NICE guidance

Electrical stimulation of the lower oesophageal sphincter for treating gastro-oesophageal reflux disease

Interventional procedures guidance
Published: 16 December 2015

www.nice.org.uk/guidance/ipg540

Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account, and specifically any special arrangements relating to the introduction of new interventional procedures. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties. Providers should ensure that governance structures are in place to review, authorise and monitor the introduction of new devices and procedures.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

1 Recommendations

1.1 Current evidence on the safety and efficacy of electrical stimulation of the lower oesophageal sphincter for treating gastro-oesophageal reflux disease (GORD) is limited in quantity and quality. Therefore, this procedure should only be used in the context of research.

1.2 NICE encourages clinicians to enter patients into controlled clinical trials. These could include crossover and cohort studies, which would allow inclusion of patients for whom other surgical options are unsuitable. These should provide a clear description of patient selection, and details of adjunctive medical and surgical treatments. Outcomes should include GORD symptoms, quality of life and objective measurements of gastric reflux. Efficacy, device durability, the need for surgical treatment for GORD in the longer term (at least 2 years) and all complications should be reported. NICE may update the guidance on publication of further evidence.

2 Indications and current treatments

2.1 Gastro-oesophageal reflux disease (GORD) is a common problem. It is caused by several conditions that disturb the sphincter function at the lower end of the oesophagus, such as hiatus hernia. Symptoms of GORD can be broadly grouped into those directly related to reflux episodes, such as heartburn, regurgitation, chest pain and nausea, and those symptoms caused by complications of reflux

disease, including dysphagia and respiratory difficulties. Repeated episodes of GORD can damage the lining of the oesophagus and lead to oesophageal ulceration, oesophageal stricture and Barrett's oesophagus.

2.2 The standard treatments for patients with symptomatic GORD are lifestyle modification and drug therapy. Patients who have refractory symptoms, who develop complications despite medication or who develop intolerance to medication may be considered for anti-reflux surgery (usually laparoscopic fundoplication). Several endoscopic techniques (such as endoscopic radiofrequency ablation or endoscopic injection of bulking agents) have also been used.

3 The procedure

3.1 Electrical stimulation of the lower oesophageal sphincter aims to strengthen a weak or improperly functioning lower oesophageal sphincter muscle, to restore the anti-reflux barrier between the stomach and oesophagus, by using low energy electrical impulses.

3.2 With the patient under general anaesthesia, 2 electrodes and a lead are implanted into the sphincter muscle using a laparoscope under endoscopic guidance. The lead is passed through the abdominal wall and is secured to a stimulator, which is implanted in a subcutaneous pocket in the abdominal wall.

3.3 The stimulator automatically delivers impulses of about 3 mA to 8 mA to the electrodes in repeated 30-minute sessions. The patient does not feel the stimulation. The stimulator is programmed and controlled wirelessly to adapt it to specific patient needs (for example, related to diet and lifestyle).

4 Efficacy

This section describes efficacy outcomes from the published literature that the committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the interventional procedure overview.

4.1 A case series of 44 patients with gastro-oesophageal reflux disease (GORD) treated by electrostimulation of the lower oesophageal sphincter (LOS) reported median (interquartile range; IQR) percentages of days with heartburn of 86% (64 to 100%, n=35) before the procedure and 17% (0 to 93%, n=34) at 6 months ($p<0.0001$). Median (IQR) percentages of nights with heartburn were 64% (43 to 86%, n=35) before the procedure and 0% (0 to 8%, n=34) at 6 months ($p<0.0001$). The evaluations used a symptom diary kept by the patients. A case series of 25 patients with GORD treated by electrostimulation of the LOS, with a 2-year follow-up, reported median percentages of days and nights with heartburn at 'baseline off proton pump inhibitors (PPIs)' (defined as 10 days after the patients had started electrostimulation and had stopped taking PPIs) and at follow-up. Median percentages of days with heartburn were 92% at 'baseline off PPIs', 14% at 6 months, 13% at 12 months and 7% at 24 months ($p<0.001$ for all times versus 'baseline off PPIs'). Median percentages of nights with heartburn were 71% at 'baseline off PPIs', and 0% at 6, 12 and 24 months ($p<0.001$ for all times versus 'baseline off PPIs').

4.2 The case series of 44 patients reported median (IQR) percentages of days with regurgitation of 79% (54 to 100%, n=35) before the procedure and 0% (0 to 21%, n=34) at 6 months ($p<0.0001$). Median (IQR) percentages of nights with regurgitation were 50% (15 to 79%, n=35) before the procedure and 0% (0 to 7%, n=34) at 6 months ($p<0.0001$). The case series of 25 patients reported median percentages of days with symptoms of regurgitation of 66% at 'baseline off PPIs', and 0% at 6, 12 and 24 months ($p<0.001$ for all times versus 'baseline off PPIs'). Median percentages of nights with regurgitation were 31% at 'baseline off PPIs', and 0% at 6, 12 and 24 months ($p<0.01$ for all times versus 'baseline off PPIs').

