



ELSEVIER

Contents lists available at [ScienceDirect](#)

## Best Practice & Research Clinical Gastroenterology



8

### Laparoscopic surgery for gastro-esophageal acid reflux disease



Marlies P. Schijven, MD, PhD, MHSc, Assistant Professor of Surgery\*, Suzanne S. Gisbertz, MD, PhD, Assistant Professor of Surgery, Mark I. van Berge Henegouwen, MD, PhD, Assistant Professor of Surgery

Department of Surgery, Academic Medical Centre, PO Box 22660, 1100 DD Amsterdam, The Netherlands

#### Keywords:

Systematic review  
Reflux  
Toupet  
Nissen  
GERD  
GORD  
Gastro-esophageal reflux disease  
Endoluminal  
Fundoplication  
Laparoscopy  
Proton pump inhibitors  
Anti-reflux procedures

#### A B S T R A C T

Gastro-esophageal reflux disease is a troublesome disease for many patients, severely affecting their quality of life. Choice of treatment depends on a combination of patient characteristics and preferences, esophageal motility and damage of reflux, symptom severity and symptom correlation to acid reflux and physician preferences. Success of treatment depends on tailoring treatment modalities to the individual patient and adequate selection of treatment choice. PubMed, Embase, The Cochrane Database of Systematic Reviews, and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) were searched for systematic reviews with an abstract, publication date within the last five years, in humans only, on key terms (laparosc\* OR laparoscopy\*) AND (fundoplication OR reflux\* OR GORD OR GERD OR nissen OR toupet) NOT (achal\* OR pediat\*). Last search was performed on July 23rd and in total 54 articles were evaluated as relevant from this search. The laparoscopic Toupet fundoplication is the therapy of choice for normal-weight GERD patients qualifying for laparoscopic surgery. No better pharmaceutical, endoluminal or surgical alternatives are present to date. No firm conclusion can be stated on its cost-effectiveness. Results have to be awaited comparing the laparoscopic 180-degree anterior fundoplication with the Toupet fundoplication to be a possible better surgical alternative. Division of the short gastric vessels is not to be recommended, nor is the use of a bougie or a mesh in the vast majority of GERD patients undergoing surgery. The use of a robot is not recommended.

\* Corresponding author. Tel.: +31 205664207.

E-mail addresses: [m.p.schijven@amc.uva.nl](mailto:m.p.schijven@amc.uva.nl), [mschijv@zonnet.nl](mailto:mschijv@zonnet.nl) (M.P. Schijven).

Anti-reflux surgery is to be considered expert surgery, but there is no clear consensus what is to be called an 'expert surgeon'. As for setting, ambulatory settings seem promising although high-level evidence is lacking.

© 2013 Elsevier Ltd. All rights reserved.

## Introduction

Gastro-esophageal reflux disease (GERD) is defined according to the Montreal Consensus as being 'a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications'. Symptoms are considered to be troublesome if they adversely affect the individual's well-being [1]. Key symptoms of GERD are heartburn and regurgitation. Many other more or less specific or common symptoms such as nausea, dysphagia, cough, laryngitis, dental erosions and gastric asthma are reported throughout literature. It is estimated that up to 20% of patients from Western countries experience heartburn, reflux, or both intermittently [2,3]. It is known that GERD indeed severely impairs the quality of life in patients, when compared to control populations and also when compared to patients with other chronic disease [4,5]. In the USA, approximately 18.6 million patients with GERD are treated annually, with direct costs approximating US \$ 9.3 billion, and anti-reflux medications accounting for US \$ 5.8 billion [3].

The treatment of GERD depends on both symptom severity and individual patient characteristics. Conservative treatment may involve lifestyle changes such as weight loss, smoking cessation, and dietary changes such as smaller meal sizes and reduction of alcohol intake. Medication regimens including proton pump inhibitors (PPI's) are introduced if symptoms persist despite lifestyle changes, but the inconvenience and cost of long-term daily medication may lead to non-compliance.

It is still debated whether medical or surgical (laparoscopic fundoplication) management is the most clinically and cost-effective treatment for controlling GERD in the long term.

Although pharmacological management is the standard initial therapy for patients suffering from GERD, an estimated five per cent of GERD patients is known to have an incomplete response to PPI's [6,7]. Moreover, a substantial number of patients are unwilling to take lifelong medications or suffer from so-called extra-esophageal manifestations of GERD. If a patient has failed medical management in terms of inadequate symptom control, intolerable medical side effects and/or severe regurgitation not controlled with acid suppression, anti-reflux surgery is to be considered as a viable option. For all patients suffering from GERD that are being considered for anti-reflux surgery, a solid preoperative workup is essential. It is important to determine if the patient is indeed suffering from GERD and not from functional heartburn; for patients suffering from functional heartburn is not likely to benefit from anti-reflux surgery. In fact, in patients with functional heartburn not suffering from GERD complaints may even worsen after anti-reflux surgery. It is believed that symptom resolution is lower in the presence of esophageal hypomotility in GERD patients. GERD patients with severe atypical symptoms or a hypomotile oesophagus may not achieve the same clinical satisfaction following anti-reflux surgery as those with normal esophageal motility [8]. Indeed, patients with poor esophageal peristalsis and prolonged supine acid exposure are at higher risk of recurrent pathological acid exposure after a Nissen fundoplication. Those patients, and the also the patient with prolonged episodes of supine acid exposure must be informed about their higher surgical re-intervention rate for recurrent GERD [9]. Good candidates for anti-reflux surgery are those who have erosive reflux disease on endoscopy and/or pathological reflux with a positive symptom index and symptom associated probability during 24 hours pH-metry, with normal esophageal motility, not satisfied with or with incomplete response to PPI use.

Since it was first described in 1991 [10], the laparoscopic procedure has now become the approach of choice for surgical treatment of GERD [11,12]. Compared to open surgery, the advantages of the laparoscopic approach include reduced hospital stay, better pain control with less medication prescribed, rapid postoperative recovery, and better cosmetic results both in adults [7,13,14] and in children [15].

Long-term results of randomized clinical trials (RCT's) comparing the open Nissen and Toupet fundoplication have demonstrated that reflux control is durable throughout ten-year follow-up after

surgery. As no differences in short-term and long-term reflux control between open and laparoscopic fundoplication exist, it seems unlikely that differences in reflux control after laparoscopic anti-reflux procedures will develop with longer follow-up [11]. Laparoscopic anti-reflux surgery, based on a meta-analysis of randomized clinical trials comparing open and laparoscopic reflux surgery, is believed to be an effective and safe alternative indeed to open anti-reflux surgery for the treatment of proven GERD [14].

