NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of flexible endoscopic treatment of pharyngeal pouch

A pharyngeal pouch is a pocket that may develop in the pharynx (throat), just above the entrance to the oesophagus (gullet); it can cause symptoms such as difficulty in swallowing, cough, and weight loss. In this procedure, an endoscope (a thin, flexible tube with a camera on the end) and special instruments are inserted through the mouth and are used to divide the tissue between the pouch and the gullet, to improve swallowing.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This IP overview was prepared in June 2014 and updated in December 2014.

Procedure name

- Flexible endoscopic treatment of pharyngeal pouch

Specialist societies

- ENT UK
- British Society of Gastroenterology.

Description

Indications and current treatment

A pharyngeal pouch, also known as Zenker's diverticulum, occurs when part of the pharyngeal lining herniates through the muscles of the pharyngeal wall. This occurs mainly in older people. Presenting symptoms include dysphagia, regurgitation of undigested food, halitosis, hoarseness, and chronic cough. It sometimes causes respiratory problems because of aspiration of the pouch contents into the lungs. As the pouch enlarges, symptoms become more severe and may result in weight loss and malnutrition. In a small proportion of patients, carcinoma may develop in the pouch.

The traditional treatment for pharyngeal pouch involves open surgery to the neck. Open diverticulectomy involves complete removal of the pouch. Alternatively, the muscle responsible for pouch formation may be divided (sometimes combined with inversion or invagination of the pouch). Endoscopic techniques using rigid endoscopes are also used, in which the wall between the pouch and the oesophagus is divided using diathermy, lasers or a stapling technique.

What the procedure involves

Flexible endoscopic treatment of a pharyngeal pouch aims to divide the septum between the diverticulum and oesophagus, without the need for hyperextension of the neck that may be necessary when using a rigid endoscope. It can be done without general anaesthesia and may be particularly useful for elderly patients with significant comorbidity or spinal stiffness.

Flexible endoscopic treatment of a pharyngeal pouch is done with the patient under sedation or general anaesthesia. Initially, a diagnostic endoscopy is done, identifying the normal oesophageal lumen and allowing a nasogastric tube to be inserted. Under flexible endoscopic guidance, the septum (containing the cricopharyngeus muscle) is exposed and divided. The flexible endoscope can be used with a variety of different accessories (hood, cap, overtube) to aid the procedure. Division of the septum reconnects the pouch lumen with the normal pharyngo-oesophageal pathway and also divides part of the sphincter muscle implicated in pouch development. More than 1 treatment session may be needed to achieve adequate division of the septum and relief of symptoms.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to flexible endoscopic treatment of pharyngeal pouch. Searches were conducted of

the following databases, covering the period from their commencement to 5 November 2014: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies, identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with pharyngeal pouch.
Intervention/test	Flexible endoscopic treatment of pharyngeal pouch.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 508 patients from 1 non-randomised comparative study and 7 case series[1–8].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on flexible endoscopic treatment of pharyngeal pouch

Study 1 Repici A (2011)

Details

Study type	**Non-randomised comparative study (retrospective)**
Country	Italy
Recruitment period	2000–6
Study population and number	**n=58 (28 flexible endoscope versus 30 endoscopic stapling)** Patients with symptomatic pharyngeal pouch Mean size of diverticulum (cm): 3.9 versus 4.2
Age and sex	Mean 72 years versus 69 years; 72% (41/58) male
Patient selection criteria	Exclusion criteria: diverticula that did not arise from the characteristic area for Zenker diverticula (Killian's triangle); post-laryngectomy pseudodiverticula; multiple oesophageal diverticula.
Technique	Flexible endoscopic treatment was done under conscious sedation with the patient in the left lateral position, using an Olympus videogastroscope with a mucosectomy, straight-end, transparent cap fixed on the scope tip. The septum was cut with a needle-knife. Endoscopic stapling was done under general anaesthesia using a bivalve diverticuloscope (Storz GMBH) introduced orally with hyperextended neck.
Follow-up	**Median 20 months (range 16–58)**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: During follow-up, 2 patients died because of unrelated causes (treatment groups not described). Long-term follow-up was obtained through telephone interview with the patients or referral doctor.

Study design issues: Retrospective review of data extracted from medical records. Patient selection was not described. The severity of dysphagia was scored according to frequency (0=absent, 1=occasional [once or twice per week], 2=frequent [daily], 3=constant [at each meal]). The scale used for measuring regurgitation was not described; the mean preoperative regurgitation score was only reported for the whole study group.

Study population issues: The 2 groups were similar with regard to gender, diverticulum size, and degree and severity of preoperative symptoms. Both groups had similar preoperative symptoms, consisting of dysphagia, regurgitation and weight loss.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **58 (28 vs 30)**

Mean dysphagia scores (0–3 with lower scores indicating less severe symptoms)

	Flexible endoscopic treatment n=28	**Endoscopic stapling n=30**
Preoperative	2.8	2.7
Postoperative	1.58	1.21

Improvements in both groups were statistically significant (p values not stated)

Mean regurgitation scores (scale not described)

	Flexible endoscopic treatment n=28	**Endoscopic stapling n=30**
Preoperative	1.42 (mean score for all patients)	
Postoperative	0.68	0.53

Improvements in both groups were statistically significant (p values not stated)

Revision within 6 months of index treatment

- Flexible endoscopic treatment=2 patients.
- Endoscopic stapling=3 patients.

Revision was done by endoscopic treatment to take down a minimal residual septum at the bottom of the diverticular wall, which produced mild but persistent dysphagia.

Recurrence of dysphagia during follow-up (among 56 surviving patients)

- Flexible endoscopic treatment=1 patient (at 14 months).
- Endoscopic stapling=2 patients (at 15 and 18 months, respectively).

