Review Article

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Endoscopic treatment of gastroesophageal reflux: a narrative review

Samuel Oliveira Lopes[a,*], Ana Raquel Gonçalves[a,b], Guilherme Macedo[a,b], João Santos-Antunes[a,b,c]

Abstract Gastroesophageal reflux disease (GERD) is a common chronic disease that affects one-third of the population worldwide. In recent years, there have been significant advances for diagnostic workup, which leads to better identification of reflux-related complications. Classically, the mainstay of therapy has been proton pump inhibitor and lifestyle and dietary modifications. For refractory GERD the gold-standard therapies are surgical antireflux procedures. Recently, endoscopic procedures have emerged as safe and efficient alternatives to surgery. These could represent a less invasive approach, with scarce morbidity and with a well-tolerated profile. Each of the existing endoscopic techniques for the treatment of GERD are addressed in this report, highlighting their potential advantages, aiming at helping decide the best management of these patients. Future studies, with larger numbers of patients, may allow a definitive role for these techniques in the management of GERD to be established.

Keywords: endoscopic treatment, gastroesophageal reflux disease

Introduction

Gastroesophageal reflux disease (GERD) is a clinical condition defined as the presence of symptoms and complications, related to the reflux of stomach contents into the esophagus.[1] GERD is a common disorder that affects quality of life, and there has been an increasing incidence and prevalence worldwide. This disease produces undesirable symptoms, such as regurgitation and heartburn, as well as other complications involving mucosal damage.[1]

The main cause for GERD is the dysfunction of the lower esophageal sphincter (LES), in which there is an inappropriate transient relaxation of the LES or a decrease in basal pressure at rest, sometimes related to anatomic alteration of the esophagogastric junction, such as the presence of a hiatal hernia.[2]

Patients with GERD report worse quality of life (QoL) because of symptoms, such as heartburn, regurgitation, dysphagia, odynophagia, atypical chest pain, and chronic cough.[3] In fact, GERD is often undervalued for its impact in patient's daily life, on the productivity, and quality of life overall,[4] so the correct management of this disease is very important to improve patient's life quality and reduce complications associated with the disorder and its treatment.

[a] Faculty of Medicine, University of Porto, Porto, Portugal, [b] Gastroenterology Department, Centro Hospitalar Universitário S. João, Porto, Portugal, [c] Ipatimup/i3S (Instituto de Investigação e Inovação em Saúde da Universidade do Porto), Porto, Portugal

* Corresponding author. Faculty of Medicine, University of Porto, Al. Prof. Hernani Monteiro, 4200-319, Porto, Portugal. E-mail address: samuelopes23@gmail.com (Samuel Oliveira Lopes).

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Treatment goals in GERD include symptom relief, cure of esophagitis if present, prevention of recurrence of symptoms, and prevention of complications such as esophageal ulcers, peptic strictures, and Barrett esophagus.[5] Medical therapy with proton pump inhibitors (PPIs) and surgical treatments have been the mainstay treatments for decades, reducing symptoms and improving the quality of life of patients with GERD. Many patients do not have a good response to PPIs or do not want to take this medication in the long term or have atypical symptoms such as dysphagia, odynophagia, chest pain, chronic cough, or asthma, which may benefit from another therapeutic approach.[5]

Recently, endoscopic therapies for GERD have emerged to improve GERD symptoms, aiming to reach the surgical results that have been described for decades, as a less invasive option, with advantages for morbidity and mortality.

In this article, we aimed to review endoscopic techniques as less invasive options for GERD treatment, such as endoscopic fundoplication with a transoral endoscopic device, nonablative radiofrequency treatment for GERD, transoral incisionless fundoplication (TIF), antireflux mucosectomy (ARMS), antireflux mucosal ablation (ARMA), endoscopic submucosal dissection, peroral endoscopic cardial constriction with band ligation, and endoscopic plication with the GERDx device.