Anti-reflux surgery aims to provide for durable control of reflux with minimal postoperative discomfort such as dysphagia and gas-related symptoms. Currently, the laparoscopic Nissen fundoplication (LNF) is the most frequently performed surgical therapy for gastro-esophageal reflux disease [16,17], although alternative surgical techniques as laparoscopic Toupet fundoplication have been suggested to have equal outcome on reflux control while overcoming post-fundoplication syndromes. It is important to assess which type of fundoplication is associated with a long-term relief of acid reflux with the lowest chance on troublesome dysphagia and other post-fundoplication symptoms for the individual patient [8].

This article aims to provide an overview of the current evidence in anti-reflux surgery using a systematic review approach of the literature.

## Methods

### *Study selection and assessment*

PubMed, Embase, The Cochrane Database of Systematic Reviews, and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) were searched for systematic reviews with an abstract, publication date within the last five years, in humans only, on key terms (laparosc\* OR laparoscop\*) AND (fundoplication OR reflux\* OR GORD OR GERD OR nissen OR toupet OR endoluminal OR endo\*) NOT (achal\* OR pediat\*).

The last search date of the databases was on July 23rd, 2013. One report was excluded based on language (Romanian). The titles and abstracts of all reports were screened for the previously mentioned search criteria. All articles deemed 'relevant', 'dubious' or 'unknown' were examined in full text. In total, 54 articles were identified as being relevant for this article (Fig. 1).

## Results

### *Medication or fundoplication?*

Long-term medication therapy using PPI's is known to be highly effective and safe for control of reflux oesophagitis [6]. However, studies have demonstrated that up to 40% of the heartburn patients reported either partial or a complete lack of response to PPI once daily. The main underlying mechanisms for PPI-failure are poor compliance, residual reflux (non-acid, bile or acidic), functional heartburn and co-morbidities (functional bowel disorders, gastroparesis etc) [18]. Some patients may experience unwanted side-effects from the use of PPI's. This may result in taking a more critical viewpoint on medication use when side-effects of PPI's outweigh the benefits for the patient, especially with long-term use [19].

Evidence exists, from four trials with a total of 1232 randomized participants, that laparoscopic fundoplication surgery is more effective than medical management in the treatment of gastro-esophageal reflux disease (GERD) in adults, at least in the short to medium term [2,20]. It is also reported that the laparoscopic Nissen fundoplication results in excellent outcomes in patients with high positivity in terms of symptom index resulting from ambulatory impedance and pH monitoring [18]. A review of literature on anti-reflux surgery for the best available evidence shows a trend for anti-reflux surgery to be superior to best medical therapy in cancer prevention in Barrett's oesophagus, but this fails to reach statistical significance [21]. Grant et al conducted a quest for the effectiveness and cost-effectiveness of minimal access surgery amongst 810 GERD patients judged suitable for either medication or a surgical fundoplication (357 randomized, 453 recruited to non-randomized preference). It is stated that amongst patients requiring long-term medication to control symptoms of GERD, surgical

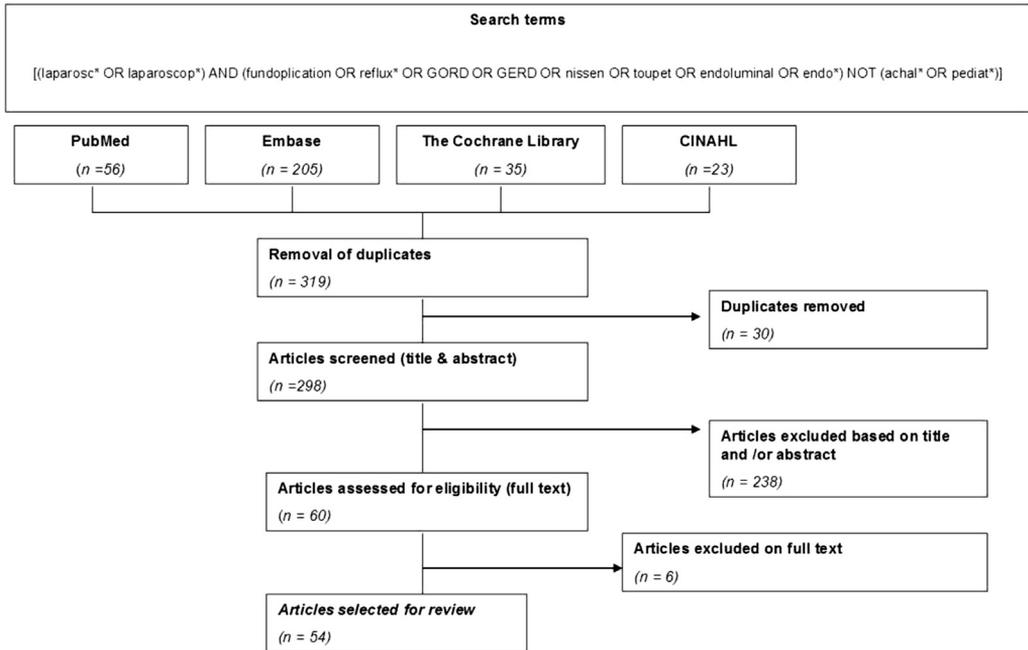


Fig. 1. Search strategy.

management provides a better relief of GERD symptoms with associated improved health-related quality of life.

Another systematic review of the literature searching for cost-effectiveness of proton pump inhibitors versus laparoscopic surgery states that results with regard to cost-effectiveness are inconclusive. In their search, it is stated that all economic models are based on high- and low-quality data. More reliable estimates of cost-effectiveness based on long-term trial data are needed [22]. Quite recently, Al Talalwah et al estimated a fundoplication is to be more cost-effective than omeprazole after eight years [20]. In general, one might state that the more troublesome the symptoms, the greater the potential benefit from surgery is believed to be and, despite being initially more costly, a surgical policy is likely to become more cost-effective in the longer run [23,24].

### Surgical standard

The number of patients suffering from GERD is on the rise, with obesity likely to be the contributing factor. Moreover, obesity is considered to be an important risk factor for developing gastro-oesophageal reflux and/or oesophagitis in itself [25]. Diet and lifestyle intervention, leading to weight reduction, appears to be beneficial with respect to GERD [26]. Although it is reasonable to assume that weight loss will result in decrease of reflux and weight reduction is often recommended as a first-line conservative treatment, there is a lack of literature supporting this recommendation [25]. A fundoplication for severely obese patients (BMI between 25–30 or over 30) is presumably not the best strategy to control GERD. Of all surgical techniques, the Roux-en-Y gastric bypass (RYGB) having both restrictive and malabsorptive properties seems to be most promising. Adjustable gastric banding is known to have anti-reflux properties, especially in the short term.