Retreatment of the residual bridge with 1 or 2 sessions of endoscopic treatment provided successful relief of symptoms.

There was no statistically significant difference in mean length of hospital stay between the 2 groups (2.4 days for flexible endoscopic treatment versus 3.4 days for endoscopic stapling).

Safety

Complications

Flexible endoscopic treatment group

- 1 cervical subcutaneous emphysema diagnosed in the first 12 hours after treatment – resolved without any sequelae.

Endoscopic stapling group

- 1 perforation of the diverticular pouch – successfully treated conservatively.
- 1 dental avulsion (no further details reported).

Note: the discussion of the paper states that there were three dental injuries, because of trauma to the central maxillary region during placement of the diverticuloscope, in the endoscopic stapling group. These were not described in the main results section.

There were no cases of mediastinitis, palsy of the recurrent laryngeal nerve, or clinical fistula.

Study 2 Huberty (2013)

Details

Study type	**Case series (retrospective)**
Country	Belgium
Recruitment period	2002–11
Study population and number	**n=150** Patients with pharyngeal pouch Median size of diverticulum=3 cm (range 1–8)
Age and sex	Median 73 years (range 42–94); 64% (96/150) male
Patient selection criteria	No inclusion or exclusion criteria were described. Diagnosis of pharyngeal pouch was based on results of barium swallow (43%), oesophagogastroscopy (24%), both (32%) or chest CT (1%).
Technique	Procedure was done under conscious sedation or general anaesthesia with patients in the left lateral position, using a soft diverticuloscope (ZD overtube, Cook Endoscopy) placed on an endoscope. A needle-knife (Endo-Flex, Voerde) was used to incise the septum. At the end of the procedure, 1–3 endoclips were placed to prevent perforation or bleeding. After treatment, all patients had a barium swallow on the same day to exclude perforation.
Follow-up	**Median 43 months (range 13–121)**
Conflict of interest/source of funding	1 of the authors received research support from Cook Endoscopy.

Analysis

Follow-up issues: The dysphagia score at 1 month follow-up was only available for 69% (103/150) of patients; the remaining patients had cancelled or declined their follow-up appointment, most of them being referred from another city or another country. At the end of follow-up, 89% (134/150) of patients were contacted: 11 patients died within 12 months of treatment and 16 (11%) were lost to follow-up.

Study design issues: Retrospective single centre study. Clinical success was defined as a residual dysphagia score ≤1 without a need for reintervention. Recurrence was defined as recurrent dysphagia (score >2) after initial clinical success, with or without complementary therapy. Dysphagia was scored from 0-4 (0=no dysphagia, 1=dysphagia to solids, 2=dysphagia to semi-solids, 3=dysphagia to liquids, 4=aphagia).

Study population issues: 5% (8/150) of patients had previous treatment in another institution but were still symptomatic (5 surgical only, 1 endoscopic only, 2 surgical and endoscopic).

Key efficacy and safety findings

Efficacy

Number of patients analysed: **150**

8 patients had no improvement of their symptoms at the time of discharge.

The mean dysphagia score dropped from 1.88 at baseline to 0.29 at 1 month follow-up ($p<0.01$). In the patients with long term follow-up, the mean dysphagia score dropped from 1.86 at baseline to 0.34 at the long term follow-up ($p<0.01$).

Dysphagia score

Score	Baseline n=150	1-month follow-up n=103	Long term follow-up (median 43 months) n=134
0	2.0% (n=3)	83.5% (n=86)	79.1% (n=106)
1	20.7% (n=31)	5.8% (n=6)	8.2% (n=11)
2	68.7% (n=103)	8.7% (n=9)	11.9% (n=16)
3	8.7% (n=13)	1.9% (n=2)	0.7% (n=1)
4	0%	0%	0%

Other symptoms, number of patients (%)

Symptom	Before treatment, n=150	Long term follow-up, n=134
Regurgitation	109 (72.7%)	16 (11.9%)
Aspiration	14 (9.3%)	2 (1.5%)
Chronic cough	40 (26.7%)	2 (1.5%)
Pneumonia	11 (7.3%)	1 (0.7%)
Weight loss	28 (18.7%)	0
Heartburn	14 (9.3%)	0
Halitosis	9 (6%)	0
Hypersialorrhea	2 (1.3%)	0
Odynophagia	2 (1.3%)	0
Dysphonia	2 (1.3%)	0

Symptom recurrence=23.1% (31/134) (after a median time of 7 months, range 1–82). 23 patients had a second treatment and 5 patients had a third treatment. After retreatment, 1 patient remained symptomatic.

Safety

Adverse events

- Increased C-reactive protein levels and fever (suspected perforations)=2.0% (3/150)
- Aspiration pneumonia after extubation=0.7% (1/150)
- Subcutaneous emphysema=0.7% (1/150) (spontaneously resolved)

All these adverse events were managed conservatively and resolved within 2–14 days without the need for reintervention.

Study 3 Mulder CJJ (1999)

Details

Study type	**Case series**
Country	The Netherlands
Recruitment period	1993–1997
Study population and number	**n=125** Patients with symptomatic pharyngeal pouch Mean size of diverticulum=4.5 cm (range 2–12)
Age and sex	Median 77 years (range 41–100); 61% (76/125) male
Patient selection criteria	Before 1995, only patients in poor condition with severe contraindications for general anaesthesia were included. After this period, patients without contraindications for surgery were also included.
Technique	Procedures were done under sedation, using a gastroscope and argon plasma coagulation with or without monopolar forceps coagulation. The number of treatment sessions ranged from 1–12 (mean=2); the interval between the endoscopies was 1 day and the maximum number of treatment sessions during 1 hospitalisation was 4. Radiography was done 2–4 hours after the last treatment session during hospitalisation.
Follow-up	**Not reported**
Conflict of interest/source of funding	Not reported

Analysis

Study design issues: Single centre study.

