased against a new intervention (Ramsay et al 2001). The costs of technology are also often higher during the early stages of dissemination when practitioners are still gaining experience in its use, making it more difficult to accurately gauge effectiveness and costs. As a result, it is often difficult to fully assess a new health technology device at an early stage, particularly those involved in/used in a surgical procedure, as most are of poor quality (Pocock 1996).

Given these limitations, this review will provide a critical appraisal of the one published study that met the eligibility criteria on ELGP. The guidelines developed by Greenhalgh (1997) will be used as the framework for critical appraisal of the study by Filipi et al (2001) on endoluminal gastroplasty in patients with GORD.

Is it safe?

Filipi et al (2001) described the endoscopic gastroplasty procedure as safe on the basis of results for 64 patients. These patients underwent 79 endoscopic gastroplasty procedures including eleven repeat procedures (17 per cent of patients) and four procedures that required more than one day for the operation to be completed satisfactorily. All repeat procedures were performed as a result of poor results from the initial procedure. Cited

reasons for procedure failure included incorrect plication positioning, inadequate tissue inclusion and poor knot tying.

Adverse events as a result of the procedure are summarised in Table 11 and include transient events. The authors stated that mucosal tears occurring during overtube placement were without sequelae. Suture site bleeding also resolved spontaneously, and in four patients oxygen desaturation occurred both before and during the procedure. One patient experienced fever and abdominal pain, and mediastinal air was noted on computerised tomography. The patient was hospitalised and treated for three days with intravenous antibiotics (Filipi et al 2001).

Filipi et al (2001) noted that ELGP is a complex procedure and that the use of an overtube adds to the potential for complications. The most serious of these peri-procedural complications include oesophageal perforation and haemorrhage. As there is only one published study on ELGP it was thought that comparison with a similar technique would be the best method of estimating the peri-procedural complication rates of ELGP. Oesophageal variceal ligation (EVL) is a similar technique that uses an overtube and it was therefore used to provide a rough estimate of the rates of complications that might be associated with the ELGP procedure.

Dennert et al (1997) in their paper on overtube-related oesophageal injury, reported that oesophageal mucosal damage occurred in the majority of patients undergoing EVL. However the damage was typically moderate and not associated with any clinical consequences. Similarly, Johnson (1993) noted that oesophageal perforation is a possible complication of undergoing EVL. However the true incidence of complications as a result of ELGP will only be known after the technique has been evaluated in a number of large controlled trials or is widely used in clinical practice. As data are based on early experience, it is probable that peri-operative complications reported by Filipi et al (2001) might not reflect accurately, the actual incidence.

Ten patients withdrew prior to completion of the six month follow-up. Patients withdrew because of unwillingness to undergo follow-up and because of poor procedural results. It is unclear whether some of these patients are included in the 17 per cent with repeat procedures. These patients may also have had additional surgical interventions following withdrawal from the study.

Prior to this study, no investigator involved in this trial had performed the procedure on a human. As a result, it would seem reasonable to assume that for ELGP, much like laparoscopic Nissen fundoplication, a learning curve is involved for surgeons to become proficient (Soot et al 1999; Watson, Baigrie, & Jamieson 1996). This can perhaps account for some of the adverse events attributed to the procedure and the high (17%) repeat procedure rate. However, more data are needed before a definite conclusion can be made about the safety of ELGP in patients with GORD.

Table 11 Summary of adverse events

Adverse event[a]	Number of patients	Percentage of total (*n*=64)
Pharyngitis	20	31
Vomiting	9	14
Abdominal pain	9	14
Chest pain	10	16
Mucosal tear	2	3
Hypoxia	4	6
Gastric bleeding	2	3
Suture perforation	1	2

a) Some of these adverse events are transient

1. Was the study original?

Sixty four patients with GORD were included in what Filipi et al (2001) describe as a prospective multicentre clinical trial. This multicentre trial sought to examine the relative risks and benefits of the endoluminal gastroplasty procedure as described by Swain et al (2000) in their preliminary report on ELGP in humans. The hypothesis of the study, according to the authors, is that endoscopic suturing is a safe procedure and can decrease heartburn and the use of acid-suppressive therapy and prokinetic agents to less than four doses per month.

The inclusion and exclusion criteria are listed below (Table 12). The authors note that the exclusion criteria are primarily based on the experience of Swain (2000). It is stated that all patients satisfying study enrolment criteria were included in the study. No mention is made of how many patients were recruited from each centre, the period in which recruitment occurred or any other details concerning recruitment or enrolment. The authors did not include a discussion of sample size or study power.