Adjustable gastric banding increases lower esophageal sphincter (LES) pressure but it decreases LES relaxation and is associated with an increase in disturbed esophageal peristalsis. Gastric banding is found to worsen GERD complaints, and is therefore not recommended. A recent multicenter study analysed 644 patients undergoing RYGB with concomitant repair of a hiatal hernia versus 1589 patients

undergoing RYGB without diagnosis or repair of a hiatal hernia. Concomitant hiatal hernia repair with laparoscopic RYGB appears to be safe and feasible; but no significant differences in morbidity, mortality, length of stay, readmission rate, or costs could be reported, and the benefit of hiatal hernia repair in regards to reflux symptoms and weight loss for laparoscopic RYGB patients is therefore unclear to date [27].

### *Laparoscopy versus open approach*

Laparoscopic fundoplication is currently considered to be the surgical approach of choice for treatment of GERD in the normal weight population [11]. The guidelines for surgical treatment of gastro-esophageal reflux disease from the SAGES guideline committee stress the importance of a consensus in the surgical community [28], but a scientific reflection of this in terms of a Delphi analysis or consensus paper other than the SAGES guidelines could not be retrieved. Most articles agree that a laparoscopic fundoplication is to be performed by or under the supervision of a senior surgeon, proficient in laparoscopy and the laparoscopic fundoplication more specifically [29].

A laparoscopic fundoplication is created by wrapping the fundus of the stomach anteriorly or posteriorly around the oesophagus just below the diaphragm. One can identify different types of funduplications for anti-reflux surgery. Most commonly known is the 360 degree posterior fundoplication (360-degree LPF or laparoscopic Nissen fundoplication, LNF). Partial funduplications have been proposed to reduce post-operative symptoms associated with the Nissen fundoplication; such as the 270 degree posterior fundoplication (270-degree LPF or laparoscopic Toupet fundoplication, LTF), the 180-degree laparoscopic anterior fundoplication (180-degree LAF) and the 90-degree anterior laparoscopic anterior fundoplication (90-degree LAF or Dor fundoplication, LDF).

### *Division of the short gastric vessels*

It is debated whether or not the short gastric vessels should be divided when constructing a laparoscopic fundoplication. Division of the short gastric vessels allow for a floppier wrap to be constructed, although five randomized trials have failed to demonstrate any advantages of full mobilization of the fundus after one and ten years follow-up [30]. Tosato states that both randomized and nonrandomized studies argue that a division of short gastric vessels is not needed for performing a 'short and floppy' fundoplication [31]. Furthermore, division of the short gastric vessels is associated with longer operative time and hospital stay. Another meta-analysis, by the group of Markar assessing five randomized trials states there is no statistically significant effect resulting from division of the short gastric vessels on the requirement for reoperation, presence of postoperative dysphagia or reflux; but division of the vessels is associated with a longer duration of operation and a reduced postoperative lower esophageal sphincter pressure [32]. A meta-analysis assessing the combined results of two randomized clinical trials shows that a fundoplication with division of the short gastric vessels is followed by a slightly poorer clinical outcome at late follow-up compared to the modified procedure where the short gastric vessels are not divided [21,33].

Surgeons should thus consider avoiding a division of the short gastric vessels when undertaking laparoscopic anti-reflux surgery.

### *Choice of fundoplication*

The most widespread technique to date, aside from diaphragmatic pillar closure with or without mesh, is the laparoscopic Nissen-Rossetti fundoplication [7,29]. In 2010, the SAGES guideline for treatment of GERD, was last revised [7]. On the debate of type of fundoplication, the guideline concludes that there is 'paucity of long-term follow-up data' and recommends 'controlled studies with long-term follow-up' [28].

A study by Fein and Seyfried comparing nine randomized trials comparing several types of wraps suggests that tailoring of type of anti-reflux surgery according to pre-operative results of esophageal motility is not indicated [17]. They state that relevant factor for selecting the type of fundoplication is the personal experience, annotating that the anterior fundoplication offers less effective long-term

reflux control. Broeders et al confirm that reflux control after a 90-degree LAF is less effective than after LNF; and reoperation rates twice as high mainly due to re-interventions for recurrent GERD. A 90-degree LAF should therefore not be considered a good option for treating GERD patients [12]. To date, the 270-degree LTF is known to be as effective as the LNF in long-term acid reflux control, with lower rates on dysphagia and gas related symptoms [11,34,35], but is more likely to be associated with early surgical complications such as perforations and bleeding reaching statistical significance in meta-analysis. A possible explanation for this finding may relate to the fact that the oesophagus has no serosal layer; during suturing of the esophageal wall, the risk of perforation may be greater with LTF [36]. Another research group believes that LNF is more successful in controlling reflux symptoms, particularly heartburn, than partial laparoscopic funduplications at 12 months follow-up, but is known to have higher post-operative dysphagia and gas-related side effects [37].

Recently, Broeders et al compared five distinct randomized trials comparing 180-degree LAF ( $n = 227$ ) with LNF ( $n = 231$ ) [12,16]. For the 180 degree LAF combined with a hiatal hernia repair, it is now known that after one and five years, dysphagia and gas-related symptoms are also lower than after LNF, and esophageal acid exposure and oesophagitis are similar, with no differences in heartburn scores, patient satisfaction, dilatations, and reoperation rate [16]. From Broeders' meta-analysis it can be concluded that the main differences between the insufficient 90- and 120-degree LAF versus a 180-degree LAF is the reduced circumference of the wrap and the lack of fixation of the 90- or 120-degree LAF wrap to the right hiatal pillar. Anchorage of the wrap to the right hiatal pillar prevents the wrap from migration into the gastro-esophageal hiatus. Fixation is believed to be the main factor contributing to recurrent reflux following various anterior funduplications, and, additionally, may be responsible for the good results following a 180-degree LAF. To date, no comparative study between outcomes and long-term reflux control after LTF, considered being the procedure of choice based on the evidence, and the 180-degree LAF could be retrieved by authors.

#### *Placement of a bougie*

As for calibration, it is proposed that use of an intra-esophageal bougie during a fundoplication reduces post-operative dysphagia. Based on a single randomized trial by Patterson et al [38], there is some evidence to suggest that the presence and size of a bougie may have an impact on the incidence of the dysphagia following a Nissen fundoplication [39].