Study population issues: 15 patients had been previously treated but remained symptomatic. About 15%–20% of the study population had Barrett's oesophagus.

Other issues: The authors note that the mean number of treatment sessions is influenced by the learning curve of the team and by the poor general condition of the patients being treated.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **125** All patients were treated successfully. In all patients, symptomatic improvement was seen after 1 or 2 treatments. 54% (67/125) of patients had a follow-up endoscopy (timing not reported) and a residual bridge 2–15 mm was diagnosed in all of them. All were treated again with argon plasma coagulation and/or precut needle. The majority had no difficulty swallowing solid food but mucus and sputum were a problem for a subgroup.	**Complications** • Subcutaneous emphysema=13.6% (17/125) • Mediastinal emphysema=4.0% (5/125) • Bleeding=1.6% (2/125) The majority of patients (70% to 90%) had a sore throat for a few days after treatment.

Study 4 Ishioka S (1995)

Details

Study type	**Case series**
Country	Brazil
Recruitment period	1982–1992
Study population and number	**n=42** Patients with symptomatic pharyngeal pouch Mean size of diverticulum=4.2 cm (range 2–11)
Age and sex	Mean 68 years (range 46–102); 69% (29/42) male
Patient selection criteria	No inclusion and exclusion criteria were described.
Technique	Procedures were done under sedation, using an Olympus endoscope with a diathermic knife and an electrosurgery system. Small diverticula were treated in only 1 session but several sessions were needed for larger diverticular (mean number of sessions=2). The intervals between sessions varied from 2–3 weeks.
Follow-up	**Mean 38 months (range 12–96)**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: No losses to follow-up were described. All patients were submitted to endoscopic evaluation 2 and 4 weeks after the end of treatment; 5 patients had manometric studies. Patients were evaluated personally or contacted by phone 12, 24 and 60 months after the procedure, and asked about dysphagia and weight loss.

Study design issues: Single centre study. Dysphagia was scored from 0–4 (0=no dysphagia, 1=dysphagia to solids, 2=dysphagia to mixed food, 3=dysphagia to liquids, 4=complete dysphagia).

Study population issues: 61% (26/42) of patients had concomitant diseases such as cardiopulmonary failure, chronic lung disease, brain stroke and choledocholithiasis; 6 patients had a sliding hiatal hernia with no signs of reflux oesophagitis.

Key efficacy and safety findings

<table>
<tr><td>Efficacy</td><td>Safety</td></tr>
<tr><td>Number of patients analysed: 42
Dysphagia score
<table>
<tr><th>Score</th><th>Baseline n=42</th><th>After treatment n=42</th></tr>
<tr><td>0</td><td>0%</td><td>92.8% (n=39)</td></tr>
<tr><td>1</td><td>21.4% (n=9)</td><td>7.2% (n=3)</td></tr>
<tr><td>2</td><td>47.6% (n=20)</td><td>0%</td></tr>
<tr><td>3</td><td>26.1% (n=11)</td><td>0%</td></tr>
<tr><td>4</td><td>4.9% (n=2)</td><td>0%</td></tr>
</table>
All patients with a significant weight loss (mean 6 kg) had a considerable recuperation during the follow-up period (mean 4 kg).

Manometric study: upper oesophageal sphincter pressure (H_2O cm) before and after treatment (5 patients)
<table>
<tr><td>Patient</td><td>Before treatment</td><td>After treatment</td></tr>
<tr><td>1</td><td>55</td><td>30</td></tr>
<tr><td>2</td><td>68</td><td>24</td></tr>
<tr><td>3</td><td>58</td><td>30</td></tr>
<tr><td>4</td><td>52</td><td>35</td></tr>
<tr><td>5</td><td>50</td><td>15</td></tr>
<tr><td>Mean</td><td>54.6</td><td>26.8</td></tr>
<tr><td>Standard deviation</td><td>10.1</td><td>7.7</td></tr>
</table>
$p<0.05$
Recurrent dysphagia during follow-up=7.1% (3/42) (at 12, 22 and 60 months after initial treatment respectively). All these patients had radiological and endoscopic evidence of a remaining diverticular septum. Retreatment improved dysphagia in all 3 patients.</td><td>Complications
Cervical emphysema=2.4% (1/42) (resolved spontaneously when the nasogastric tube was left in place and antibiotics were administered for 1 week)
Bleeding=2.4% (1/42) (endoscopic haemostasis with injection of an adrenaline solution resulted in permanent haemostasis; the patient received 1 unit of blood transfusion)</td></tr>
</table>

Study 5 Rabenstein T (2007)

Details

Study type	**Case series (retrospective)**
Country	Germany
Recruitment period	2002–6
Study population and number	**n=41** Patients with symptomatic pharyngeal pouch
Age and sex	Mean 73 years; 66% (27/41) male
Patient selection criteria	Inclusion and exclusion criteria not reported. 86% of patients had a barium study to diagnose the pharyngeal pouch. All patients had at least moderate dysphagia and at least mild regurgitation before treatment.
Technique	Procedures were done under sedation, generally using a gastroscope (Fujinon) and a standard mucosectomy cap on the tip of the scope. Argon plasma coagulation was used to cut the diverticulum. Treatment was done in 1–10 sessions (mean=3).
Follow-up	**Mean 16 months (range 6–43)**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Follow-up started 3 months after the last scheduled treatment. Longer term follow-up data were only used from patients treated between 2002 and 2005 (n=34). These patients and/or their family doctors were contacted by phone and were questioned about clinical success, including patient satisfaction and late complications.

