



# How I do it: laparoscopic implantation of lower esophageal sphincter stimulator for the treatment of gastro-esophageal reflux disease

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**Abstract:** The principal medical treatment of gastro-esophageal reflux disease (GERD) is proton pump inhibitor (PPI) therapy. PPI lowers gastric acid secretion, but its long-term use is not free from adverse effects. However, PPI therapy has no effects on the dysfunctional lower esophageal sphincter (LES) and on reflux of stomach contents. Prior to the introduction of medical therapy, surgical gastric fundoplication was originally proposed in order to create a mechanical valve to prevent reflux. The postoperative results obtained after fundoplication depend on the surgical volume of the centers in which surgery is performed, and important functional sequelae, including dysphagia and gas bloat syndrome, have been reported. LES electrical stimulation therapy (EST) has been recently introduced as an alternative treatment option in the management of GERD. The rationale of this strategy is to electrically stimulate the LES in order to increase its tone and to reduce reflux. LES stimulator implantation is a feasible and safe minimally invasive technique. Data reported in the literature regarding the postoperative functional outcomes related to GERD, evaluated by 24 h-pH-manometry, and GERD specific questionnaire after the implantation of LES-EST, show significant improvement at both short and long-term follow up, up to three years after surgery. Although these data are encouraging, further prospective and randomized studies are required to draw definitive conclusions. We report the technique of laparoscopic LES stimulator surgical implantation, together with an explanatory video.

**Keywords:** Gastro-esophageal reflux disease (GERD); lower esophageal sphincter (LES); electrical stimulation; laparoscopic surgery

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## Introduction

According to the Montreal Consensus conference, gastro-esophageal reflux disease (GERD) is defined as a “condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications” (1). In Europe and North America, GERD prevalence is reported to range between 10% and 20% (2). GERD causes both

typical (heartburn, regurgitation, dysphagia) and atypical (chest pain, cough, wheezing) symptoms, and may cause mucosal damage even though often the endoscopic findings do not correlate with symptoms (3-6).

The principal medical treatment of GERD is by proton pump inhibitor (PPI) therapy, which reduces gastric acid secretion, but its long-term use is also not free from adverse effects (7). However, PPI therapy has no effects on

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the dysfunctional lower esophageal sphincter (LES) and reflux (8). Prior to the introduction of medical therapy, surgical gastric fundoplication was originally proposed so as to create a mechanical valve to prevent reflux (9,10). The postoperative results obtained after fundoplication are highly dependent on the surgical volume of the centers in which surgery is performed, and important functional sequelae, including dysphagia and gas bloat syndrome, are reported (9,10).

LES electrical stimulation therapy (EST) has been recently introduced as an alternative surgical option for the treatment of GERD (11,12). The rationale of this strategy is to electrically stimulate the LES in order to increase its tone and to reduce reflux (11,12).

We report the laparoscopic surgical technique to implant the LES stimulator together with an explanatory video.

## Methods

### *Protocol and patients selection*

The study was conducted in accordance with the Declaration of Helsinki. The study was approved by Institutional review board of Sapienza University of Rome (n. 3436) and informed consent from the participants included in the study were obtained.

According to our study protocol, patients undergo upper gastrointestinal endoscopy, barium swallow and 24 h-pH-manometry prior to surgery. The Gastroesophageal Reflux Disease Health-Related Quality of Life (GERD-HRQL) questionnaire is also administered (13). These exams are repeated 12 and 24 months after surgery.

### *Inclusion and exclusion criteria*

Patients between 21 and 65 years of age, classified as American Society of Anaesthesiologists (ASA) grade I–III, who have been suffering from heartburn, regurgitation, or both for more than 6 months and necessitating daily use of PPI, with baseline GERD-HRQL heartburn score  $\geq 20$  off PPI therapy and with at least a 10-point improvement upon resumption of PPI therapy, distal esophageal pH  $< 4$  on 24-h pH-metry off PPI therapy for  $> 5\%$  of the time, resting LES expiratory pressure (EEP)  $\geq 5$  and  $\leq 15$  mmHg, esophageal body contraction amplitude  $> 30$  mmHg for  $> 70\%$  of swallows and  $> 50\%$  peristaltic contractions, esophagitis  $\leq$  grade C [according to Los Angeles Classification (14)], failure or poor compliance with medical therapy and with

signed informed consent, were included.