However, no evidence to date could be retrieved on the use of a bougie in partial funduplications. The proposed benefit of using a bougie must be weighed against the reasonable risk of esophageal injury which patients should be consented for. The 2010 Guidelines for Surgical Treatment of Gastro-esophageal Reflux disease by the Society of American Gastrointestinal and Endoscopic Surgeons give a Grade B recommendation for the placement of a 56 French bougie; this is however solely based on the afore-mentioned outcomes of the study by Patterson et al and does not apply to partial funduplications much less at risk for being 'too tight'.

#### *Crural reinforcement in hiatus hernia*

On the issue of using a mesh for reinforcement of hiatal hernia repair in GERD patients, much debate exists. Use of a mesh is believed to have beneficial effects on the recurrent rate of hernias, but it may have adverse postoperative outcome due to foreign body reactions. Dysphagia, wrap migration, hernia recurrence, peri-esophageal mesh-induced fibrosis and intraluminal mesh erosion are reported. In essence, it is important to adhere primarily to diagnosis and management guidelines for GERD upon the presence of a hiatal hernia [40]. If the patient is a GERD patient with a concomitant hiatal hernia, consideration for surgical treatment using a mesh may apply. It is important to realize that the patient with a hiatal hernia is not necessarily a patient suffering from GERD; nor is it a patient that needs an operation per se in the mere presence of a hernia without accompanying symptoms.

A wide range in the incidence of hernia recurrence following suture hiatoplasty in patients with para-esophageal hernias – without mesh – is reported in literature, reaching up to 42%. It is to be stressed that a para-esophageal hernia is not the same situation, nor nearly as common as a sliding hernia at the GE junction, where the LES is believed to be positioned more than 2 cm upwards in the

hiatus of the diaphragm. Despite wide application of mesh hiatoplasty worldwide, with polypropylene (PP) being the most commonly used prosthetic material, there is currently no available evidence supporting a clear benefit with regard to recurrence rates for patients without a para-esophageal hiatal hernia [13].

Recurrence rates of hernias after the use of a PP mesh vary between 0% and 22.7%, with a median of 1.9%. The incidence of dysphagia after PP-mesh reinforced hiatoplasty ranged from 0% to 21.7%, with a median value of 3.9%.

Reported dysphagia rates after the use of a mesh are reported to be lower when using a PP mesh, whereas PTFE and ePTFE meshes are believed to exhibit considerably higher dysphagia rates and have unacceptably high recurrence rates [13]. Indications for mesh reinforcement according to the type or the size of the hernia are poorly defined. Antoniou et al report that several studies consider GERD as the sole inclusion criterion for mesh hiatoplasty, but study populations were an aggregate of patients with and without hiatal hernia, thus not allowing comparative evaluation of the clinical effect of mesh hiatoplasty in patient groups with specific hernia characteristics. Although surgeons prefer to excise the herniac sac, no comparative data exists on recurrence risk and dysphagia with or without excision of the herniac sac.

Hiatal hernias at original operation have been reported to be predictors for anatomic failure of a non-mesh reinforced suture cruraplasty. A proposed treatment protocol includes mesh augmentation depending on the size of the hiatal defect of a para-esophageal hernia. For defects smaller than 4 cm<sup>2</sup> simple suture hiatorraphy is proposed. For defects between 4 cm<sup>2</sup> and 8 cm<sup>2</sup>, hiatorraphy and online mesh is proposed, for defects up to 8 cm<sup>2</sup> tension-free hiatoplasty is advised. Furnee et al conclude from their analysis of 26 studies, in which anti-reflux surgery was in fact an exclusion criteria for selection, that the use of mesh in the repair of large hiatal hernias is promising with regard to the reduction of anatomical recurrences; but high quality randomized controlled trials are lacking and no conclusions can be stated in terms of what the most effective and safe mesh is to use on the long term [41]. Currently, there is no evidence to support application of biologic implants in widespread clinical practice. In the lack of randomized studies, surgical modalities at the moment remain empirical, guided by the surgeon's preferences, experience, and intuition.

A careful evacuation of pneumoperitoneum is to be performed at all times, and a drain is not indicated [29]. Literature reports other supplemental surgical interventions taking place simultaneously, but it is unclear if this influences outcome of the fundoplication and/or increases operative risk. Hence, this should only be suggested to patients after careful consideration. A systematic review of Kahokehr including five randomized trials of which two focusing on fundoplication suggest there is evidence in favour of administering an intraperitoneal local anaesthetic for pain reduction. There were no reports of adverse effects [42].

Upon closure, to avoid laparoscopic port site hernia's, it is advised to close all the fascial defects larger or equal to 10 mm under direct vision to prevent herniation and re-intervention [43].

#### *Robotic surgical techniques in anti-reflux surgery*

On the use of a robotic surgical Da Vinci-system, four RCT's and five non-randomized studies were assessed by Maeso et al detecting no differences between use of the Da Vinci surgical system compared to conventional laparoscopic surgery with respect to surgery time, length of hospital stay, complications, or conversion to another surgical technique [44]. This was supported by another meta-analysis from the group of Mi, assessing seven RCT's and four clinical controlled trials on the issue and by Zhang et al, assessing five studies with a total of 181 patients in comparative studies [45]. Their systematic review of the literature indicates that the use of a laparoscopic robot is a safe alternative to laparoscopic surgery, but it lacks obvious advantages with respect to operating time, length of hospital stay and cost and thus has limitations for its extensive application in clinics. Another meta-analysis by Markar included six randomized trials on robotic versus laparoscopic Nissen fundoplication, concluding that there was no significant difference between robotic and laparoscopic groups for hospital stay or operative complications. Clinical results from robotic Nissen fundoplication were comparable to the standard laparoscopic approach besides increased operation time and costs for the robotic procedure [46]. Wang et al state that, since clinical outcome of both approaches are comparable with prolonged

operation time for robotic surgery, conventional laparoscopic surgery is preferred [47]. At present, there is no evidence in literature for the use of a robot in terms of better outcome for surgical anti-reflux procedure.

#### *Redo surgery after failed anti-reflux surgery*

The evidence base for revision or re-do laparoscopic anti-reflux surgery is currently limited to case series and one comparative study. An estimated 4% of patients are believed to be eligible for such surgery. The overall conversion rate is a reported 3.5% higher than in primary approach, and operation time 20% longer.