In this narrative review, searches were performed in the PubMed, EMBASE, and Cochrane Library databases from September 2022 to March 2023. The terms "endoscopic treatment," "gastroesophageal reflux disease," "endoscopic fundoplication with a transoral endoscopic device," "nonablative radiofrequency treatment for gastroesophageal reflux disease," "transoral incisionless fundoplication," "anti-reflux mucosectomy," "anti-reflux mucosal ablation," "endoscopic submucosal dissection," "peroral endoscopic cardial constriction with band ligation," "endoscopic plication with the GERDx device" were used, but not limited to, as search terms. Selected literature types include research articles, systematic reviews, narrative reviews, letters, commentaries, and opinion articles. Studies not written in English were excluded.

Epidemiology of GERD

GERD affects between 8% and 33% of the world's population and affects all age groups and sex.[3,6] It is a very common disease, with a

higher prevalence in South Asia, Southeast Europe, and America. The prevalence in Europe is approximately 8.8%–25.9%.[7] In the United States, the annual expenditure on diagnosing and treating the disease exceeds 9 billion dollars.[6,8]

Pathophysiology

The pathophysiology of GERD can be mechanical and/or acid related. The pathophysiology of GERD is complex, and it is determined by the balance of protective factors against reflux such as the antireflux barrier, esophageal acid clearance, and tissue resistance and aggressive factors such as gastric acidity, volume, and duodenal contents.[9] Gastroesophageal reflux is not pathognomonic of GERD because it occurs in healthy people.[10] There are physiological factors that promote GERD such as LES dysfunction, hiatal hernia, and increased numbers of transient lower esophageal sphincter relaxations that is a brief moment of inhibition of the tone of the LES, independent of a swallow. Antireflux procedures, such as the Nissen fundoplication, promotes the decrease of these transient events, as well as the amount of gastric reflux, ineffective esophageal clearance, the presence of an acid pocket, and delayed gastric emptying.[10-13]

Diagnosis

To make the diagnosis of GERD, it is necessary to take a detailed medical history. If there are symptoms suggestive of GERD such as heartburn and regurgitation, with no alarm symptoms, an 8-week using PPIs could be performed to confirm the diagnosis[14]; if the symptoms are not resolved or if alarm symptoms are present, such as dysphagia, odynophagia, melena, hematemesis, or abnormal weight loss, an upper digestive endoscopy must be performed to determine whether there is any acid reflux complication, such as esophagitis, ulcers, strictures, or Barrett esophagus,[15] or other types of diseases.

Twenty Four-hour esophageal pH monitoring is done to measure the severity of the patient's acid reflux. This diagnostic tool is indicated for patients for who do not respond or have an incomplete response to PPIs, for patients with atypical symptoms, those who experience medication side effects, and those being evaluated for antireflux surgery.[16] Ambulatory 24-hour esophageal pH monitoring is considered the gold standard for diagnosing GERD.[17]

Esophageal manometry is a study of esophageal function, which evaluates peristalsis, amplitudes of contraction and pressure, elongation, and length of the LES. This test provides information about esophageal motility, the strength of peristaltic contractions, and the function of the LES and helps distinguish motility disorders from GERD and adjust GERD treatment. Esophageal manometry should be performed in patients with suspected achalasia and in all patients evaluated for antireflux surgery.[18]

Complications

Acid reflux causes damage to the esophageal squamous epithelium, which leads to cell loss with basal cell hyperplasia and the release of inflammatory cytokines, such as interleukins, because of epithelial aggression, leading to esophagitis.[1]

The Los Angeles Esophagitis Classification System is used to assess the degree of esophagitis which uses an A, B, C, D grading system, and it is based on the number, length, location, and circumferential severity of breaks in the mucosa.[19] Over time, this inflammation causes ulcerations and erosions in the esophageal wall, which can lead to esophageal stricture.[11] Because of chronic mucosal damage, the squamous epithelium is replaced by the columnar epithelium (columnar metaplasia).[20] With time, caliciform cells appear, and Barrett esophagus is established. Each year 0.25% of patients progress from Barrett esophagus to esophageal adenocarcinoma.[1,11,20]

Medical treatment

Currently, PPI-based pharmacological therapy in combination with lifestyle modifications (e.g., elevating the head of the bed while sleeping, changing eating habits, restricting alcohol and tobacco consumption, controlling body weight, avoiding the supine position after meals, and avoiding meals 2–3 hours before sleep) continues to be the mainstay of GERD treatment and the first measures to adopt.[21-23]