Table 12 Inclusion and exclusion criteria for study

Inclusion	1) symptomatic GORD, defined as heartburn frequency score of 2 or higher when not taking medication, with or without erosive oesophagitis grade 0–2 on the modified Savary–Miller scale;
	2) successful treatment but with dependence on anti-secretory medications, which could include antacids, H_2-receptor blocking drugs and PPIs;
	3) documented reflux by pH monitoring as evidenced by a sustained pH of less than 4 for more than 4% of the time after discontinuation of GORD medications, except antacids, for 7 days; and
	4) willingness to undergo clinical follow-up for six months.
Exclusion	1) dysphagia;
	2) grade 3 or 4 erosive oesophagitis noted while taking medication;
	3) a body mass index (BMI) higher than 40kg/m^2;
	4) GORD refractory to PPIs;
	5) a hiatus hernia larger than 2 cm.

As indicated above, not all patients with symptomatic GORD were eligible for the procedure. According to Lehman (2000) the initial studies in humans have largely been restricted to GORD patients with a small or no hiatal hernia, no dysphagia or stricture, absence of Barrett's mucosa and good symptom control with acid-suppressing medications. This means that patient selection was biased towardsthose with a fairly

good prognosis. Patients with such uncomplicated disease, as stated by Lehman (2000), are a select portion of those seeking medical evaluation, and it is this group who are thought to benefit from ELGP (Haber et al 2001; Raijman et al 2001; Singh et al 1999).

The paper by Filipi et al (2001) is the only full text paper to be published on ELGP in more than 10 patients. Three other papers have been published on the technique: one being a pilot study on six patients and the remaining two studies relating to animals (Kadirkamanathan et al 1996; Kadirkamanathan et al 1999).

2. Was the study design sensible?

As previously mentioned, Filipi et al (2001) state that the hypothesis of the study is that endoscopic suturing is a safe procedure and one that can reduce the symptoms of GORD. The authors base this statement on the premise that the initial procedure should be half as effective as laparoscopic Nissen fundoplication. The basis of this assumption is unclear. In the introductory section of the article Filipi et al (2001) noted that the development of the endoscopic suturing machine was intended to be an alternative to surgical therapy. Later on in the article it is also suggested as being a replacement to continuous medical therapy.

The study, however, does not compare laparoscopic Nissen fundoplication or medical therapy with endoscopic gastroplication. The authors indicate that patients were randomised to two different plication configurations although most of the data are presented as a single group. As no control group (either surgical or pharmacological) was included, it is not possible to draw conclusions regarding the comparative efficacy of ELGP to these treatment options.

A more appropriate study design might have been a randomised controlled trial comparing endoscopic suturing with either laparoscopic Nissen fundoplication and/or continuous medical therapy. Endoscopic suturing is a relatively recent procedure, and while both sewing machines and endoscopic techniques have been used in surgery, it has only been in the last two decades that studies of suturing techniques have been initiated (Lehman 2000). According to Pocock (1996), development of new surgical procedures broadly follows the phase I-III classification system, with phase I considered to be basic development of surgical techniques. Prior published studies on ELGP have been on animals (Kadirkamanathan et al 1996; Kadirkamanathan et al 1999), not humans, so it is difficult to ascertain whether the authors perceived the trial as being a phase I study or a preliminary study to determine the feasibility of a larger study. If it is the latter, a comparison group could still have been included in the design.

Unfortunately, there seems to be a paucity of rigorous surgical trials evaluating new procedures. Russell (1995) cites several reasons for this shortage, including the difficulty of recruitment and blinding, although inability to blind does not preclude inclusion of a control group. Practical issues such as accounting for the learning curve between new and old procedures also means trials may be difficult. This issue of the learning curve has already been mentioned. Lilford et al (2000) advocate the use of 'tracker trials' in such circumstances. Tracker trials are flexible randomised trials that track progress of new technology over time, enabling researchers to monitor the learning curve so that when the technology has stabilised there is enough information available for decisions not to be based on poor quality evidence (Ramsay et al 2001).

Study outcomes

Most of the outcomes measured by the authors are the standard outcomes assessed in patients with GORD (Table 13). The exception is dysphagia which, while acknowledged as a common and debilitating preoperative and postoperative condition with a significant impact on quality of life (Wills & Hunt 2001), is not explicitly included as an outcome of interest by the authors. The reason for not measuring dysphagia would seem to be related to the statement by Filipi et al (2001) that, "the plication barrier does not create post-procedural dysphagia", unlike open or laparoscopic fundoplication, and as such, "transient dysphagia was not experienced by any patient" in the study (p. 420).