Study design issues: Retrospective, single-centre centre with consecutive patients. Symptoms were assessed using 3 grades (none=complete success, mild=partial success, moderate or unchanged=no success). Recurrence was defined as moderate to severe symptoms after initial complete or partial success.

Study population issues: The patients were largely elderly, with significant comorbidity. 61% of patients had severe dysphagia and significant regurgitation. At the time of admission, 5 patients had pneumonia or tracheobronchitis due to recurrent aspiration, 3 patients had significant malnutrition or cachexia, and 4 patients had significant impaction of food in the pharyngeal pouch with incomplete clearance during the first endoscopy. Medical treatment was given before flexible endoscopic treatment could be started.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **41** **Clinical success of treatment after 3 months=95.1% (39/41)** • Complete relief of symptoms=58.5% (24/41) • Major relief of symptoms=36.6% (15/41) • No or insufficient relief of symptoms=4.9% (2/41) **Symptomatic recurrence during follow-up=14.7% (5/34)** (at 8, 9, 13, 15 and 18 months respectively) **Retreatment=14.7% (5/34)** No patients had a rigid endoscopic procedure.	**Complications** • Fever lasting <24 hours=7.3% (3/41) • Infections with fever lasting >24 hours=9.8% (4/41) (there were no organ manifestations in 3 patients and tracheobronchitis and pneumonia in 1 patient. Antibiotics were given and perforation and mediastinitis were excluded by appropriate diagnostic tests.) • Perforation=2.4% (1/41) (a 4 cm deep bridge was dissected in 1 session; the patient developed skin emphysema some hours after endoscopy and the perforation was confirmed by repeat endoscopy. The patient was kept nil by mouth, with tube feeding, for 7 days, and received antibiotic therapy for 10 days, leading to complete resolution.)

Study 6 Costamagna C (2007)

Details

Study type	**Case series** (comparing 2 different techniques for flexible endoscopic treatment)
Country	Italy
Recruitment period	2001–2006
Study population and number	**n=39** Patients with symptomatic pharyngeal pouch Median length of diverticulum=4 cm (range 2–8)
Age and sex	Age range 47–86 years; 59% (23/39) male
Patient selection criteria	Not reported. Pharyngeal pouch was diagnosed at endoscopy in 67% (26/39) and by barium swallow in the remaining patients. All patients complained of moderate to severe dysphagia and /or pharyngo-oral regurgitation.
Technique	Procedures were done under conscious or deep sedation, with the patient in the left lateral position, and using video endoscopes (Olympus Optical company, Japan) with an oblique-end transparent cap fixed at the tip (2001–5) or a soft diverticuloscope (ZD overtube, Wilson-Cook, USA) specifically designed for flexible diverticulotomy (2005–6). The septum was cut with a needle-knife. During the last 3 years of the study, a long endoclip was placed at the bottom of the cut for prophylaxis against microscopic perforation.
Follow-up	**Range 3–60 months (median 6.5 months in diverticuloscope group and 36 months in the cap group)**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Patients in the diverticuloscope group were treated more recently and so have a shorter follow-up than patients treated by the cap technique. No losses to follow-up were described.

Study design issues: Retrospective analysis of prospectively collected data, consecutive patients, single-centre study.

Study population issues: 28% (11/39) of patients had severe comorbidities, such as coronary artery disease, congestive heart failure, hypertension, and pulmonary insufficiency.

Other issues: The authors note that the clinical remission rates are based on the presence or absence of a pool of symptoms, including achalasia. If dysphagia alone were used, the remission rate for cap-assisted treatment would have been 54% rather than the reported 29%.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **39** The procedure time was significantly longer in the cap-assisted group than it was for the diverticuloscope group (median 30 versus 15 minutes, p=0.002). All symptoms had decreased significantly at 1 month after treatment. Remission rates after 1 month (defined as the disappearance of all symptoms or the occasional persistence of no more than 2 symptoms) • Cap-assisted technique=43% (12/28) • Diverticuloscope technique=91% (10/11) Remission rates at follow-up (mean 36 months for cap-assisted group, 6.5 months for diverticuloscope group) • Cap-assisted technique=29% (8/28) • Diverticuloscope technique=82% (9/11), p=0.004 **Retreatments=20.5% (8/39)** (4 diverticuloscope, 1 cap, 2 open surgery, 1 endostapling)	**Complications** *Cap-assisted group (n=28)* • Minor bleeding=14.3% (4/28) (controlled with thermal contact and noncontact methods) • Macroscopic perforation=10.7% (3/28) (immediately closed using endoclips) • Microscopic perforation=7.1% (2/28) (cervical emphysema and mild pneumomediastinum were observed within the first 24 hours. Patients were treated conservatively and symptoms resolved within 2–4 days.) There were no complications in the group of patients treated by the diverticuloscope approach.

Study 7 Vogelsang A (2007)

Details

Study type	**Case series (retrospective)**
Country	Germany
Recruitment period	2001–4
Study population and number	**n=31** Patients with symptomatic pharyngeal pouch
Age and sex	Median 69 years (range 52–92); 58% (18/31) male
Patient selection criteria	Not reported. Pharyngeal pouch diagnosis was confirmed by barium swallow.
Technique	Procedures were done under conscious sedation, using a gastroscope (Olympus, Japan) with a transparent cap fixed at the tip. The septum was cut with a needle-knife. Bleeding was treated by electrocoagulation.
Follow-up	**Mean 26 months (range 14–49)**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: There were no losses to follow-up. Patients were contacted by telephone to collect follow-up data.