Acid suppression with PPI therapy is the most commonly used treatment option because it is highly effective in alleviating GERD-related symptoms, as well as resolving and maintaining remission of this disease.[5,21,24,25]

However, this pharmacological therapy is less effective for extraesophageal symptoms of GERD and in patients with symptomatic regurgitation.[26] In addition, PPIs, which are daily medications that sometimes need to be prescribed for prolonged periods or even for life, may lead to relevant side effects, such as the increased risk of bone fracture, infectious complications, interference with antiplatelet drugs, and modified absorption of vitamins and minerals, causing deficiencies of vitamin B12, calcium, magnesium, and iron.[3,5,21-23,25,26]

Furthermore, approximately 40% of patients do not respond completely to PPI treatment.[5,6,22,27,28] If the patient does not feel relief from symptoms despite the use of an optimized dose of PPIs for 8 weeks, the condition is called refractory GERD.[27]

Surgical treatment

The two most popular surgical procedures performed laparoscopically to treat GERD are the Nissen 360-degree fundoplication and the Toupet partial fundoplication.[29]

Antireflux surgery is an option in healthy patients with typical or atypical GERD symptoms well controlled on PPIs, desiring alternative therapy because of poor medication compliance, or fear of possible long-term side effects. Patients with volume regurgitation and aspiration symptoms not controlled with PPIs, or recurrent peptic strictures in younger patients are also suitable for surgical antireflux treatment. Patients with contraindication to the use of PPIs are also candidates.[30] These surgical procedures allow a significant improvement in symptoms (92%), as well as a great reduction in PPI intake (85%).[31]

Surgical treatment, most often laparoscopic Nissen fundoplication (LNF), is indicated when the above measures do not yield satisfactory results in patients. Although laparoscopic fundoplication is the gold standard in the surgical treatment of GERD,[5,24,27] this procedure has become less preferred by patients in recent years, because of the inherent invasiveness of the procedure.[27]

Mortality is rare (<1%) after antireflux surgery, but some patients refer dysphagia, gas bloat, diarrhea, and increased flatus.[32] Because of complications and the degree of invasion inherent to the procedure, alternative therapies such as endoscopic therapies have emerged (Table 1).

Endoscopic treatment

As an alternative to medications and surgery for GERD's treatment, several endoscopic techniques have been developed since the late

Table 1.

Summary of the main studies addressing different endoscopic techniques for the treatment of GERD.