Table 13 Outcomes listed in the study

Category	Outcome	Measurement tool
Change in gastro-oesophageal reflux disease symptoms	Heartburn severity	Study specific: 0–10 visual analogue scale
	Heartburn frequency	Study specific: 0–3 scale
	Heartburn score	Heartburn score: frequency x severity
	Regurgitation	Study specific
	Quality of life	SF-36
Changes in objective measures	LOS pressure	Manometer
	Oesophagitis	Savary-Miller scale
	pH	pH probe
Changes in medication	Medication intake	Observational
Complications of surgery	Adverse events	Observational

Outcomes concerning health care utilisation and costs are also absent from the paper although reductions in health care costs are promoted as one of the main potential benefits of this procedure (Swain et al 2000). Filipi et al (2001) state that the cost of the procedure could not be determined because of the absence of professional fees, varying hospital costs and the variety of sedation and anaesthetic techniques. It should also be noted that the makers of the endoscopic suturing device, C.R. Bard Inc, assisted with the management of the trial. Additionally, as previously noted, the costs are typically higher during the early phases of a technology (Ramsay et al 2001). However, the implementation of a tracker trial might have allowed these costs, both clinical and economic, to be monitored during the evaluation of the new procedure (Russell 1995).

Medication use before and after the procedure, is also reported poorly in relation to this study population. Information on medication use by patients undergoing ELGP is presented both in the full text paper by Filipi et al (2001) and in the application forwarded to the Department of Health and Ageing by Bard Australia Pty Ltd (Table 15). In the paper by Filipi et al (2001), the percentage of patients taking particular drug classes are reported, while the raw data are stated in the application. These two sources of information, however, do not reconcile, thereby raising questions regarding the value of this information.

As noted in Table 13, the tool used to measure a number of these outcomes is a study-specific tool rather than a validated measurement. This is a recognised problem in studies of patients with GORD (Talley et al 2001) in that many different symptom rating scales are used. Two more common and validated scales that the authors could have used would have been the DeMeester symptom score or the gastrointestinal symptom rating

scale (GSRS). As both these scales have been validated (Revicki et al 1998b), data for ELGP could have been compared with data available for other management strategies. This is of particular importance, given that changes in symptoms determine the efficacy of the procedure. It is also possible that changes in these scales are not clinically relevant and that they do not adequately reflect changes in the status of the patient.

3. Was systematic bias avoided or minimised?

As indicated, patients were not randomised to ELGP or a comparator procedure or surgery. Patients were randomised to different plication techniques. This was done by means of a numbered sealed envelope, and as noted by Torgerson and Roberts (1999), this is not the ideal method of randomisation because of the possibility of concealment being compromised, resulting in selection bias. As most data have been presented for the group as a whole, rather than by plication configuration, the method of randomisation is probably not crucial.

The recruitment process of subjects for the multicentre trial was also a little unclear. It has already been established that the inclusion and exclusion criteria of the study meant that a select group of patients with uncomplicated GORD were included and it is probably these patients who would have the best outcomes.

Stirrart et al (1992) also make the point that new surgical procedures are often done by skilled surgeons. If the results are compared with those of other procedures, such as fundoplication, it should be remembered that most surgeons in the gastroenterology field practise these techniques.

C.R. Bard Inc, the maker of the Bard® EndoCinch™ suturing device, was also involved in the management of the multicentre clinical trial.

4. Was assessment blind?

The authors do not state whether outcomes were assessed blind, although this is less of an issue because there was no control treatment and the data for ELGP were reported for the whole group. Greenhalgh (1997) cites an example of expectation bias as a result of non-blinding of patients where better postoperative recovery might have been a result of the beliefs of patients and carers rather than a more effective intervention (Majeed et al 1996). It is also true that further bias may accrue because new surgical techniques are usually introduced by enthusiastic surgeons, whose beliefs and convictions could also affect the assessment of outcomes. These factors need to be taken into account when the results of this trial are considered, particularly because subjective measures such as symptom scores and quality of life are the primary measures of efficacy.

5. Statistics

The authors provide a section in the paper on the statistical analysis of the results. While the statistical tests appear to be appropriate for the data, not all values have been reported. Filipi et al (2001) have chosen in some cases to report on significant but not non-significant values (that is, $P>0.05$).

6. Follow-up

Ten patients withdrew from the study and for three patients data were incomplete at the six month follow-up (Table 14). Reasons for withdrawal included unwillingness to undergo post-procedure testing, poor results and moving to a different city. As a result, data on 51 patients were used for most outcomes. The exception to this is in relation to GORD symptom scores, for which dropout patients were included in a second analysis; although no significant difference was reported.