Quality of outcome is lower and rate of reoperation in revision surgery is higher than of primary anti-reflux surgery [Symons, 2011 #13]. A study by van Beek, assessing 17 series representing 1167 cases state that complications occur in a reported 18.6% of cases, with gastrointestinal perforations being the most common complication (14.2%) [van Beek, 2011 #29]. This is in line with the results of an earlier meta-analysis of Peters et al from 2009 drawing upon a total of 1036 patients and reporting a significantly, 79% higher rate of re-operations in the laparoscopic anti-reflux surgery group compared to patients in the open surgery group [14]. The relatively disappointing results of a structured literature search on the issue of redo anti-reflux surgery with regard to morbidity, mortality, and symptomatic outcome support the opinion that redo surgery is tertiary referral center surgery, and that these centers should continue their efforts to collect prospective subjective and objective data [48].

#### *Fundoplication in day care admission*

Ambulatory laparoscopic fundoplication for GERD is on the rise. Ambulatory settings are appealing in terms of increasing patients' satisfaction, reducing time away from home and in saving on bed costs for society. A systematic search performed by Kraft et al yielded 12 publications, but no prospective randomized trial or meta-analysis. Another systematic review of Thomas et al reflects 13 cohort studies. Thomas et al conclude that most patients were satisfied with day-case laparoscopic fundoplication and could be discharged as scheduled in 93% of cases, with a 4% complication and 5% readmission rate. Dysphagia and pain were the main reasons for readmission, and nausea, pain, fatigue and pneumothorax the commonest causes for overnight admission [49]. Analysis of the literature by Kraft shows significant experience with laparoscopic ambulatory surgery for the treatment of gastroesophageal reflux disease, with 751 patients treated in less than 12-h and 583 in less than 24-h care settings. With the reservation that these studies were all of level-4 evidence, the procedure appears to be feasible with very low postoperative mortality and rates of conversion, reoperation and overall morbidity of 3.6, 0.6 and 1.1%, respectively. The most common causes of failure are uncontrolled postoperative pain or postoperative nausea–vomiting. There is no study comparing the functional outcomes after surgery performed in the ambulatory setting versus the non-ambulatory setting. The rate of self-assessed patient satisfaction is high [50]. As a remark, data mentioned in the study by Kraft are all based on level-3b and mostly level 4 evidence, being case series only [51].

Mariette et al reviewed 13 articles with a total of 1459 adult patients who underwent ambulatory laparoscopic fundoplication, 876 patients in a day-case setting and 583 in an outpatient setting [29]. According to this study, ambulant laparoscopic fundoplication is considered to be feasible in selected patients in the hand of expert surgeons. The main inclusion criteria for a day-case fundoplication reported were an ASA grade I or II, with some stabilized and selected ASA grade III patients, a body mass index less than 35 or 40 kg/m<sup>2</sup>, patients living nearby the hospital (from 30 min up to 1.5 h away), a hotel near the hospital, availability of a responsible adult for the first postoperative night, fully motivated and informed patients with a frequently required written consent, patients under the care of a general practitioner, and telephonic accessibility.

Relative contraindications were the existence of a large hiatal hernia, a brachy-oesophagus, history of abdominal (laparoscopic) surgery, a history of surgical intervention for GERD and co morbidity requiring hospitalization (ASA III or IV, with III being a relative contra-indication).

To date, no randomized controlled trials are reported to support the promising data on anti-reflux surgery in the ambulatory setting.

## Discussion

The treatment of gastro-esophageal reflux disease has changed over the past two decades with the development of laparoscopic fundoplication techniques and of more effective medical therapy. Various types of fundoplication have been introduced in the hope of minimizing the risk of postoperative side effects such as dysphagia or gas bloat symptoms.

From the results above, surgical therapy for GERD is to be considered as an effective alternative to medical therapy, especially in the younger patient, and should be offered to appropriately selected patients by appropriately skilled surgeons. Clearly patients who have erosive reflux disease on endoscopy and/or pathologic reflux with a positive symptom index and symptom associated probability during 24 hours pH-metry, with normal esophageal motility, with poor results on medical therapy and/or with side effects of medical therapy are good surgical candidates.

Unfortunately, no clear definition or consensus could be retrieved what an 'expert surgeon' in anti-reflux surgery is believed to be. Like any other surgical procedure, laparoscopic anti-reflux surgery is subject to a learning curve, which may impact patient outcomes. As the meta-analysis of Peters suggests in order to prevent re-operations, it is very important that patients are both carefully selected for the appropriate procedure and that the procedure is performed by a dedicated anti-reflux surgeon.

According to the SAGES guidelines, level III evidence exists that surgeons seek experienced supervision during their first 15–20 laparoscopic anti-reflux procedures to minimize adverse outcomes as a result of the learning curve [7]. Level II evidence is reported from the literature suggesting that redo anti-reflux surgery should be undertaken in high volume tertiary centers by experienced anti-reflux surgeons only, citing a decreased conversion rate compared with lower volume centers.

It is now known that both the laparoscopic Toupet fundoplication and 180-degree anterior fundoplication equal the 360 degree Nissen fundoplication in terms of long-term reduction of acid reflux; and it is to be advised not to perform Nissen fundoplication for GERD patients.

To date, it is not known if postoperative symptom reduction is significantly reduced in 180 degrees LAF patients, compared to Toupet patients. But having a similar outcome on acid reflux, one might hypothesize that a less invasive procedure such as the 180 degrees LAF, not necessarily requiring division of short gastric vessels nor extensive mobilization, might have a lower operation risks over-all. It is not known if dysphagia and gas-related symptoms are reduced by LAF compared to Toupet and Nissen fundoplication. It does seem that Toupet fundoplication has a lower incidence of postoperative dysphagia as compared to Nissen fundoplication in large volume centers. To evaluate postoperative outcome in LAF compared to Toupet fundoplication more evidence is needed.

It seems that ambulatory laparoscopic fundoplication for GERD is an attractive option for selected patient groups in the hand of expert surgeons. That being stated, promising results for ambulatory laparoscopic fundoplication need to be supported by research from high methodological quality that is currently missing.

In patients with mild to moderate GERD who are dependent on medication, but are reluctant to use them or reluctant or unable to undergo surgery, endoscopic procedures to treat GERD may be very interesting both to patient and physician. No systematic reviews were obtained from literature, hence it was not mentioned in the results section of this article.