Study design issues: Retrospective analysis, consecutive patients, single-centre study. Dysphagia was assessed on a numeric analogue scale from 0 (no dysphagia) to 10 (dysphagia on every swallow). The indication for repeat treatment was an increase in the grade of dysphagia of greater than 2 on the scale and patient request for retreatment. Clinical success was defined as dysphagia scores of between 0 and 5, without demand for reintervention.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **31**

All patients had improvement in dysphagia at time of discharge from hospital.

Group 1: 21 patients treated in a single session (mean follow-up=24 months)

Dysphagia score	Before treatment	At follow-up
Intensity		
Drinking	3.4	0.4
Semi-solid food	4.6	0.1
Solid food	7.3	1.2
Very solid food	8.6	2.4
Frequency		
Drinking	3.1	0.5
Solid food	7.6	1.4
Very solid food	9.0	2.2

Group 2 –10 patients with repeat treatment because of recurrent symptoms (mean follow-up=29 months; mean interval between treatments=6 months)

Dysphagia score	Before treatment	At follow-up
Intensity		
Drinking	5.3	0.9
Semi-solid food	5.4	1.0
Solid food	8.2	2.4
Very solid food	9.0	3.5
Frequency		
Drinking	6.8	0.9
Solid food	9.2	2.3
Very solid food	9.4	3.4

At the time of follow-up interview, 12.9% (4/31) of patients wanted further treatment. One patient decided to undergo surgery because of persistent dysphagia 8 months after the last procedure.

Clinical success=84% (26/31) (based on intention to treat)

Patients successfully treated with a single session=61% (19/31)

Of 31 patients, 13 reported weight loss before the procedure with a mean loss of 8.5 kg. The weight of these patients increased by an average of 5.7 kg during the study period.

Safety

Complications

- Mild intraoperative bleeding=3.2% (1/31) (managed with argon plasma coagulation)
- Minor perforation=22.6% (7/31) (patients developed mediastinal or cervical emphysema confirmed by x-ray or CT scan, without perforation seen on contrast swallow. These patients received antibiotics for 5–7 days.)

There were no major complications such as obvious perforation or severe bleeding needing re-intervention or surgery.

Study 8 Case DJ (2010)

Details

Study type	**Case series**
Country	USA
Recruitment period	2006–10
Study population and number	**n=22** Patients with symptomatic pharyngeal pouch
Age and sex	Median age 84.5 years; 59% (13/22) male
Patient selection criteria	Not reported. Pharyngeal pouch was diagnosed by barium swallow and confirmed at the time of endoscopy.
Technique	Procedures were done under moderate sedation (general anaesthesia was needed in 2 patients and monitored anaesthesia care in 1), with the patient in the left lateral position, and using standard flexible endoscopes. The septum was cut with a needle-knife. A transparent cap was used for 3 patients. All patients had only 1 treatment session.
Follow-up	**Mean 13 months**
Conflict of interest/source of funding	Not reported

Analysis

Follow-up issues: There were no losses to follow-up. Follow up continued until patient death or last telephone contact.

Study design issues: Retrospective analysis, consecutive patients, single-centre study.

Study population issues: 23% (5/22) of patients were deemed to be nonoperative candidates; 18% (4/22) of patients had prior therapy that was unsuccessful.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **22** Initial symptomatic improvement=100% (22/22) Outcome at last follow-up: • Complete/near-complete symptom resolution=68.2% (15/22) • Moderate symptom improvement=13.6% (3/22) • Complete symptom recurrence=18.2% (4/22)	**Complications** • Minor bleeding=22.7% (5/22) (described as 'not clinically meaningful') • Oesophageal perforation=27.3% (6/22) (4 patients were hospitalised for 3–5 days and 2 were observed overnight.) • Neck abscess=4.5% (1/22) (developed 1 week after treatment; abscess was surgically drained and the patient stayed in hospital for 9 days.)

Efficacy

Symptom resolution

A non-randomised study of 58 patients who had flexible endoscopic treatment or endoscopic stapling using a rigid endoscope reported mean dysphagia scores (measured on a scale of 0 to 3, with lower values meaning less severe symptoms) of 1.6 and 1.2 respectively after treatment compared with 2.8 and 2.7 respectively before treatment (improvements in both groups were stated as being statistically significant but p values were not reported)[1]. A case series of 150 patients reported that the mean dysphagia score dropped from 1.9 at baseline to 0.3 at 1 month follow-up ($p<0.01$). This improvement was reported in the 134 patients with longer-term follow-up (median follow-up=43 months). Of the 150 patients, 8 had no improvement of their symptoms at the time of discharge from hospital[2]. A case series of 42 patients reported that 93% (39/42) of patients had no dysphagia after a mean follow-up of 38 months[4]. A case series of 31 patients reported that 61% (19/31) of patients were successfully treated by a single procedure, with a mean follow-up of 24 months; the clinical success rate based on intention to treat was 84% (26/31)[7]. A case series of 22 patients treated by a single procedure reported initial symptomatic improvement in 100% (22/22) of patients. After a mean follow-up of 13 months, 68% (15/22) of patients had complete or near-complete symptom resolution and 14% (3/22) had moderate symptom improvement[8].

Symptom recurrence

The non-randomised study of 58 patients reported recurrence of dysphagia in 1 patient treated by flexible endoscopic treatment (at 14 months) and in 2 patients treated by endoscopic stapling (at 15 and 18 months respectively). Retreatment of the residual bridge with 1 or 2 sessions of endoscopic treatment provided successful relief of symptoms in all 3 patients[1]. The case series of 150 patients reported symptom recurrence in 23% (31/134) of patients after a median follow-up of 7 months (range 1–82). Of the 31 patients with recurrence, 23 patients had a second treatment and 5 patients had a third treatment. After retreatment, 1 patient remained symptomatic[2]. The case series of 42 patients reported recurrent dysphagia in 7% (3/42) of patients during follow-up; these occurred at 12, 22 and 60 months after initial treatment respectively. Retreatment improved dysphagia in all 3 patients[4]. A case series of 41 patients reported symptomatic recurrence during follow-up in 15% (5/34) of patients (at 8, 9, 13, 15 and 18 months respectively)[5].