Table 14 Follow-up numbers for ELGP outcomes

Outcome	Baseline (*n*)	Three months (*n*)	Six months (*n*)
HB severity	64	56	51
HB frequency	64	56	51
HB score	64	54	51
Regurgitation	64	56	51
Quality of life	64	a	56
LOS pressure	Not reported; assume 51 patients		
Oesophagitis	Not reported; assume 51 patients		
pH	64	53	29
Medication intake	Not reported		

a) Not reported

Note: Adverse events were also presented as a % of the study population but are described elsewhere

The duration of follow-up in this trial was also quite short. Filipi et al (2001) noted that long term follow-up is planned as an extension of this study. Good quality long term data are needed to make any type of reliable assessment on the efficacy of ELGP. While ELGP appears to reduce symptoms in the short term, the possible long term efficacy and safety is unclear at this stage.

Is it effective?

Filipi et al (2001) state that changes to the mean six month symptom score changes demonstrated procedural efficacy. As can be seen from Table 16, heartburn severity and frequency improved. According to Filipi et al (2001) the number of patients experiencing moderate to severe regurgitation decreased from 39 of 64 (61%) patients to 4 of 51 patients (8%) six months after the endoluminal gastroplasty procedure. This may have been as high as 22 per cent (14/64) if all patients who withdrew were still experiencing regurgitation. The authors report, however, that even if dropout patients are included in the analysis, symptom scores remain significantly improved.

Filipi et al (2001) also claim that 62 per cent of surgical patients at three month and six month follow-up were taking less than four doses of medication per month, compared with 86 per cent of patients who were taking PPIs, 39 per cent H_2 receptor antagonists, 20 per cent magnesium compounds and 19 per cent prokinetic agents at baseline. Baseline information on medication dose and frequency of use, while not reported in the article by Filipi et al, was included in the application submitted by Bard Australia Pty Ltd (Table 15). In the application it is stated that there was a 76 per cent reduction in the number of patients taking either multiple medications or daily PPIs. While this statement

would seem to be true on the basis of the additional data, the difficulty is that these numbers do not reconcile with what Filipi et al (2001) published in their report. Patients taking prokinetics are not mentioned in the table, despite Filipi et al (2001) reporting that 19 per cent of patients (12) were taking prokinetics. In addition, baseline information is presented for only 58 patients, with no mention on the missing data on eight patients. Consequently, caution should be exercised in interpreting these results.

Table 15 Medication use at baseline and six month follow-up

	% and no. of patients					
	Baseline		3 months		6 months	
Medication	**%**	***n***	**%**	***n***	**%**	***n***
Multiple	12.1	7	0	0	0	0
PPI daily	75.9	44	22.4	13	21.4	12
PPI weekly	0	0	8.6	5	8.9	5
H_2 blockers	10.3	6	8.6	5	5.4	3
Antacids daily	1.7	1	10.3	6	8.9	5
Antacids weekly	0	0	29.3	17	32.1	18
None	0	0	20.7	12	23.2	13
Total no. of patients		58		58		56

As shown in Table 16, only two of the eight subscales in the quality of life questionnaire (SF-36), bodily pain (P =0.012) and social functioning (P =0.0075) showed improvement over the six month period. A statistically significant reduction in the total number of reflux episodes was noted at six months (P =0.0002) and a reduction in oesophageal acid reflux. However, the mean percentage of time that pH was less than four at six months was still above normal at 8.5 per cent. It should be remembered that these results are based on 29 patients.

Erosive oesophagitis, oesophageal body and LOS pressure, had not improved six months after the procedure. This, in addition to the modest change in oesophageal acid reflux in patients after the procedure, may have implications for the long term control of oesophagitis and reflux symptoms (Sugiura et al 2001). It also brings into question, as stated by Raju (2001), the effectiveness of ELGP in patients with more severe disease.

There are a number of factors that limit the ability to draw conclusions about the overall efficacy of the procedure. While the authors make the statement that ELGP is associated with reduced symptoms and medication use at six months, factors such as the reliability and validity of the measures and the duration of follow-up must also be taken into consideration.