The transoral incisionless endoluminal fundoplication (ELF) is a relatively new endoscopic technique that has been examined by a number of authors. In this technique, a device is used for the formation of an intraluminal wrap [52]. The two year results of the group of Cadière includes only fourteen patients; of the original group of 17 patients, two patients underwent retreatment. Complete cure from GERD was obtained in 30% of patients and remission only in 50% of patients [53]. The group of Witteman et al state that the endoluminal fundoplication improved quality of life and reduced the need for PPI's in only a subgroup of patients at three years follow-up. The amount of patients requiring additional medication and revision surgery was high [54]. Another study by Testoni et al, including 42 GERD patients states that about 77% of patients to stop or at least halve PPI use at six-month follow-up after ELF; and that this proportion dropped to about 69% at 24-month evaluation, raising some concern about how long fundoplication lasts with the current technique [55]. Long-term outcome results at the moment are lacking, and so are well-designed randomized trails between ELF

and fundoplication surgery. ELF at the moment cannot be considered a valid alternative for anti-reflux surgery as of yet [56].

A second alternative to the surgical fundoplication to be found in literature is a ringed magnetic device which is placed in a laparoscopic procedure around the LES and which enables food bolus to pass but inhibits regurgitation of gastric contents [57]. Initial studies show promising results. Intake of a proton pump inhibitor decreased in majority of patients and reflux oesophagitis was 40% at baseline and decreased to 11% at two years follow up. Most important side effect was dysphagia, which decreased from 68% directly after the procedure to 4% at three years. The device was, however, not tested in a randomized study compared to standard surgical fundoplication so these study results have to be awaited.

Another novel device is an electrical lower esophageal sphincter pacing device [58]. During a laparoscopic procedure, electrodes are placed at the lower esophageal sphincter. The electrodes are exteriorized and electric pulses generate an increased lower esophageal sphincter pressure. Short-term stimulation of the lower esophageal sphincter in patients with GERD significantly increases resting lower esophageal sphincter pressure without affecting esophageal peristalsis or lower esophageal sphincter relaxation. Therefore, electrical stimulation of the lower esophageal sphincter may offer a novel therapy for patients with GERD. For this device results from randomized studies have to be awaited as well.

At present, there is insufficient evidence to determine both safety and efficacy of a variety of endoscopic procedures such as for gastro-esophageal reflux disease, particularly in the long term [3].

Results have to be awaited comparing the laparoscopic 180-degree anterior fundoplication with the Toupet fundoplication to be a possible better surgical alternative. Division of the short gastric vessels is not to be recommended, nor is the use of a bougie or a mesh in the vast majority of GERD patients undergoing surgery. The use of a robot is not recommended. Anti-reflux surgery is to be considered expert surgery, but there is no clear consensus what is to be called an 'expert surgeon'. As for setting, ambulatory settings seem promising although high-level evidence is lacking.

### Practice points

- Good candidates for anti-reflux surgery are patients who have erosive reflux disease visible on endoscopy and/or pathological reflux with a positive symptom index and symptom associated probability during 24 hours pH-metry; with normal esophageal motility; not satisfied with – or with an incomplete response to – proton pump inhibitors
- Laparoscopic fundoplication surgery is more effective than medical management in the treatment of GERD in adults
- In case a diet and lifestyle intervention fails for the severely obese patient (BMI between 25–30 or over 30), a Roux-en-Y gastric bypass is a better strategy than a fundoplication in order to control GERD
- The laparoscopic Toupet fundoplication is the therapy of choice for normal-weight GERD patients qualifying for laparoscopic anti-reflux surgery
- A division of the short gastric vessels in constructing a fundoplication is to be avoided
- The use of a bougie is to be avoided in constructing partial fundoplications in anti-reflux surgery
- The use of a mesh is not to be recommended in standard anti-reflux surgery; unless there is a large, concomitant paraoesophageal hernia. Polypropylene is the material of choice.
- The use of a robot is not recommended in performing laparoscopic anti-reflux surgery
- Day care settings seem feasible for selected patient groups in laparoscopic anti-reflux surgery
- Laparoscopic anti-reflux surgery and especially redo surgery after failed anti reflux surgery should be performed by experts/in expert centers
- There is not sufficient evidence to conclude on the safety and efficacy of a variety of endoscopic procedures in gastro-esophageal reflux disease, particularly in the long term.

## Research agenda

- A randomized clinical trial between outcomes and long-term reflux control after laparoscopic toupet fundoplication considered being the procedure of choice based on the evidence, and the 180-degree laparoscopic anterior fundoplication is to be undertaken to establish best procedure for GERD symptom control and post-operative symptoms resulting from type of fundoplication
- Anti-reflux surgery is to be considered expert surgery, but there is no clear consensus what is to be called an 'expert surgeon'. A consensus statement based on Delphi analysis and outcome results related to volume is needed
- A randomized clinical trial between in-hospital and ambulatory settings is needed to address best operative setting for outcome and patient satisfaction in anti-reflux surgery

## Conflict of interest

No conflict of interest reported.