Safety

Oesophageal perforation

Oesophageal perforation was reported in 27% (6/22) of patients in a case series of 22 patients (method of diagnosis not described): 4 patients were hospitalised

for 3–5 days and 2 were observed overnight[8]. Perforation (confirmed by endoscopy) was reported in 1 patient in a case series of 41 patients: the patient was kept nil by mouth, with tube feeding, for 7 days, and received antibiotic therapy for 10 days, leading to complete resolution[5]. Macroscopic perforations were reported in 11% (3/28) of patients treated by cap-assisted flexible endoscopic treatment in a case series of 39 patients: these were immediately closed using endoclips. In the same study, microscopic perforation was reported in 7% (2/28) of patients treated by cap-assisted flexible endoscopic treatment: cervical emphysema and mild pneumomediastinum were observed within the first 24 hours; patients were treated conservatively and symptoms resolved within 2–4 days[6]. Suspected perforation was reported in 2% (3/150) of patients in a case series of 150 patients; the patients had increased C-reactive protein levels and fever. They were managed conservatively and their symptoms and signs resolved within 2–14 days[2]. 'Minor perforation' was reported in 23% (7/31) of patients in a case series of 31 patients: the patients developed mediastinal or cervical emphysema confirmed by x-ray or CT scan, without perforation seen on contrast swallow, and were treated with antibiotics for 5–7 days[7].Cervical subcutaneous emphysema was reported in 1 patient treated by flexible endoscopic treatment in a non-randomised comparative study of 58 patients treated by flexible endoscopic treatment or endoscopic stapling; it was diagnosed in the first 12 hours after treatment and resolved without any sequelae[1]. Subcutaneous emphysema that spontaneously resolved was reported in 1 patient in a case series of 150 patients[2]. Subcutaneous emphysema was reported in 14% (17/125) of patients and mediastinal emphysema was reported in 4% (5/125) in a case series of 125 patients (management not described)[3]. Cervical emphysema was reported in 1 patient in a case series of 42 patients: it resolved spontaneously when the nasogastric tube was left in place and antibiotics were administered for 1 week[4].

Bleeding

Bleeding was reported in 2% (2/125) of patients in the case series of 125 patients (not further described)[3]. Bleeding was reported in 1 patient in the case series of 42 patients: endoscopic haemostasis with injection of an adrenaline solution resulted in permanent haemostasis; the patient received 1 unit of blood transfusion[4].

Infection

A neck abscess developed 1 week after treatment in 1 patient in the case series of 22 patients. This was surgically drained and the patient stayed in hospital for 9 days[8]. Infection with fever lasting more than 24 hours was reported in 10% (4/41) of patients in the case series of 41 patients: there were no organ manifestations in 3 patients and tracheobronchitis and pneumonia in 1 patient. Antibiotics were given and perforation and mediastinitis were excluded by appropriate diagnostic tests[5].

Aspiration pneumonia

Aspiration pneumonia after extubation was reported in 1 patient in the case series of 150 patients[2].

Validity and generalisability of the studies

- There are no randomised controlled trials. Some of the studies note that for patients treated by this technique other surgical treatments such as rigid endoscopy or open surgery would not be suitable.
- Most of the studies are small, retrospective case series.
- None of the studies list detailed inclusion and exclusion criteria but most state that a proportion of patients had significant comorbidities. In 1 study, only patients in poor condition with severe contraindications for general anaesthesia were initially included in the study. After 1995, patients without contraindications for surgery were also included[3].
- The techniques used vary between studies. There are a number of different devices that can be used: 1 study compares cap-assisted flexible treatment with a flexible diverticuloscope[6].
- The definition of clinical success is not consistent between studies – it may be defined as symptom resolution or improvement.
- Some studies report efficacy outcomes after just 1 treatment session whereas other report efficacy outcomes after repeated sessions.
- Most studies lack objective symptom assessments.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Endoscopic stapling of pharyngeal pouch. NICE interventional procedure guidance 22 (2003). Available from http://www.nice.org.uk/guidance/IPG22

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their specialist society or royal college. The advice received is their individual opinion and does not represent the view of the society.

Dr M Banks, Professor S Ishaq, Professor K Ragunath (British Society of Gastroenterology), Professor N Kumar, Mr V Paleri (ENT UK).

- Four specialist advisers have never performed the procedure and 1 performs it regularly.
- Four specialist advisers consider the procedure to be definitely novel and of uncertain safety and efficacy; 1 considers it to be established practice in Europe but new to the UK.
- Comparators are open diverticulotomy and rigid endoscopy under general anaesthesia and endoscopic stapling.
- Theoretical adverse events: bleeding, perforation, infection, mediastinal or cervical emphysema, aspiration, pneumonia, cervical abscess, mediastinitis, septicaemia, death.
- Adverse events reported in literature: bleeding, perforation, mediastinal or cervical emphysema, aspiration, pneumonia, cervical abscess, mediastinitis.
- The key efficacy outcome is resolution or reduction of dysphagia.
- There are concerns about the efficacy of the procedure because there are no randomised controlled trials.
- One adviser noted that the procedure is not widely taken up by the gastrointestinal community in the UK. This may be due to awareness of the flexible endoscopic approach and training issues. Also, there are competing specialties (ear nose and throat [ENT] compared with gastroenterology).
- Four advisers thought that the procedure will have a minor impact on the NHS, in terms of numbers of patients and use of resources; 1 adviser thought it would have a moderate impact.