Procedure	First Author	Year	Study design	Limitations	Conclusions
MUSE	Johannes Zacherl[26]	2014	Prospective study	Short follow-up period and the lack of control group Exclusion of a subset of patients with relatively common complications of GERD, such as large hiatal hernia, severe erosive esophagitis, and symptoms unresponsive to PPI therapy, Barrett esophagus, and esophageal motility disorders	It is an option to offer patients seeking reduction or discontinuation of medical therapy for GERD and to avoid troublesome side effects associated with incisional therapies such as LNF.
MUSE	Hong Joo Kim[5]	2015	Prospective study	Small number of patients enrolled and the lack of a dummy or control group Subjective improvements in outcomes such as symptoms and quality of life may not necessarily correlate with objective measurements such as gastroesophageal acid reflux	The MUSE endoscopic stapling device appears to be safe and effective in improving symptom scores as well as reducing PPI use in patients with GERD.
STRETTA	Rakesh Kalapala[3]	2017	Prospective study	Study from a single center and short follow-up time Small sample	Short-term efficacy procedure for the treatment of patients with PPI-refractory GERD Safe, well tolerated, and minimally invasive
STRETTA	Wei-Tao Liang[21]	2014	Prospective study	Not referred by the authors	Stretta procedure was able to control GERD symptoms effectively and safely Reliable treatment modality for adult patients with drug-refractory GERD
STRETTA	J. Arts[34]	2022	Double-blind randomized cross-over study	Reflux evaluation did not include impedance monitoring.	Significant improvement of GERD symptoms. Decreases the distensibility of the GEJ. These data suggest that altered distensibility may be an important pathophysiological factor and a therapeutic target in the treatment of GERD.
TIF	Ninh T. Nguyen[21]	2021	Retrospective study	Not referred by the authors	Collaboration between a GI surgeon and a gastroenterologist has led to new perspectives on the optimal surgically constructed GEFV.
TIF	Munyaradzi Chimukangara[22]	2018	Retrospective study	Small size, single-institution cohort, and lack of a corresponding LARS cohort to compare data Long-term outcome data are lacking Study is based on a telephone questionnaire	TIF can produce lasting improvements in disease-specific quality of life. Although most patients resume long-term antisecretory medications, most patients are satisfied with the control of GERD symptoms and experience a sustained improvement in quality of life.
TIF	Karim S. Trad[38]	2018	Randomized study	Small number of patients Results are reported regardless of PPI use at the time of postprocedural evaluation (with or without PPI therapy)	Five years after the application of TIF 2.0, most patients in the TEMPO study showed lasting elimination of all types of problematic manifestations of GERD, including regurgitation and atypical symptoms. No SAEs or any safety concerns. It also appears that, in the appropriate patient population, the TIF 2.0 procedure may be a cost-effective alternative to LNF.
TIF	Karim S. Trad[36]	2015	Randomized study	Short-term follow-up and the potential placebo effect in the TIF group Small sample size The study population was heterogeneous in relation to the predominant symptomatology.	TIF, compared with the maximum standard dose of PPI therapy, resulted in better control of regurgitation and a wider range of chronic GERD symptoms.
ARMS	Xinke Sui[33]	2022	Retrospective study	Single-center, noncontrolled, nonrandomized study with a small sample size	The clinical efficacy of ARMS and SRF 6 months after the operation were equivalent. The results showed that treatment with ARMS and SRF was acceptable for patients with GEFV grades II and III, whereas ARMS should be selected for patients with GEFV grade IV.
ARMS	Xinyi Yang[27]	2021	Retrospective study	Limited sample size Short follow-up period Lack of an adequate control group	No significant differences between 180° and 270° ARMS in patients with GERD in terms of reflux control, relief of GERD symptoms, improvement in quality of life, and objective GERD parameters. However, notable efficacy in symptom relief was noted between pre- and post-ARMS treatment. The 180° ARMS may be more recommended for the treatment of GERD because of the lower incidence of dysphagia. However, the balance between effective reflux control and dysphagia prevention needs to be further investigated.

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Table 1. (*continued*)

Procedure	First Author	Year	Study design	Limitations	Conclusions
ARMS	Haruhiro Inoue[24]	2014	Pilot study	In almost half of the cases, pH monitoring was not accepted by the patients after the procedure.	ARMS for GERD without sliding hernia showed excellent short-term and medium-term control of GERD. Future larger studies with objective evaluation and long follow-up are warranted.
ARMS	Gaurav Patil[23]	2020	Prospective study	Highly specialized unit with a selective subset of referred patients, the results of which may not be generalizable. Only a few patients were following up at 1 year.	ARMS is an effective antireflux treatment modality for GERD with small hiatal hernia.
ARMA	Oscar Víctor Hernández Mondragón[42]	2020	Prospective study	Did not have a comparison group Single-center study	ARAT is clinically feasible, safe, and effective ablative therapy at early and mid-term evaluations for the control of GERD in patients without sliding hiatal hernia.
ARMA	Haruhiro Inoue[39]	2020	Prospective study	Small number of patients Short follow-up Assessment by an unblinded single operator Lack of pH monitoring data	It is simple, safe, and improves GERD-related symptoms and objective acid reflux parameters.
ARMA	Mayo Tanabe[40]	2020	Retrospective study	Not referred by the authors	Both ARMS and ARMA were effective antireflux therapy methods for PPI-refractory GERD which improved GERD-related symptoms and objective acid reflux parameters. ARMA may be advantageous on its easiness and simplicity regarding operative time.
ARMA	R. Kalapala[41]	2021	Prospective study	Not referred by the authors	ARMA is a safe endoscopic therapeutic option for PPI-refractory GERD with significant improvement in symptoms.
ESD-G	Kazuhiro Ota[43]	2021	Prospective study	Sample size was small, as this was a single-center, single-arm study without a comparison group There are many missing data points The mechanism by which ESD-G improves GERD-related symptoms remains ambiguous The results of the 24-h pH monitoring study could not be assessed because some patients were unable to withdraw gastric acid suppressants	ESD-G may be effective in patients with refractory GERD-related symptoms without a history of distal gastrectomy in the long term.
PECC-B	Zhi-Tong Li[25]	2021	Retrospective study	Small number of enrolled patients prevents controls and double-blind analysis Less evaluation measures and inconsistent standard procedures may make postoperative results less valuable It is not clear whether PECC-B has long-lasting effects	PECC-b is a new, effective, and safe method. It not only can control reflux symptoms, but also relieve reflux-related extra-esophageal symptoms. The postoperative results are stable and satisfactory.
GERDx	Michael Weitzendorfer[44]	2018	Prospective study	Single-arm study 25% lost to follow-up-rate Included only patients with hiatal hernia measuring <2 cm and excluded individuals with Barrett esophagus or esophageal motility disorders.	Endoscopic full-thickness plication using the GERDx device improves the distal acid exposure of the esophagus, typical reflux-related symptoms, and QoL in well-selected patients. This procedure might constitute an option for patients with mild GERD.