Table 16 Efficacy outcomes for ELGP

Outcome measure	Baseline mean (SD)	Three-month mean (SD)	Six-month mean (SD)
HB severity	23.0 (5.7)	9.2 (8.3) *P*=0.0001	9.5 (7.4) *P*=0.0001
HB frequency	2.75 (0.5)	1.46 (1.0) *P*=0.0001	1.31 (0.8) *P*=0.0001
HB score	62.7 (18.6)	16.7 (22.3) *P*=0.0001	17.0 (20.2) *P*=0.0001
Regurgitation	1.81 (0.8)	0.59 (0.8) *P*=0.0001	0.61 (0.6) *P*=0.0001
Quality of life			
Physical functioning	80.9 (26.5)	-	88.6 (21.2) *P*= 0.07
Role–physical	78.5 (35.9)	-	87.1 (30.9) (NS)
Bodily pain	68.0 (19.0)	-	75.2 (18.7) *P*=0.012
General health	67.8 (22.0)	-	71.6 (19.9) (NS)
Vitality	58.4 (19.8)	-	62.6 (20.4) (NS)
Social functioning	77.3 (25.1)	-	86.2 (20.6) *P*=0.0075
Role–emotional	76.2 (38.1)	-	79.2 (34.0) (NS)
Mental health	73.1 (17.9)	-	74.4 (16.2) (NS)
LOS pressure	16.1 mm Hg	-	20.6 mm Hg
Oesophagitis	25% grade II	-	19% grade II
PH			
% upright time	11.5 (8.0)	10.6 (8.7) (NS)	9.70 (9.1) *P*=0.005
% supine time	6.77 (8.6)	7.08 (11) (NS)	5.92 (7.0) (NS)
longest single episode	15.0 (15.0)	21.0 (21.0) *P*=0.06	17.7 (16.7) (NS)
total number of episodes	158 (97)	112 (77) *P*=0.0007	117 (104) *P*=0.0002
% time pH <4	9.63 (6.8)	9.34 (7.5) (NS)	8.50 (8.3) *P*=0.011

NS=Not significant, *P*>0.05

Conclusions

In summary the following conclusions can be drawn from the available evidence on the safety and effectiveness of ELGP:

- There is a paucity of evidence on ELGP in humans.
- From the very limited data reported in the one case-series paper it seems that patients may experience some short term symptom control.
- Short term follow-up (only six months) limits our ability to draw conclusions on the long term efficacy or effectiveness of ELGP.
- It appears from the limited reports published on the procedure, that ELGP may benefit a select group of patients with uncomplicated GORD.
- Long term randomised evidence is needed on patients receiving ELGP.
- Good quality long term evidence comparing the ELGP procedure with fundoplication and pharmacotherapy is also needed.

What are the economic considerations?

The information on the effectiveness of ELGP is based on one trial of 64 patients with uncomplicated GORD. From the very limited data reported, it seems that some patients may experience some short term symptom control.

GORD is a chronic condition, and as such, the short-term follow-up (six months) limits our ability to draw conclusions on the long-term efficacy or effectiveness of ELGP. The availability of only short term data only means that it is difficult to estimate the long term benefit realised (for example, in life years saved or quality adjusted life years). As a result, it is difficult to provide an estimate of the likely additional cost to government that may be incurred if the Bard® EndoCinch ™ 1 is listed on the Medicare Benefits Schedule.

As only six month efficacy data from a small number of patients are available it would be inappropriate to extrapolate costs (or cost savings) beyond this period. For this reason the information below provides only a very crude estimate of short-term costs.

It has been assumed that the ELGP procedure, once successful, will remove the need for all medication. This is considered a 'best case' scenario for ELGP, as the data from Filipi et al (2001) suggest that this may not be the case.

Estimates of costs of the ELGP procedure

The applicant has provided some estimates of costs. These costs have been used to calculate an approximate cost for the ELGP procedure.

Staff costs

The applicant has indicated the following professional fees for the ELGP procedure. It has not provided an indication of the other likely staff required for the procedure (for example nursing staff).

Table 17 Estimated staff costs for ELGP procedure

Staff	Hourly rate	Procedure duration	Professional fee
Surgeon	Not reported	Not reported	$481.23
Assistant surgeon	Not reported	Not reported	$120.31
Anaesthetist	Not reported	Not reported	$118.40
Nursing staff (not included by applicant)	Not reported	Not reported	Not reported
Total staff costs			**$719.94**

Disposable costs

The applicant has provided the following estimates of disposable costs for the first model of the EndoCinch™ system. C.R. Bard Inc is also in the process of finalising the development of the EndoCinch™ 2 system, which has lower disposable costs, estimated at $3,500 (personal communication, Alex McMichael, Bard Australia Pty Ltd, 22 March 2002).

Since the application is based on the Bard® EndoCinch™ version 1 system, and these details have been supplied, the following costs are based on this model. Table 20 provides a crude estimate of costs if the Bard® EndoCinch™ 2 system were to be used in clinical practice.

Table 18 Estimated disposable costs for the Bard ® EndoCinch ™ 1 device

Device	Cost	Number of times used	Cost per use
Endoscopic suturing handle	$3,500	50 times	$70.00
Endoscopic suturing kit	$2,000	single use	$2,000.00
Endoscopic overtube 1	$180	25 times	$7.20
Total disposable costs			$2,077.20

Capital costs

It is unclear whether there are any additional capital costs required for the use of the Bard® EndoCinch™ device.