Patient commentators' opinions

NICE's Public Involvement Programme sent 10 questionnaires to 1 NHS trust for distribution to patients who had the procedure (or their carers). NICE received 2 completed questionnaires.

The patient commentators' views on the procedure were consistent with the published evidence and the opinions of the specialist advisers.

Issues for consideration by IPAC

None other than those described above.

References

1. Repici A, Pagano N, Fumagalli U et al. (2011) Transoral treatment of Zenker diverticulum: flexible endoscopy versus endoscopic stapling. A retrospective comparison of outcomes. Diseases of the Esophagus 24: 235–9
2. Huberty V, El Bacha S, Blero D et al. (2013) Endoscopic treatment for Zenker's diverticulum: long-term results (with video). Gastrointestinal Endoscopy 77: 701–7
3. Mulder CJ (1999) Zapping Zenker's diverticulum: gastroscopic treatment. Canadian Journal of Gastroenterology 13: 405–7
4. Ishioka S, Sakai P, Maluf Filho F et al. (1995) Endoscopic incision of Zenker's diverticula. Endoscopy 27: 433–7
5. Rabenstein T, May A, Michel J et al. (2007) Argon plasma coagulation for flexible endoscopic Zenker's diverticulotomy. Endoscopy 39: 141–5
6. Costamagna G, Iacopini F, Tringali A et al. (2007) Flexible endoscopic Zenker's diverticulotomy: cap-assisted technique vs. diverticuloscope-assisted technique. Endoscopy 39: 146–52
7. Vogelsang A, Preiss C, Neuhaus H et al. (2007) Endotherapy of Zenker's diverticulum using the needle-knife technique: long-term follow-up. Endoscopy 39: 131–6
8. Case DJ, Baron TH (2010) Flexible endoscopic management of Zenker diverticulum: the Mayo Clinic experience. Mayo Clinic Proceedings 85: 719–22

Appendix A: Additional papers on flexible endoscopic treatment of pharyngeal pouch

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Al-Kadi AS, Maghrabi AA, Thomson D et al. (2010) Endoscopic treatment of Zenker diverticulum: results of a 7-year experience. Journal of the American College of Surgeons 211: 239-243	n=18 FU=mean 28 months	Dysphagia score and regurgitation symptoms improved substantially after treatment. 1 patient had a microperforation treated conservatively and 2 patients had re-do procedures for persistence of dysphagia.	Studies with more patients or longer follow-up are included.
Christiaens P, De Roock W, Van Olmen A et al. (2007) Treatment of Zenker's diverticulum through a flexible endoscope with a transparent oblique-end hood attached to the tip and a monopolar forceps. Endoscopy 39: 137–40	n=21 FU=1 month	Complete relief of dysphagia at 1 month=100% (21/21) Recurrence=9.5% (2/21) after the first session. These patients were successfully treated again in the same way. Adverse events=transient cervical emphysema in 1 patient.	Studies with more patients or longer follow-up are included.
Dzeletovic I, Ekbom DC, Baron TH (2012) Flexible endoscopic and surgical management of Zenker's diverticulum. Expert review of gastroenterology & hepatology 6: 449-465	Review n=449	The flexible endoscopic technique is used when there is a high risk of general anesthesia, or neck extension is contraindicated. Some centres use flexible endoscopy as the initial treatment option. Due to a lack of prospective studies, the treatment choice should be tailored to the individual patient and local expertise	No meta-analysis – all the described studies are included in table 2 or the appendix.
Efthymiou M, Raftopoulos S, Marcon N (2012) Flexible endoscopic septoplasty for bilobed Zenker's diverticulum. Gastrointestinal Endoscopy 75: 1110-1111	n=1	Flexible endoscopic septoplasty with a needle-knife can be a successful therapy for bilobed diverticular.	Case report.
Evrard S, Le Moine O, Hassid S et al. (2003) Zenker's diverticulum: a new endoscopic treatment with a soft diverticuloscope. Gastrointestinal Endoscopy 58: 116-120	n=30 FU=median 12.5 months	All patients were successfully treated in a single session. In one patient, dysphagia persisted but was milder than before the treatment. A complication occurred in 4 patients (13%); in one (3%), it was severe. During follow-up dysphagia recurred in one patient 1 year after the initial procedure.	Studies with more patients or longer follow-up are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Hashiba K, de Paula AL, da Silva JG et al. (1999) Endoscopic treatment of Zenker's diverticulum. Gastrointestinal Endoscopy 49: 93-97	n=47 FU=1 day-1 year	96% (45/47) of patients had no dysphagia or only occasional, mild dysphagia during the postoperative course. No fistula, no recurrent laryngeal paralysis, and no deaths occurred.	Studies with more patients or longer follow-up are included.
Hondo FY, Maluf-Filho F, Giordano-Nappi, JH et al. (2011) Endoscopic treatment of Zenker's diverticulum by harmonic scalpel. Gastrointestinal Endoscopy 74: 666-671	n=5	4 out of 5 patients were successfully treated in 1 session. No hemorrhage or perforation occurred. One patient needed a second session to complete dissection of the septum. All patients demonstrated improvement of dysphagia score after treatment.	Studies with more patients or longer follow-up are included.
Manno M, Manta R, Caruso A et al. (2014) Alternative endoscopic treatment of Zenker's diverticulum: A case series (with video). Gastrointestinal Endoscopy 79: 168-70	n=19 FU=median 27 months	Dysphagia recurred in 10.5% (2/19) of patients (at 6 and 8 months respectively). There were no adverse events.	Studies with more patients or longer follow-up are included.
Mulder CJ, den Hartog G, Robijn RJ et al. (1995) Flexible endoscopic treatment of Zenker's diverticulum: a new approach. Endoscopy 27: 438-442	n=20 FU=mean 6 months	Treatment using a mean of 3 sessions per patient was successful, with a good symptomatic response in all patients. There were no severe complications associated with the therapy. During follow-up, 17 patients remained asymptomatic	Studies with more patients or longer follow-up are included. A larger study by the same author is included.
Ramchandani M, Nageshwar Reddy D (2013) New endoscopic "scissors" to treat Zenker's diverticulum (with video). Gastrointestinal Endoscopy 78: 645-648	n=3	Cricopharyngeal myotomy was successfully performed in all patients. There were no major adverse events. Minor intraprocedure bleeding occurred in 1 patient.	Studies with more patients or longer follow-up are included.
Repici A, Pagano N, Romeo F et al. (2010) Endoscopic flexible treatment of Zenker's diverticulum: a modification of the needle-knife technique. Endoscopy 42: 532-535	n=32 FU=24 months	Complications= 6% (2/32) At 1 month follow-up, the mean dysphagia score was significantly improved from 2.9 to 0.6 ($p<0.001$) with 88% of patients free of symptoms. Three patients underwent a successful second endoscopic treatment with complete relief of dysphagia. During the follow-up period, 2 patients developed dysphagia recurrence. The overall success rate was 91%.	A more recent non-comparative study from the same author is included.
Sakai P, Ishioka S, Maluf-Filho F et al. (2001) Endoscopic treatment of Zenker's diverticulum with an oblique-end hood attached to the endoscope. Gastrointestinal Endoscopy 54: 760-763	n=10 FU=2–12 months	Complete incision of the septum was achieved in a single session in all cases. Bleeding or perforation did not occur. Complete relief of dysphagia was reported by all patients during follow-up.	Studies with more patients or longer follow-up are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Tang SJ, Jazrawi SF, Chen E et al. (2008) Flexible endoscopic clip-assisted Zenker's diverticulotomy: the first case series (with videos). Laryngoscope 118: 1199-1205	n=7 FU=at least 6 months	The 6 patients who had endoscopic clip-assisted procedure had complete resolution of esophageal symptoms at follow-up. There were no procedural complications. The remaining patient developed an esophageal perforation. She was managed conservatively without surgical intervention. On follow-up, her dysphagia was completely resolved.	Studies with more patients or longer follow-up are included.
Tang SJ, Lara LF (2008) Flexible endoscopic clip-assisted Zenker's diverticulotomy (with videos). Gastrointestinal Endoscopy 67: 704-708	n=1	Patient had complete symptom resolution without complications.	Case report.
Tang SJ, Myers LL (2010) Flexible endoscopic diverticulotomies for bilateral Zenker's Diverticula (with videos). Laryngoscope 120: 1553-1556	n=1 FU=18 months	After up to 18 months follow-up, the patient has near complete symptomatic resolution with associated radiological improvements.	Case report.