Patients with non-GERD esophageal motility disorders or gastroparesis, significant multisystem disease (e.g., scleroderma, dermatomyositis, Sjogren's syndrome, Sharp's syndrome, etc.), Barrett's esophagus ( $> M2; > C1$ ) [according to Prague Classification (15)] or any dysplasia, hiatal hernia  $> 3$  cm, body mass index (BMI)  $> 35$  kg/m<sup>2</sup>, type 1 diabetes mellitus, uncontrolled type 2 diabetes mellitus (T2DM) defined as HbA1c  $> 9.5\%$  in the previous 6 months, T2DM for  $> 10$  years, suspected or confirmed esophageal or gastric malignancy, portal hypertension with esophago-gastric varices, significant cardiac arrhythmia or cardiovascular disease, implanted electromedical device (cardiac pacemaker) or pregnancy, were excluded.

### *Stimulation system*

The system includes three components: an implantable pulse generator (IPG) connected to a bipolar stimulation lead by two stitch electrodes, and an external IPG wireless programmer with dedicated software (EndoStim B.V., The Hague, The Netherlands) (12). The IPG is a hermetically sealed, titanium casing which contains a medical-grade lithium battery, microelectronics, coils and an inclinometer for sensing the patient's posture. Its top edge is composed by an implantable medical-grade epoxy which includes the stainless-steel contacts for the connection with the lead (12). Two platinum-iridium electrodes, measuring 10 mm in length and 0.5 mm in diameter, constitute the stimulation lead which is 45 cm long overall (12). The external programmer has an interface box which communicates with the IPG and with a laptop to set the stimulation (12). The stimulation system provides a monophasic pulse (215  $\mu$ s wide and nominally 5 mA in amplitude, delivered at 20 Hz in 30 minutes sessions) followed by a charge-balancing phase. By means of the external programmer, it is possible to adjust the stimulation by changing the electrode polarity, the number or timing of stimulation sessions, and the amplitude (12).

### *Surgical technique*

The patient is positioned supine on the operative table with abducted legs. The surgeon stands between the patient legs and the first assistant stands on the right side of the patient holding a 30° forward oblique optic. The second assistant stands on the left side of the patient. The camera with video monitor, the light source and insufflator are placed at the patient's head on the left side. Pneumoperitoneum

is established at a pressure of 12–13 mmHg with the open technique and Hasson cannula (T1) in supra-umbilical position. Another two 12 mm trocars are introduced under vision in the left (T2) and right (T3) hypochondrium along the midclavicular lines. One 12 mm subxiphoid midline trocar is placed under vision (T4) and a 5 mm trocar (T5) is introduced under vision in the left flank along the anterior axillary line. T2 and T3 are the working trocars that are used by the surgeon. A liver retractor (Nathanson retractor, Cook Medical, Bloomington, Indiana, USA, or Endo Paddle retractor, Covidien, Mansfield, Massachusetts, USA) is introduced from T4. A grasper introduced from T5 is used to apply traction during the surgical maneuvers. The operating table is turned in slight anti-Trendelenburg position. Surgical dissection is performed with an ultrasonic device (Ultracision, Harmonic Scalpel, Ethicon Endo Surgery, Cincinnati, Ohio, USA) (*Video 1*).

#### **Step 1—Hiatus dissection**

The first step of the procedure is removal of the Belsey fat pad and division of the phreno-esophageal membrane, in order to expose the left and right diaphragmatic crura and the anterior wall of the abdominal esophagus. Careful dissection is required in order to avoid injury of the esophagus or of the anterior vagus nerve. If a small hiatal hernia is present, the mediastinal space is opened and the abdominal esophagus is mobilized so as to reduce it in the abdomen (*Video 1*).

#### **Step 2—electrodes placement**

In order to prevent perforation of the esophageal lumen by the electrodes, and to make sure that they are correctly positioned at the level of the LES, the two electrodes are placed under endoscopic control. One is placed on the midline of the esophagus and one on its right lateral side into the muscularis propria of the LES, at a distance of about 1 cm from each other and parallel to the longitudinal axis of the esophagus. Both electrodes are fixed by titanium clips on the proximal nylon wire and by a 3.0 silk stitch at the distal anchoring “butterfly” located on the back end of the electrodes (*Video 1*).

#### **Step 3—anterior hiatoplasty**

After positioning of the two electrodes, the left and right bundles of the right diaphragmatic crus are sutured

together anteriorly to the esophagus, with two stitches of non-absorbable, 2.0 braided polyester suture (Ethibond, Ethicon, Cincinnati, Ohio, USA) (*Video 1*).

#### **Step 4—IPG placement and lead connection**

A subcutaneous pouch is prepared along the transverse umbilical line on the left. One 5 mm trocar is inserted in the upper left corner of the pouch, in order to extract the lead, which is connected to the titanium IPG. Finally, the redundant lead is positioned in the left parietocolic groove (*Video 1*).