ARAT, antireflux ablation therapy; ARMA, anti-reflux mucosal ablation; ARMS, anti-reflux mucosectomy; ESD-G, endoscopic submucosal dissection for GERD; GEFV, gastroesophageal flap valve; GEJ, gastroesophageal junction; GERD, gastroesophageal reflux disease; GerdQ, gastroesophageal reflux disease questionnaire; LARS, laparoscopic antireflux surgery; LNF, laparoscopic Nissen fundoplication; PECC-b, peroral endoscopic cardial constriction with band ligation; PPI, proton pump inhibitors; QoL, quality of life; SAEs, severe adverse events; SRF, Stretta radiofrequency; TIF, transoral incisionless fundoplication.

1990s to modify the gastroesophageal junction (GEJ) to decrease stomach-esophageal reflux.[5,24,25] In patients who have a virtually intact LES (absence of hiatal hernia or hiatal hernia, Hill Grade 1 or 2), it may be beneficial to use an endoscopic technique to restore the LES. Endoscopic methods can be considered less invasive methods compared with surgery.[28,33]

Endoscopic fundoplication with a transoral endoscopic device

Endoscopic fundoplication with a transoral endoscopic device, MUSE, was developed as an endoscopic therapy for GERD. This procedure is performed by a transoral approach using a video-guided surgical stapler. The device contains a camera for direct viewing during insertion and selection of the place where the staple will be placed. The procedure aims to treat LES dysfunction and thus preventing acid reflux into the esophagus.[26]

According to a prospective study with 6 months of follow-up[26], there was a significant decrease in the reduction of GERD-related symptoms using the gastroesophageal reflux disease-health-related quality of life (GERD-HRQL) score (73%) and a 65% reduction in the number of patients taking PPIs daily. Approximately 85% of the patients reported a decrease in dose or frequency of use of PPIs, and there were statistically significant reductions in the total time of esophageal pH below 4. In this study, 8 side effects were reported in the first 24 participants, 2 were rated as severe and required intervention (empyema and pneumothorax needed mechanical ventilation and antibiotic therapy and an upper gastrointestinal hemorrhage, which presented 8 days after the procedure, but no endoscopic treatment was necessary).

In the prospective 4-year follow-up study by Kim et al,[5] 37 participants showed an improvement in GERD symptoms, which was measured as a reduction in the GERD-HRQL score. Sixty Nine percent of patients reported to decrease or stopped taking PPIs, as well as a decrease in the dose or frequency of use of PPIs. There was also a reduction of the total time in which the esophageal pH was <4, but not statistically significant.

These articles showed that this procedure seems to be safe and effective in improving symptoms, as well in reducing the use of PPIs in patients with GERD. It could be a safe and less invasive option to patients who seek to reduce or discontinue GERD drug therapy and avoid side effects.