Hospital costs

It has been estimated by the applicant that hospital costs, including operating theatre and recovery, (facility fee and consumables), would be about $1,275.

Total costs

The total cost for one ELGP procedure using the Bard® EndoCinch™1 device is estimated to be **$4,072**.

Filipi et al (2001) indicated that 17 per cent of patients required repeat procedures, all as a result of poor results from the original procedure. If the repeat procedure rate is taken into consideration, the cost per successful procedure would be **$4,764** (that is, $4,072 x 1.17).

Estimates of costs of comparator (continuous pharmacotherapy)

Costs of the non-surgical comparator, continuous pharmacotherapy, have been calculated out to six months as the efficacy data for the ELGP procedure are available only up to this time. For simplicity it has been assumed that patients will be treated with H_2RAs and PPIs, and will receive the maximum recommended therapeutic dose. Treatment is assumed to be continuous for the six months and the prices below represent the branded drugs (and include a brand price premium where appropriate). These assumptions are considered to be a 'worst case' scenario for pharmacotherapy as patients are likely to be using cheaper medications, and may only be using medication on an as-needed basis rather than constantly. Costs are based on the schedule of pharmaceutical benefits for approved pharmacists and medical practitioners (Department of Health and Ageing, February 2002).

Table 19 Estimated pharmacotherapy costs for six months

Generic name	Brand name	Dose	Cost per month	Total cost per six months
Omeprazole	Losec	40 mg, 4/day	$93.08	$562.80
Ranitidine	Zantac	300 mg, 2/day	$48.02	$288.12

One standard general practitioner consultation ($21.00) has also been factored in to the costs of treating GORD medically.

Therefore the total costs for six months of medical treatment of GORD is **$583.80** for PPIs and **$309.12** for H_2RAs.

Net cost at six months

If it is assumed that all medication use ceases after the ELGP procedure, the net cost is as follows:

= cost of ELGP (at six months) – cost of pharmacotherapy (for six months both PPIs and H_2RAs)

PPIs

= $4,072 – $584

= $3,488

H_2RAs

= $4,072 – $309

= $3,763

If the repeat procedure rate of ELGP is considered the net cost of ELGP is **$4,180** or **$4,455** respectively.

The table below indicates how the net cost of ELGP might differ if the medication use assumption is varied.

Table 20 Estimates of net cost of ELGP varied by proportion of medication use averted

Proportion of medication use averted at six months	Cost of medication for six months		Cost of medication use averted		Cost of ELGP		Net cost ELGP at six months: PPIs		Net cost ELGP at six months: H_2RAs	
	PPIs	H_2RAs	PPIs	H_2RAs	Endo 1	Endo 2	Endo 1	Endo 2	Endo 1	Endo 2
100%	$584	$309	$584	$309	$4,072	$3,500	**$3,488**	$2,916	**$3,763**	$3,191
75%	$584	$309	$438	$232	$4,072	$3,500	**$3,634**	$3,062	**$3,840**	$3,268
50%	$584	$309	$292	$154.5	$4,072	$3,500	**$3,780**	$3,208	**$3,918**	$3,346

This is considered a reasonably generous estimate as it has been assumed that medication use prior to the procedure is daily rather than as needed, and that as a result of ELGP, all concomitant medication ceases (that is, ELGP is 100 per cent effective in reducing

medication intake). The data from Filipi et al (2001) suggests that while it is likely that ELGP reduces medication use at six months, it is not likely to remove the need for medication completely. This is illustrated in Table 20. The short duration of follow-up in this study limits our ability to draw conclusions regarding the likely longer term efficacy and costs of the procedure.

Conclusions

Based on the available evidence the following conclusions can be drawn on the cost-effectiveness of the ELGP procedure:

- There is a paucity of data on the effectiveness of ELGP beyond six months of follow-up. It appears that medication use at six months is reduced but the duration of this effect is as yet unknown.
- Total costs of the ELGP procedure are based on information provided by the applicant. Costs of pharmacotherapy are based on PBS data.
- At six months the net cost of ELGP (taking into consideration that patients are receiving no medication or repeat procedures) ranges from $3,488 –$4,455, although caution should be exercised when interpreting these cost estimates.
- A comprehensive economic evaluation should be conducted on ELGP when there are sufficient data available to do so.

Conclusions

Safety

Limited evidence was available to assess the safety of endoluminal gastroplication in patients with gastro-oesophageal reflux disease. From the data provided in the one case-series paper, it would appear that six months after the procedure a minority of patients had suffered adverse events. Some of the adverse events may be explained by the limited experience of surgeons performing the procedure. However more data are needed before a decision can be made regarding the safety of the procedure in patients with gastro-oesophageal reflux disease.