## References

- [1] Kahrilas P, Shaheen N, Vaezi M, Hiltz S, Black E, Modlin I, et al. American Gastroenterological Association Medical Position Statement on the management of gastroesophageal reflux disease. *Gastroenterology* 2008;135:1383–91.
- [2] Wileman SM, McCann S, Grant AM, Krukowski ZH, Bruce J. Medical versus surgical management for gastro-oesophageal reflux disease (GORD) in adults. *Cochrane Database Syst Rev* 2010;17(3). CD003243.
- [3] Chen D, Barber C, McLoughlin P, Thavaneswaran P, Jamieson GG, Maddern GJ. Systematic review of endoscopic treatments for gastro-oesophageal reflux disease. *Br J Surg* 2009 Feb;96(2):128–36.
- [4] Dimenäs E. Methodological aspects of evaluation of Quality of Life in upper gastrointestinal diseases. *Scand J Gastroenterol Suppl* 1993;199:18–21.
- [5] Revicki DA, Wood M, Maton PN, Sorensen S. The impact of gastroesophageal reflux disease on health-related quality of life. *Am J Med* 1998;104(3):252–8.
- [6] Klinkenberg-Knol E, Nelis F, Dent J, Snel P, Mitchell B, Prichard P, et al. Long-term omeprazole treatment in resistant gastroesophageal reflux disease: efficacy, safety, and influence on gastric mucosa. *Gastroenterology* 2000 Apr;118(4):661–9.
- [7] (SAGES). SoAGES. Revised SAGES guidelines for surgical treatment of gastroesophageal reflux disease (GERD); 2010.
- [8] Brown SR, Gyawali CP, Melman L, Jenkins ED, Bader J, Frisella MM, et al. Clinical outcomes of atypical extra-esophageal reflux symptoms following laparoscopic antireflux surgery. *Surg Endosc* 2011 Dec;25(12):3852–8.
- [9] Broeders JA, Roks DJ, Draaisma WA, Hazebroek EJ, Broeders IA, Smout AJ. Predictors of objectively identified recurrent reflux after primary Nissen fundoplication. *Dis Esophagus* 2010 Aug;23:43A.
- [10] Dallemagne B, Weerts JM, Jehaes C, Markiewicz S, Lombard R. Laparoscopic Nissen fundoplication: preliminary report. *Surg Laparosc Endosc* 1991;1(3):138–43.
- [11] Broeders JA, Mauritz FA, Ahmed Ali U, Draaisma WA, Ruurda JP, Gooszen HG, et al. Systematic review and meta-analysis of laparoscopic Nissen (posterior total) versus Toupet (posterior partial) fundoplication for gastro-oesophageal reflux disease. *Br J Surg* 2010 Sep;97(9):1318–30.
- [12] Broeders JA, Roks DJ, Ahmed Ali U, Draaisma WA, Smout AJ, Hazebroek EJ. Laparoscopic anterior versus posterior fundoplication for gastroesophageal reflux disease: systematic review and meta-analysis of randomized clinical trials. *Ann Surg* 2011 Jul;254(1):39–47.
- [13] Antoniou SA, Koch OO, Antoniou GA, Pointner R, Granderath FA. Mesh-reinforced hiatal hernia repair: a review on the effect on postoperative dysphagia and recurrence. *Langenbeck's Arch Surg* 2012;397(1):19–27.
- [14] Peters MJ, Mukhtar A, Yunus RM, Khan S, Pappalardo J, Memon B, et al. Meta-analysis of randomized clinical trials comparing open and laparoscopic anti-reflux surgery. *Am J Gastroenterol* 2009 Jun;104(6):1548–61. quiz 7, 62.
- [15] Siddiqui M, Abdulaal Y, Nisar A, Ali H, Hasan F. A meta-analysis of outcomes after open and laparoscopic Nissen's fundoplication for gastro-oesophageal reflux disease in children. *Pediatr Surg Int* 2011;27(4):359–66.
- [16] Broeders JA, Roks DJ, Ahmed Ali U, Watson DJ, Baigrie RJ, Cao Z, et al. Laparoscopic anterior 180-degree versus nissen fundoplication for gastroesophageal reflux disease: systematic review and meta-analysis of randomized clinical trials. *Ann Surg* 2013 May;257(5):850–9.
- [17] Fein M, Seyfried F. Is there a role for anything other than a Nissen's operation? *J Gastrointest Surg* 2010 Feb;14 Suppl 1: S67–74.
- [18] Lundell LR. Risks and benefits of surgery in refractory GERD. *Dis Esophagus* 2012 Oct;25 Suppl.:26 A. C20705.
- [19] von Rahden BH, Scheurlen M, Filser J, Stein HJ, Germer CT. Newly recognized side-effects of proton pump inhibitors. Arguments in favour of fundoplication for GERD? *Chirurg* 2012 Jan;83(1):38–44.
- [20] Al Talalwah N, Woodward S. Gastro-oesophageal reflux part 3: medical and surgical treatment. *Br J Nurs* 2013;22(7):409–15.