Nonablative radiofrequency treatment for GERD

The Stretta procedure is a minimally invasive endoscopic procedure that uses radiofrequency energy in the muscles of the LES and in the gastric cardia to decrease gastroesophageal junction compliance, resulting in an improvement of reflux symptoms.[34] This procedure corrects the defect underlying gastroesophageal reflux, while irrigating the overlying mucosa to prevent heat injury because of radiofrequency energy delivered to the esophageal wall.

According to a prospective study with 5 years of follow-up,[21] the disease symptom assessment score decreased after the procedure. This study with 138 patients showed at 6 months that about 29% of the patients stopped taking PPIs, and at the end of 5 years the percentage raised to 43%.

In another prospective study,[3] in which the follow-up lasted 3 months, a higher percentage of patients who abandoned PPI use was found (around 60%). This study also showed a slight increase in LES pressure and also a significant improvement in GERD symptoms.

Studies have reported that approximately 75%–80% of patients were fully or partially satisfied with the results of this procedure,[3,21] and there were no relevant postprocedural complications, except abdominal distension, which was moderately alleviated, after treatment with trimebutine maleate tablets in combination with lifestyle modifications.

This technique is a safe, well-tolerated, minimally invasive procedure, with improvements observed in symptoms and the medication required by the patient.

TIF

TIF is a minimally invasive procedure for the treatment of GERD. TIF is an endoscopic procedure that involves the use of an endoscopic device, called an EsophyX, which is inserted through the mouth and positioned in the esophagus and stomach. This device creates a mechanical antireflux valve between the esophagus and the stomach, creating folds of tissue that are held together by clamps.[35] This procedure is performed without external incisions and does not require a prolonged hospital stay.

The benefits of TIF include a shorter recovery time compared with open surgery, less postoperative pain, and a lower rate of complications compared with surgery.[35]

Analyzing the retrospective study by Chimukangara et al,[22] around 47% of the patients discontinued the PPI at 12 months of follow-up, and this percentage raised to 27% at the end of 97 months. There was an approximately 26% reduction in GERD symptoms at the long-term follow-up, with significant decrease in the GERD-HRQL score from 24 to 7 at the short-term analysis, and to 10 at the 97-month long-term follow-up, with an improvement in quality of patient's lives. However, most patients required PPI therapy to maintain these improvements over time. About 21% of patients underwent a laparoscopic antireflux surgery (LARS) for the failure of the TIF procedure during the study period.

In a randomized clinical trial with 63 patients,[36] the TIF 2.0 technique was used, and all patients underwent this technique with the EsophyX 2 device, under general endotracheal anesthesia. The TIF 2.0 procedure created a full-thickness partial gastroesophageal fundoplication fixed above the Z-line with polypropylene "H" fasteners, which were placed through the thickness of the apposed stomach and esophageal walls. In 62% of patients, evaluated over 6 months, GERD symptoms disappeared, and 90% of them stopped taking PPIs after this time. With the extension of the patient's follow-up to 5 years, there was the elimination of GERD symptoms in about 80–86% of the patients, and about 46% of them stopped taking PPIs after 5 years. There was a 70% patient satisfaction rate with the procedure after 5 years. Elimination of regurgitation, atypical symptoms, and heartburn, as assessed by validated disease-specific scores, was maintained without significant deterioration over time. No complications were reported during and after the procedure.

The ability of the TIF 2.0 procedure to provide durable, long-term resolution of troublesome GERD symptoms improved quality of life and reduced PPI use. It was demonstrated that this technique can be performed on patients with grade 1 or 2 Hill classification. If the classification is higher, performing TIF is not recommended.[37] The reoperation rate was 5% after 5 years, which is comparable with published reoperation rates after laparoscopic Nissen fundoplication.[38]

ARMS

ARMS is an endoscopic procedure that involves the removal of mucosa in the cardia by mucosectomy. Removing this layer creates a scar that helps strengthen the junction between the esophagus and stomach, preventing acid reflux.[24]