Effectiveness

Data at six months' follow-up, from the one case-series paper, indicate that ELGP may reduce some symptoms of GORD. However the paucity of good quality data limits the ability to draw any conclusions regarding the efficacy of this procedure. Further research focusing on randomised trials is needed in this area.

Cost-effectiveness

There is a paucity of data on the effectiveness of ELGP beyond six months of follow-up. It appears that medication use at six months is reduced but the duration of the effect is unknown as yet. A comprehensive economic evaluation should be conducted on ELGP when there are sufficient data available to do so.

Recommendation

Since there is currently insufficient evidence pertaining to endoluminal gastroplication for gastro-oesophageal reflux disease, public funding should not be supported at this time for this procedure.

The Minister for Health and Ageing accepted this recommendation on 26 June 2002.

Appendix A MSAC terms of reference and membership

The terms of reference of the MSAC are to advise the Commonwealth Minister for Health and Ageing on:

- the strength of evidence pertaining to new and emerging medical technologies and procedures in relation to their safety, effectiveness and cost-effectiveness and under what circumstances public funding should be supported;
- which new medical technologies and procedures should be funded on an interim basis to allow data to be assembled to determine their safety, effectiveness and cost-effectiveness;
- references related either to new and/or existing medical technologies and procedures; and
- undertake health technology assessment work referred by the Australian Health Ministers' Advisory Council (AHMAC), and report its findings to AHMAC.

The membership of the MSAC comprises a mix of clinical expertise covering pathology, nuclear medicine, surgery, specialist medicine and general practice, plus clinical epidemiology and clinical trials, health economics, consumers and health administration and planning:

Member	**Expertise or affiliation**
Dr Stephen Blamey (Chair)	general surgery
Professor Bruce Barraclough	general surgery
Professor Syd Bell	pathology
Dr Paul Craft	clinical epidemiology and oncology
Professor Ian Fraser	reproductive medicine
Associate Professor Jane Hall	health economics
Dr Terri Jackson	health economics
Ms Rebecca James	consumer health issues
Professor Brendon Kearney	health administration and planning
Mr Alan Keith	Assistant Secretary, Diagnostics and Technology Branch, Commonwealth Department of Health and Ageing
Associate Professor Richard King	internal medicine

Member	Expertise or affiliation
Dr Ray Kirk	health research
Dr Michael Kitchener	nuclear medicine
Mr Lou McCallum	consumer health issues
Emeritus Professor Peter Phelan	paediatrics
Dr Ewa Piejko	general practice
Dr David Robinson	plastic surgery
Professor John Simes	clinical epidemiology and clinical trials
Professor Richard Smallwood	Chief Medical Officer, Commonwealth Department of Health and Ageing
Professor Bryant Stokes	neurological surgery, representing the Australian Health Ministers' Advisory Council
Associate Professor Ken Thomson	radiology
Dr Douglas Travis	urology

Appendix B Supporting committee

Supporting committee for MSAC application 1047- Endoluminal gastroplication for gastro-oesophageal reflux disease

Dr John Primrose (Chair until 19 March 2002) MBBS (Hons) FRANZCR Senior Medical Adviser Diagnostics and Technology Branch Department of Health and Ageing	Medical Advisor to MSAC
Dr David Barton (Chair from 20 March 2002) MBBS, FRACGP Medical Adviser Diagnostics and Technology Branch Department of Health and Ageing	Co-opted Medical Adviser
Dr Don Cameron MBBS, FRACP Paediatric Gastroenterologist Royal Children's Hospital, Parkville	Co-opted Paediatric Gastroenterologist
Professor David Gotley MBBS, FRACS, DM Professor of Surgical Research University of Queensland and Consultant Surgeon Princess Alexandra Hospital, Brisbane	Nominated by the Royal Australasian College of Surgeons
Dr David Jarvis MBChB, FRACGP, BA, BLitt General Practitioner, ACT	Nominated by the Royal Australian College of General Practitioners
Mr Lou McCallum Member of MSAC and Chairperson, Consumers' Health Forum of Australia	Co-opted consumer representative
Dr Mark Schoeman MBBS, FRACP, PhD (Medicine) Head of Gastrointestinal Endoscopic Services Department of Gastrointestinal Medicine Royal Adelaide Hospital	Nominated by the Gastroenterological Society of Australia
Dr Doug Travis MBBS, FRACS Head of Urology Western Health, Melbourne	Member of MSAC
Ms Linda Marshall BSc, BA, MBA MSAC Project Manager	Diagnostic and Technology Branch Department of Health and Ageing