Appendix B: Related NICE guidance for flexible endoscopic treatment of pharyngeal pouch

Guidance	Recommendations
Interventional procedures	**Endoscopic stapling of pharyngeal pouch. NICE interventional procedure guidance 22 (2003)** 1.1 Current evidence on the safety and efficacy of endoscopic stapling of pharyngeal pouch appears adequate to support the use of the procedure, provided that normal arrangements are in place for consent, audit and clinical governance.

Appendix C: Literature search for flexible endoscopic treatment of pharyngeal pouch

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	05/11/2014	Issue 11 of 12, November 2014
Database of Abstracts of Reviews of Effects – DARE (Cochrane Library)	05/11/2014	Issue 4 of 4, October 2014
HTA database (Cochrane Library)	05/11/2014	Issue 4 of 4, October 2014
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	05/11/2014	Issue 10 of 12, October 2014
MEDLINE (Ovid)	05/11/2014	Ovid MEDLINE(R) <1946 to October Week 4 2014>
MEDLINE In-Process (Ovid)	05/11/2014	Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <November 03, 2014>
EMBASE (Ovid)	05/11/2014	Embase <1974 to 2014 Week 44>
CINAHL (NLH Search 2.0)		n/a
PubMed		n/a
JournalTOCS		n/a

Trial sources searched on 22 05 2014:

- National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC) Portfolio Database
- Current Controlled Trials *meta*Register of Controlled Trials – *m*RCT
- Clinicaltrials.gov

Websites searched on 22 05 2014 & 23 05 2014:

- National Institute for Health and Clinical Excellence (NICE)
- Food and Drug Administration (FDA) - MAUDE database
- French Health Authority (FHA)
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- Conference websites <<BLIC>>
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Endoscopy/
2	Esophagoscopy/
3	Esophagoscopes/
4	(esophagoscop* or oesophagoscop*).tw.
5	endoscopy, gastrointestinal/
6	diverticuloscop*.tw.
7	(endoscop* or telescop* or endotherap* or endosurg* or scope*).tw.
8	(needle* adj4 knife).tw.
9	pharyngolaryngoscop*.tw.
10	Endoscopes/
11	Surgical Procedures, Minimally Invasive/
12	Video-Assisted Surgery/
13	Surgery, Computer-Assisted/
14	((minimal* or non) adj4 invasive* adj4 (surg* or procedure* or technique*)).tw.
15	((video* or comput*) adj4 (surg* or procedure* or technique*)).tw.
16	or/1-15
17	(pharyngeal adj4 pouch*).tw.
18	Zenker Diverticulum/
19	((zenker* or esophagopharyngeal* or hypopharyngeal*) adj4 divert*).tw.
20	(blind adj4 end* adj4 sac*).tw.
21	or/17-20
22	16 and 21
23	animals/ not humans/
24	22 not 23 (427)