- [21] Gatenby PA, Bann SD. Antireflux surgery. *Minerva Chir* 2009 Apr;64(2):169–81.
- [22] Thijssen AS, Broeders IA, de Wit GA, Draaisma WA. Cost-effectiveness of proton pump inhibitors versus laparoscopic Nissen fundoplication for patients with gastroesophageal reflux disease: a systematic review of the literature. *Surg Endosc* 2011 Oct;25(10):3127–34.
- [23] Grant A, Wileman S, Ramsay C, Bojke L, Epstein D, Sculpher M, et al. The effectiveness and cost-effectiveness of minimal access surgery amongst people with gastro-oesophageal reflux disease – a UK collaborative study. The REFLUX trial. *Health Technol Assess* 2008 Sep;12(31):1–181 [iii–iv].
- [24] Grant AM, Boachie C, Cotton SC, Faria R, Bojke L, Epstein DM, et al. Clinical and economic evaluation of laparoscopic surgery compared with medical management for gastro-oesophageal reflux disease: 5-year follow-up of multicentre randomised trial (the REFLUX trial). *Health Technol Assess* 2013;17(22):1–167.
- [25] De Jong JR, Besselink MGH, Van Ramshorst B, Gooszen HG, Smout AJPM. Effects of adjustable gastric banding on gastroesophageal reflux and esophageal motility: a systematic review. *Obes Rev* 2009;11(4):297–305.
- [26] De Groot NL, Burgerhart JS, Van De Meeberg PC, de Vries DR, Smout AJ, Siersema PD. Systematic review: the effects of conservative and surgical treatment for obesity on gastro-oesophageal reflux disease. *Aliment Pharmacol Ther* 2009 Dec 1;30(11–12):1091–102.
- [27] Kothari V, Shaligram A, Reynoso J, Schmidt E, McBride CL, Oleynikov D. Impact on perioperative outcomes of concomitant hiatal hernia repair with laparoscopic gastric bypass. *Obes Surg* 2012 Oct;22(10):1607–10.
- [28] Stefanidis D, Hope WW, Kohn GP, Reardon PR, Richardson WS, Fanelli RD. Guidelines for surgical treatment of gastroesophageal reflux disease. *Surg Endosc* 2010 Nov;24(11):2647–69.
- [29] Mariette C, Pessaux P. Ambulatory laparoscopic fundoplication for gastroesophageal reflux disease: a systematic review. *Surg Endosc* 2011 Sep;25(9):2859–64.
- [30] Khatri K, Sajid MS, Brodrick R, Baig MK, Sayegh M, Singh KK. Laparoscopic Nissen fundoplication with or without short gastric vessel division: a meta-analysis. *Surg Endosc Interv Tech* 2012 Apr;26(4):970–8.
- [31] Tosato F, Marano S, Luongo B, Paltrinieri G, Portale G, Mattacchione S, et al. Partial or total fundoplication (with or without division of the short gastric vessels): which is the best laparoscopic choice in GERD surgical treatment? *Surg Laparosc Endosc Percutan Tech* 2010;20(6):371–7.
- [32] Markar SR, Karthikesalingam AP, Wagner OJ, Jackson D, Hewes JC, Vyas S, et al. Systematic review and meta-analysis of laparoscopic Nissen fundoplication with or without division of the short gastric vessels. *Br J Surg* 2011 Aug;98(8):1056–62.
- [33] Engstrom C, Jamieson CG, Devitt PG, Watson DI. Meta-analysis of two randomized controlled trials to identify long-term symptoms after division of the short gastric vessels during Nissen fundoplication. *Br J Surg* 2011 Aug;98(8):1063–7.
- [34] Shan CX, Zhang W, Zheng XM, Jiang DZ, Liu S, Qiu M. Evidence-based appraisal in laparoscopic Nissen and Toupet fundoplications for gastroesophageal reflux disease. *World J Gastroenterol* 2010 Jun 28;16(24):3063–71.
- [35] Broeders IAJL, Maurits FA, Ali UA, Draaisma WA, Ruurda JP, Gooszen HG, et al. Laparoscopic nissen (POSTERIOR TOTAL) versus toupet (POSTERIOR PARTIAL) fundoplication for gastroesophageal reflux disease – a meta-analysis of RCTs. *Surg Endosc Interv Tech* 2011 Mar;25S42.
- [36] Tan G, Yang Z, Wang Z. Meta-analysis of laparoscopic total (Nissen) versus posterior (Toupet) fundoplication for gastroesophageal reflux disease based on randomized clinical trials. *ANZ J Surg* 2011 Apr;81(4):246–52.
- [37] Ma S, Qian B, Shang L, Shi R, Zhang G. A meta-analysis comparing laparoscopic partial versus Nissen fundoplication. *ANZ J Surg* 2012 Jan–Feb;82(1–2):17–22.
- [38] Patterson E, Herron D, Hansen P, Ramzi N, Standage B, Swanstrom L. Effect of an esophageal bougie on the incidence of dysphagia following nissen fundoplication: a prospective, blinded, randomized clinical trial. *Arch Surg* 2000;135:1055–61.
- [39] Jarral OA, Athanasiou T, Hanna GB, Zacharakis E. Is an intra-oesophageal bougie of use during Nissen fundoplication? *Journal* 2012 June;14(6):828–33.
- [40] Kohn G, Price R, Demeester S, Zehetner J, Muensterer O, Awad Z, et al. SAGES guidelines for the management of hiatal hernia; 2013.
- [41] Furnee E, Hazebroek E. Mesh in laparoscopic large hiatal hernia repair: a systematic review of the literature. *Surg Endosc* 2013 June. <http://dx.doi.org/10.1007/s00464-013-3036-y> [Epub ahead of print].
- [42] Kahokehr A, Sammour T, Srinivasa S, Hill AG. Systematic review and meta-analysis of intraperitoneal local anaesthetic for pain reduction after laparoscopic gastric procedures. *Br J Surg* 2011 Jan;98(1):29–36.
- [43] Owens M, Barry M, Janjua AZ, Winter DC. A systematic review of laparoscopic port site hernias in gastrointestinal surgery. *Surgeon* 2011 Aug;9(4):218–24.
- [44] Maeso S, Reza M, Mayol JA, Blasco JA, Guerra M, Andradas E, et al. Efficacy of the Da Vinci surgical system in abdominal surgery compared with that of laparoscopy: a systematic review and meta-analysis. *Ann Surg* 2010 Aug;252(2):254–62.
- [45] Zhang P, Tian JH, Yang KH, Li J, Jia WQ, Sun SL, et al. Robot-assisted laparoscopic fundoplication for gastroesophageal reflux disease: a systematic review of randomized controlled trials. *Digestion* 2010 Feb;81(1):1–9.
- [46] Markar SR, Karthikesalingam AP, Hagen ME, Talamini M, Horgan S, Wagner OJ. Robotic vs. laparoscopic Nissen fundoplication for gastro-oesophageal reflux disease: systematic review and meta-analysis. *Int J Med Robot* 2011 Jun;6(2):125–31.
- [47] Wang Z, Zheng Q, Jin Z. Meta-analysis of robot-assisted versus conventional laparoscopic Nissen fundoplication for gastroesophageal reflux disease. *ANZ J Surg* 2012 Mar;82(3):112–7.
- [48] Furnee EJ, Draaisma WA, Broeders IA, Gooszen HG. Surgical reintervention after failed antireflux surgery: a systematic review of the literature. *J Gastrointest Surg* 2009 Aug;13(8):1539–49.
- [49] Thomas H, Agrawal S. Systematic review of day-case laparoscopic fundoplication. *J Laparoendosc Adv Surg Tech A* 2011 Nov;21(9):781–8.
- [50] Kraft K, Mariette C, Sauvanet A, Balon JM, Douard R, Fabre S, et al. Indications for ambulatory gastrointestinal and endocrine surgery in adults. *J Visc Surg* 2011 Feb;148(1):69–74.
- [51] Phillips B, Ball C, Sackett D, Badenoch D, Straus S, Haynes B, et al. Levels of evidence and grades of recommendation: Oxford Centre for Evidence-based Medicine Levels of Evidence [accessed July 2013].
- [52] Cadière GB, Rajan A, Germay O, Himpens J. Endoluminal fundoplication by a transoral device for the treatment of GERD: a feasibility study. *Surg Endosc* 2008;22(2):333–42.

- [53] Cadière GB, Van Sante N, Graves JE, Gawlicka AK, Rajan A. Two-year results of a feasibility study on antireflux transoral incisionless fundoplication using Esophyx. *Surg Endosc* 2009;23(5):957–64.
- [54] Witteman BP, Strijkers R, de Vries E, Toemen L, Conchillo JM, Hameeteman W, et al. Transoral incisionless fundoplication for treatment of gastroesophageal reflux disease in clinical practice. *Surg Endosc* 2012 Nov;26(11):3307–15.
- [55] Testoni PA, Vailati C, Testoni S, Corsetti M. Transoral incisionless fundoplication (TIF 2.0) with EsophyX for gastroesophageal reflux disease: long-term results and findings affecting outcome. *Surg Endosc* 2012 May;26(5):1425–35.
- [56] Nicolau AE, Lobontiu A, Constantinescu G. Endoluminal fundoplication (ELF) with EsophyX2 for gastroesophageal reflux disease (GERD). *Chirurgia (Bucur)* 2009 Jul–Aug;104(4):381–7.
- [57] Ganz RA, Peters JH, Horgan S, Bemelman WA, Dunst CM, Edmundowicz SA, et al. Esophageal sphincter device for gastroesophageal reflux disease. *N Engl J Med* 2013;368(21):2039–40.
- [58] Rodríguez L, Rodríguez P, Neto MG, Ayala JC, Saba J, Berel D, et al. Short-term electrical stimulation of the lower esophageal sphincter increases sphincter pressure in patients with gastroesophageal reflux disease. *Neurogastroenterol Motil* 2012; 24(5):446–50.