4.3 The case series of 25 patients reported dysphagia caused by GORD in 38% (9/24) of patients at 'baseline on PPIs' and in 71% (17/24) at 'baseline off PPIs'. Dysphagia was reported in 13% (n=23) of patients at 12-month follow-up, and in 5% (1/21) at 24-month follow-up (level of significance not stated).

4.4 The case series of 44 patients reported median gastro-oesophageal reflux disease health-related quality of life (GORD-HRQL) scores (IQR) at baseline of 16.5 (9.0 to 22.8) when patients (n=42) were still taking PPIs and of 31.0 (26.2 to 36.8) when patients (n=42) had stopped taking PPIs. The scores improved significantly to 5.0 (3.0 to 9.0) at 6 months, (n=41, $p<0.0001$ for the

comparison against 'baseline on PPI' and 'baseline off PPI' scores). The case series of 25 patients reported median GORD-HRQL scores (IQR) at baseline of 9.0 (6.0 to 10.0) when patients (n=24) were still taking PPIs, and of 23.5 (21.0 to 25.8) when patients (n=24) had stopped taking PPIs. The scores improved significantly to 2.0 at 12 months (IQR and number of patients not given) and to 0 (0 to 3.0) at 24 months (n=21; $p \leq 0.002$ versus 'baseline on PPI' and 'baseline off PPI' scores at 12- and 24-month follow-up respectively). A publication reporting on 15 patients from the case series of 25 patients with GORD treated by electrostimulation of the LOS after 3 years of follow-up, reported median GORD-HRQL scores (IQR) at baseline of 9.0 (6.0 to 10.0) when patients were still taking PPIs and of 23.5 (21.0 to 25.0) when patients had stopped taking PPIs. The scores improved significantly to 1.0 (0.0 to 2.0) at 3 years ($p<0.001$).

4.5 In the case series of 44 patients, 74% (31/42) of patients reported dissatisfaction with GORD control at 'baseline on PPIs' and 21% (8/39) reported it 6 months after the procedure. In the case series of 25 patients, 71% (17/24) of patients reported dissatisfaction with GORD control at 'baseline on PPIs' and 92% (22/24) reported dissatisfaction at 'baseline off PPIs'. At 24-month follow-up, dissatisfaction was reported in none (0/21) of the patients ($p<0.001$ for both groups of patients).

4.6 The case series of 25 patients reported that GORD had an impact on their sleep in 71% (17/24) of patients at 'baseline on PPIs' and in 96% (23/24) of patients at 'baseline off PPIs'. At 12-month follow-up, GORD was reported to have an impact on their sleep by 17% of patients (n=23, absolute numbers not given) and, at 24-month follow-up, by 10% (2/21) of patients.

4.7 The case series of 44 patients reported that the median (IQR) percentages of the 24-hour period for which there was a distal oesophageal pH of less than 4 was 10% (8 to 13%, n=42) before the procedure compared against 4% (2 to 7%, n=40) after 6 months ($p<0.0001$). The case series of 25 patients reported that the median percentage of the 24-hour period for which there was a distal oesophageal pH of less than 4 was 10% (IQR 8 to 13%) at baseline (n=24; defined for this measure as at least 5 days after the patients had started electrostimulation and had stopped taking PPIs) compared against 5% (3 to 7%) at 24 months (n=18; $p=0.001$ versus baseline). At baseline, 96% (23/24) of patients had an abnormal distal oesophageal pH (less than 4 for more than 4% of a 24-hour recording) and, at 24 months, 61% (11/18) had an abnormal pH. The

publication reporting on 15 patients from the case series of 25 patients with a 3-year follow-up reported that the median (IQR) percentages of the 24-hour period for which there was a distal oesophageal pH of less than 4 was 10% (8 to 12%) at baseline compared against 3% (2 to 5%) at 3 years ($p<0.001$ for the comparison against baseline scores).

4.8 In the case series of 44 patients, 90% (37/41) of patients were completely off PPI, 5% (2/41) reported intermittent use of PPIs and 7% (3/41) reported regular use of PPIs at 6 months ($p<0.001$). In the case series of 25 patients, all patients still included in the study (24/24) were taking PPIs for GORD after implantation. At 24 months, 76% (16/21) of patients were not taking any PPIs, 14% (3/21) reported occasional PPI use and 10% (2/21) reported regular PPI use. The publication reporting on 15 patients from the case series of 25 patients with a 3-year follow-up reported that 73% of patients were free from PPI dependence (defined as 50% or more diary days with PPI use) at 3 years.