Appendix C Studies included in the review

n	Period	Population	Study type and level of evidence	Intervention	Comparator	Outcomes	Comments
Filipi et al 2001							
64	Not stated	Symptomatic GORD	Case series IV	Bard® EndoCinch™ device	None	GORD symptoms Quality of life Heartburn Regurgitation pH LOS pressure Oesophagitis Medication use Adverse events	Participants randomised to different plication techniques No investigators had performed procedure on human prior to study Unclear whether outcomes were assessed blinded Bias
Shafer et al 2001							
6	Not stated	Symptomatic GORD	Case series IV	Bard® EndoCinch™ device	None	pH LOS pressure Oesophagitis	Small study

Appendix D Endoluminal gastroplication abstracts

n	Entry criteria	Follow-up time	Outcomes assessed	Results (significance level, if reported)	Comments and adverse effects (no. patients)
Haber et al 2001					
25	Symptomatic GORD	24 months	Symptom scores Antisecretory medication use Need for subsequent surgery	Follow-up was available in 23/25 patients Complete success in 5 patients, partial in 7 patients and failure in 11 patients	8/11 patients underwent subsequent laparoscopic fundoplication Minimal and mild dysphagia (2)
Mahmood et al 2001					
20	Symptomatic GORD Inclusion and exclusion criteria stated	3 months	GORD symptoms pH scores Medication use Quality of life	Noted that only 11 patients have so far completed 3 months of follow-up Heartburn reduction 79% to 27% (P<0.01), heartburn severity from 72% to 24% (P<0.01) and regurgitation 64% to 18% (P<0.01). Mean pH DeMeester score reduced from 42 to 25 (P<0.01) 80% reduction in the use of PPIs and H_2RAs	Mild transient dysphagia (3) Oesophageal mucosal lacerations (2)
Park et al 2002; Swain et al 2000					
142	Symptomatic GORD	12 weeks (median)	GORD symptoms Manometry pH studies	Symptoms assessed by DeMeester symptom score improved from 1 to 5 (P<0.01). Median LES length increased from 2 to 3 cm (P<0.05); pressure increased from 5 to 8 mm Hg (P<0.05). The median % time pH <4 decreased from 8.5 to 3.7(P<0.05)	Minor haematemesis (2) Transient dysphagia (3) Endotracheal intubation (1) Underwent Nissen fundoplication (1)

n	Entry criteria	Follow-up time	Outcomes assessed	Results (significance level, if reported)	Comments and adverse effects (no. patients)
Raijman et al 2001					
88	Symptomatic GORD	Not stated	GORD symptoms	Heartburn resolved in 75/88 patients (85.2%), and <3 episodes a week in 5/88 pts (6%). Regurgitation resolved in 80/88 pts (90%), while the remainder reported no improvement.	
			Medication use	65 patients discontinued medication (74%).	
Singh et al 1999					
15	Symptomatic GORD without hiatus hernia, oesophageal ulcers or strictures	6 months (unclear)	Heartburn severity	Heartburn severity scores improved from 3 to 1.2	Misplaced stitches (3)
			Heartburn frequency	Heartburn frequency scores improved from 3 to 1	Broken suture (1)
			DeMeester scores	Regurgitation scores improved from 1.3 to 0.3	Device malfunction (1)
				Noted that all patients had stopped their anti reflux medication	Respiratory depression (1)
					Minor bleeding (1)

Appendix E Los Angeles classification of oesophagitis

Grade A	One (or more) mucosal break, no longer than 5 mm, that does not extend between the tops of mucosal folds
Grade B	One (or more) mucosal break, more than 5 mm long, that does not extend between the tops of two mucosal folds
Grade C	One (or more) mucosal break that is continuous between the tops of two or more mucosal folds but which involves less than 75% of the circumference
Grade D	One (or more) mucosal break that involves at least 75% of the oesophageal circumference

Source: Lundell et al 1999

Abbreviations

AIHW	Australian Institute of Health and Welfare
BESS	Bard EndoCinch Suturing System
BMI	body mass index
CCOHTA	Canadian Coordinating Office for HealthTechnology Assessment
ELGP	Endoluminal gastroplication
ENRD	Endoscopic-negative reflux disease
EVL	Oesophageal variceal ligation
GERD	Gastro-esophageal reflux disease
GORD	Gastro-oesophageal reflux disease
GSRS	Gastrointestinal symptom rating scale
H_2RAs	Histamine receptor antagonists
HTA	Health technology assessment
LES	Lower esophageal sphincter
LOS	Lower oesophageal sphincter
MSAC	Medical Services Advisory Committee
NHMRC	National Health and Medical Research Council
PBS	Pharmaceutical Benefits Scheme
PPIs	Proton pump inhibitors
RPBS	Repatriation Pharmaceutical Benefits Scheme

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