In a retrospective study,[33] the ARMS and Stretta techniques were compared in 69 patients, and it was found that the scores that assess the symptoms of GERD decreased significantly in both procedures. There was no significant difference between these two techniques, and there was no significant difference in the discontinuation of PPI use between procedures and between gastroesophageal flap valve (GEFV) grade II and III patients. However, for GEFV grade IV patients, 9 of 12 patients in the ARMS group discontinued PPI use, whereas only 3 of 11 patients in the Stretta radiofrequency (SRF) group discontinued PPI use. That is, ARMS was significantly more effective than SRF for GEFV grade IV patients.[33]

ARMS 180° and 270° procedure, in which the crescent resection of the mucosa of 50% and 75% of the esophagogastric junction circumference, respectively, was performed in 39 patients, with a 6-month follow-up, in a retrospective study by Yang et al.[27] The mean GERD-Q score was 11.38, which decreased to 6.60 after 6 months of operation. There were significant differences in the results of the GERD-Q scores before and after the operation in both groups, but there was no significant difference between groups regarding GERD-HRQL scores and changes in PPI use. After the operation, 58.97% (23 of 39, 9 in the ARMS 180° group and 14 in the ARMS 270° group) discontinued PPI use, and a reduction in PPI dose or frequency was reported in 5 patients treated with ARMS 180° and 4 patients treated with 270° ARMS. Postoperative dysphagia was more frequent in the group that performed ARM at 270°.

In a prospective study,[23] using the ARMS procedure with a follow-up up to 12 months, approximately 61% of patients reported symptomatic improvements. There was a significant decrease in the GERD-HRQL score and the use of PPI. The most common adverse effect was dysphagia, and it was managed successfully with balloon dilatation.[23]

ARMA

ARMA is another endoscopic technique for the treatment of GERD. In this technique, marks were made with a triangular-tipped knife J connected to an electrocautery generator in a spray coagulation mode. Mucosal ablation is performed around the cardia in a butterfly shape, leaving two areas of normal mucosa to avoid stenosis. The depth of the ablation was until reaching the submucosal layer, which was confirmed by observing the indigo carmine dye during the ablation.[39]

In a prospective study by Inoue et al,[39] GERD-HRQL scores, median FSSG score, median Hill flap grade, and median DeMeester score improved significantly. There were no immediate adverse events such as bleeding or perforation. One patient developed dysphagia 2 weeks after ARMA because of stenosis at the esophagogastric junction, which was successfully controlled by two sessions of balloon dilations. The mean length of hospital stay was 4 days.

In another prospective study,[40] 24 patients underwent ARMA, with a reduction in the FSSG score from 25 to 10.5, a reduction in the median acid exposure time (AET) from 9 to 0.5, and the DeMeester score significantly reduced from 33.5 to 2.8. Kalapala et al showed that among 29 patients with PPI refractory GERD, the mean GERD-HRQL reduced from 39.90 to 9.15 and at 6 months to 4.85.[41] There was significant improvement in heartburn and regurgitation score at 3 and 6 months. After 3 months, the DeMeester score went from 41.52 to 25.66 and AET from 24.48 to 8.23. This study showed that the ARMA technique is safe and significantly improves GERD symptoms.[41]

In a larger prospective study,[42] a total of 108 patients were included. At the 3-month postprocedure assessment, there was a decrease from 18.8 to 2.8, 42.5 to 9.1, and 36.5 to 10 points between preprocedure and postprocedure 3 months for AET, DeMeester scores, and GERD-HRQL, respectively. At the 36-month evaluation, 78.6% of the patients were without PPI. After the procedure, there were no major adverse events. However, there was thoracic pain in 13 patients (12%), odynophagia in 9 patients (8.3%), mild abdominal pain in 6 patients (5.3%), mild transprocedural bleeding in 4 patients (3.7%), and about 76 patients (70.4%) had no complications. ARMA was demonstrated to be a clinically feasible, safe, and effective ablative therapy at baseline and intermediate evaluations for the control of GERD in patients without sliding hiatal hernia.

Endoscopic submucosal dissection

Endoscopic submucosal dissection for GERD (ESD-G) is a treatment option for GERD. This technique makes it possible to reduce the opening of the hiatus, performing a resection of the mucosa of the esophagogastric junction with endoscopic dissection of the submucosa. The rationale is the same from ARMS technique, and the resulting scar is expected to reduce gastric reflux.