4.9 The case series of 44 patients reported that, at baseline, 41% (16/39) of patients had no oesophagitis, 31% (12/39) had Los Angeles classification (LA) grade A oesophagitis (grades A to D range from less severe to more severe oesophagitis assessed by endoscopy), 23% (9/39) had LA grade B oesophagitis and 5% (2/39) had LA grade C oesophagitis. At 6 months, 51% (20/39) of patients had no oesophagitis, 31% (12/39) had LA grade A, 18% (7/39) had LA grade B and none (0/39) had LA grade C oesophagitis ($p=0.02$ for the improvement in oesophagitis grade at 6 months). A publication about the case series of 25 patients with GORD treated by electrostimulation of the LOS after only 1 year of follow-up reported that, at baseline (within 6 months before enrolment), 67% (16/24) of patients had LA grade A oesophagitis, 25% (6/24) had LA grade B and 8% (2/24) had LA grade C oesophagitis. At 12 months, 31% (7/23) of patients had no oesophagitis, 52% (12/23) had LA grade A, 13% (3/23) had LA grade B and 4% (1/23) had LA grade C oesophagitis ($p=0.01$). Oesophagitis had improved by at least 1 grade in 58% (14/24) of patients at 3 months and in 57% (13/23) of patients at 12 months compared against baseline. The publication reporting on 15 patients from the case series of 25 patients with a 3-year follow-up reported that 50% (6/12) of the patients who had an endoscopy at 3 years showed an improvement in their oesophagitis by more than 1 grade.

4.10 The specialist advisers listed the following key efficacy outcomes: reduction in

symptoms of acid reflux, elimination (remission) of pre-operative GORD-related symptoms assessed by GORD-HRQL questionnaire, subjective and objective maintenance of remission, healing of any pre-operatively noted oesophagitis (assessed according to LA grading), improved 24-hour ambulatory pH studies, and lack of side effects such as dysphagia, bloating, fullness, increased wind and abdominal pain.

5 Safety

This section describes safety outcomes from the published literature that the committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the interventional procedure overview.

5.1 Trocar perforation of the small bowel during laparoscopy was reported in 1 patient in a cases series of 44 patients with gastro-oesophageal reflux disease (GORD) treated by electrostimulation of the lower oesophageal sphincter (LOS). This was repaired and the device was removed to avoid the possibility of subsequent complications.

5.2 Pain or discomfort was reported on 24 occasions in 46% (19/41) of patients in the case series of 44 patients; the adverse events were reported as related to the procedure (no details on timing given). Pain or discomfort in the abdomen was reported on 6 occasions in 6 patients in a case series of 25 patients with GORD treated by electrostimulation of the LOS with a 2-year follow-up; the adverse events were reported as related to the device (no details on timing given). In addition, 1 patient had transient discomfort in the shoulder. Epigastric pain was reported once in 1 patient in the case series of 44 patients; the adverse event was reported as related to the procedure (no details on timing given).

5.3 Mild or moderate dysphagia related to the procedure was reported on 5 occasions in 10% (4/41) of patients in the case series of 44 patients; it resolved without intervention. It was reported that crural repair was done in all 4 patients during device implantation (no details on timing given).

5.4 Nausea or vomiting was reported on 4 occasions in 7% (3/41) of patients in the case series of 44 patients; the adverse events were reported as related to the

procedure (no details on timing given). Nausea or vomiting on the day or the day after the procedure was reported on 3 occasions in 3 patients in the case series of 25 patients with 2-year follow-up.

5.5 Weight loss or anorexia was reported on 5 occasions in 12% (5/41) of patients in the case series of 44 patients; the adverse events were reported as related to the procedure (no details on timing given).

5.6 Fever was reported once in 1 patient in the case series of 44 patients; the adverse event was reported as related to the procedure (no details on timing given).

5.7 Superficial skin infection at the abdominal wall pocket site was reported in 1 patient in the case series of 25 patients.

5.8 Mesh repair hernia cicatricalis was reported once in 1 patient in the case series of 44 patients; the adverse event was reported as related to the procedure (no details on timing given).

5.9 Lead erosion was reported in 1 patient at the 6-month endoscopy in the case series of 44 patients. The device was removed and the patient was treated by fundoplication during the same procedure. Out-of-range impedance was reported on 2 occasions in 5% (2/41) of patients in the case series of 44 patients; the adverse events were reported as related to the procedure (no details on timing given).

5.10 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers listed the following anecdotal adverse events: deep vein thrombosis and chest infection. They considered that the following were theoretical adverse events: all laparoscopic-surgery-related adverse events, including port insertion vascular/visceral bleeding events; pneumoperitoneum-related cardio-pulmonary complications; oesophageal injury (perforation); device malfunction/failure; and lead migration.

6 Committee comments

6.1 The committee considered electrical stimulation of the lower oesophageal sphincter for the treatment of gastro-oesophageal reflux disease to be a promising intervention for a common condition. This underpinned the recommendation for further research, which should provide data to identify subgroups of patients who might derive particular benefit from the procedure.

ISBN: 978-1-4731-1597-2

Endorsing organisation

This guidance has been endorsed by Healthcare Improvement Scotland.

Accreditation