### **Discussion**

Laparoscopic implantation of the IPG-LES stimulator for the treatment of GERD is feasible and safe (11,12,16-21), and the surgical technique does not require a specific learning curve. In fact, due to the simplicity of the technique as shown in the video, an upper gastrointestinal surgeon does not require any specific experience for implantation of the two stitch electrodes and IPG. However, isolation of the abdominal esophagus and correct positioning of the electrodes at the level of the cardia without perforation of the esophago-gastric mucosa must be performed cautiously (11,12,16-21). For this the reason the procedure is best performed under endoscopic control. Failure of IPG stimulator implantation, intra or postoperative complications up to 30-days after surgery, or conversion to open surgery related to implantation of the device have not been reported (11,12,16-21). A median operating time of 45 minutes is reported (11) and is consistent with our experience.

Patients with hiatal hernia greater than 3 cm are excluded from the protocol, hence a posterior hiatoplasty is not required. Should a small hiatal hernia be present, an anterior hiatoplasty is recommended and is more than adequate to prevent hiatal hernia recurrence, due to the close distance between the left and right bundles of the right crus. Moreover, complete esophageal mobilization to expose the anterior esophageal wall for stimulator implantation is not required, so the choice to perform anterior hiatoplasty is simply to restore the physiological diaphragmatic crura and LES anatomy. The exclusion of patients with hiatal hernia more than 3 cm is widely accepted in the published case series (12,16-21), except for Paireder *et al.* although even in their study patients with large hiatal hernias were not included (11). Concomitant hiatal hernia repair is described only in two studies, but without specifying whether it was done by anterior or posterior hiatoplasty (11,16).

Regarding GERD-related postoperative functional outcomes, the implantation of LES-EST showed significant improvement at short and long-term follow up as evaluated by 24h-pH-manometry (11,12,16-21). At manometry evaluation, a few days after stimulator implantation an almost doubled LES pressure was observed in ten patients in the study published by Rodríguez *et al.* (17). One month after surgery, Paireder *et al.* report an improvement in GERD symptoms evaluated by the GERD-HRQL questionnaire in 17 patients (questionnaire score 37.53 *vs.* 10.93,  $P=0.001$ ), even though an objective evaluation by 24h-pH-manometry was not performed (11).

Six months after surgery, Kappelle *et al.* report statistically significant improvements in GERD symptoms as evaluated by GERD-HRQL questionnaire, in esophageal acid exposure time (pH <4%: median 9.9 *vs.* 4.4,  $P\leq 0.0001$ ) and in De Meester score (median 35.1 *vs.* 17.5,  $P\leq 0.0001$ ) evaluated by 24 h-pH-metry in 41 patients, even if little increase in LES pressure at manometry was observed (median 13.1 *vs.* 15,  $P=0.2195$ ) (16). These 24h-pH-manometry data at six months after surgery are confirmed by Rodríguez *et al.* reporting a median reduction in esophageal acid exposure (pH <4%) from 10.1 to 5.1,  $P\leq 0.001$  (18). Data regarding time of acid exposure, De Meester score and GERD-HRQL questionnaire score continue to show statistically significantly improvement up to 3 years after surgery, with no reported adverse effects on esophageal body function, confirming that LES stimulator implantation improves both symptoms and objective instrumental exam data (19-21).

The LES-EST implantation could be a valid alternative to treat patients who underwent previous sleeve gastrectomy, and in case of patients with severe chronic respiratory failure waiting for lung transplant with severe GERD who are refractory to medical treatment (21,22). In this group of patients, anti-reflux fundoplication often is not performed due to compromised cardiorespiratory conditions and high surgical risk (22).

The indication for stimulator removal is its failure in the management of GERD. To date, IPG removal has been reported only in one case (20). In this case the patient decided to have the stimulator removed two weeks after its implantation, due to anxiety related to presence of the device and the need for invasive assessment of device functioning that are required by the study protocol, despite GERD symptoms improvement (20). Stimulator removal can be performed under local anaesthesia, leaving the leads intraabdominally, or under general anaesthesia by

laparoscopy, removing both leads and stimulator. In the latter case, construction of a laparoscopic fundoplication may be added, if necessary.

Analysing the costs related to this procedure, in patients with PPI-refractory GERD, LES stimulator implantation is reported to cost less than high-dose PPI for more than 10 years (20). However, the lack of long-term data about the effects of LES stimulator should be taken into account (20).

In conclusion, LES stimulator implantation is a feasible and safe minimally invasive technique. Although present data reported in the literature on improvement of GERD symptoms and 24h-pH-manometry assessment are encouraging, further prospective, randomized studies are required to draw definitive conclusions.

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