In the single-arm trial by Ota et al,[43] 35 cases in which ESD-G was performed were analyzed. The clinical efficiency of this procedure was only moderate, and this article revealed that the ESD-G technique may be less effective for patients with a history of distal gastrectomy. Complications were observed in 4 patients: 3 patients developed stenosis and underwent endoscopic balloon dilation, and 1 patient experienced bleeding and underwent endoscopic hemostasis.

Peroral endoscopic cardial constriction with band ligation

Peroral endoscopic cardial constriction with band ligation technique is a recent endoscopic treatment option for GERD. The procedure is minimally invasive and is performed through a transoral endoscopy. In this technique, the mucosa is captured individually with the band ligation at the level of the GEJ and cardia toward the lesser curvature of the stomach, being treated with ligation rings.

In the retrospective study by Li et al,[25] 68 patients were evaluated. 3 and 12 months after the procedure, symptom scores were significantly lower. Medications to treat GERD symptoms were discontinued in approximately 64% of patients, and approximately 77% of patients were completely or partially satisfied with the procedure and with the symptoms control. Esophagitis was documented in about 29% of patients. Post-operatively, 25 patients had mild retrosternal pain and discomfort that disappeared after 3 days; 28 patients had mild dysphagia, which did not require additional balloon dilation, and disappeared after 2 weeks; 10 patients had abdominal distention; 2 patients had mild hemoptysis; and 1 patient had diarrhea, but these problems resolved within 1–2 weeks. There were no serious complications during the follow-up period.

Endoscopic plication with the GERDx device

The GERDx technique is an endoscopic treatment option for GERD. Endoscopic full thickness plication was performed using the GERDx system.

The distal end of the device is retroflexed to the anterior gastric cardia. The arms of the GERDx device were opened, and when they closed, a pretied transmural suture is performed.

In a prospective study,[44] 40 patients were included. Thirty patients completed 3-month follow-up and showed an improvement in the GIQLI score after endoscopic full-thickness plication with the GERDx device. The mean overall reflux-specific symptom (SCL) score was significantly reduced; overall, 93.3% of patients showed SCL improvement after this procedure. Scores for typical reflux symptoms, bowel dysfunction, atypical reflux symptoms, and gas/bloating scores also improved significantly; 10.0% of the patients stated that they were using PPI daily, 26.7% on demand, and 63.3% were without medication after the plication. From the 40 patients, 7 (17.5%) underwent LARS before the 3-month follow-up, 6 because of persistent symptoms and 1 because of a post-therapy complication after endoscopic plication with GERDx.

Conclusions

The prevalence of GERD is increasing worldwide and techniques have been developed to optimize patient's treatment, showing good results in the short and long term,[45] with minimal complications.

GERD treatment is complex, and there is a wide variety of medical and surgical options, such as lifestyle modifications, PPIs therapy, surgical fundoplication, and, more recently, endoscopic procedures. In this review, we explored endoscopy treatment as an option for refractory GERD and as a less invasive alternative to antireflux surgery. GERD's endoscopic treatments bridge the gap between medical and classical surgical treatment, being not as invasive as surgery and avoiding potential side effects of long-term PPI.

Globally, endoscopic procedures are safe, well tolerated, and minimally invasive, with specific particularities that sometimes make them preferred over other techniques. Overall, the procedures evaluated in this review allowed a better quality of life for patients, improvement in symptoms related to GERD, and a decrease in the dosage/frequency of PPIs.

Future directions

The endoscopic treatment for GERD is complex, and many of these techniques require expensive add-on devices. Moreover, the learning process of these procedures is sometimes difficult and limits their popularization. With this review, we can see that more studies are needed to evaluate its long-term effects, as well as to compare their results with Nissen fundoplication. Although some results were promising and encouraging, only a small subset of patients are suitable for endoscopy therapy, and many failed to achieve the long-term goal. Because the pathogenesis of GERD is complex and many times multifactorial, combined techniques could be the future, and an option to consider when the workup shows that more than one GERD mechanism may exist in a particular patient.

Conflict of interest

The authors declare no conflicts of interest.

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