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REVIEW PAPER

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New endoscopic treatment methods for PPI-resistant GERD

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ABSTRACT

Introduction. Gastroesophageal reflux disease (GERD) is a common disease with the highest prevalence in North America. Up to 40% of patients report persistent gastroesophageal reflux disease (GERD) symptoms despite proton pump inhibitor (PPI) therapy.
Aim. The aim of this article is to complete discuss the GERD characterized by heartburn and/or regurgitation symptoms.
Material and methods. We discuss here the evidence for medical therapy for PPI nonresponsive GERD.
Analysis of the literature. GERD may present with a variety of other symptoms, including water brash, chest pain or discomfort, dysphagia, belching, epigastric pain, nausea, and bloating. In addition, patients may experience extraesophageal symptoms like cough, hoarseness, throat clearing, throat pain or burning, wheezing, and sleep disturbances.
Conclusion. There has been an increase in GERD prevalence. GERD is one of the most common gastrointestinal disorders managed by gastroenterologists and primary care physicians.
Keywords. diagnostics, endoscopic treatment, gastrology

Introduction

Gastroesophageal reflux disease (GERD) is a chronic condition of the upper gastrointestinal tract. An international consensus group in Montreal has defined GERD as a condition that develops when reflux of stomach contents causes troublesome symptoms with or without complications.[1] The typical GERD syndrome is characterized by heartburn and regurgitation, and proton pump inhibitor (PPI) therapy represents the mainstay of medical treatment for typical GERD, with very high efficacy in heartburn relief and healing of erosive reflux disease (ERD).[2]

Aim

We performed a systematic literature search and present a narrative review. We investigated factors related to proton pump inhibitor (PPI)-refractory gastroesophageal reflux disease (GERD) symptoms.

Material and methods

According to the recommendations, a new endoscopic treatment method for PPI-resistant GERD have been investigated in data base such as Pubmed, Science Direct and Medline.

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Analysis of the literature

A recent systematic review showed that the prevalence of GERD is 18.1–27.8% in North America, 8.8–25.9% in Europe, 2.5–7.8% in East Asia, 8.7–33.1% in the Middle East, 11.6% in Australia, and 23.0% in South America.[3] Eusebi et al. made global meta-analysis of global prevalescence GERD stated the prevalence of gastro-oesophageal reflux symptoms varied strikingly among countries, prevalence was significantly higher in subjects ≥50 years, smokers, NSAID users and obese individuals, although these associations were modest.[4] Yamasaki et al noticed that over the last decade, there has been a significant increase in the proportion of younger patients with GERD, especially those within the age range of 30–39 years.[5]

There are several important factors like age ≥50 years, male sex, white rase associated with the risk of complications from GERD, but none are strongly associated with GERD symptoms. Environmental factors are strongly related to both GERD symptoms and complications, including obesity, tobacco use, and inversely with infection with *Helicobacter pylori*.[6]

GERD is mainly a clinical diagnosis based on typical symptoms. Patients with typical symptoms should first be given a trial of PPI treatment. Patients with alarm symptoms including dysphagia, anemia, weight loss, bleeding, and recurrent vomiting should proceed directly to upper endoscopy.[7]

To describing endoscopic assessment of oesophagitis there is used the Los Angeles scale (Tab. 1).

Table 1. The Los Angeles scale

Grade	Endoscopic view
A	One (or more) mucosal break no longer than 5 mm, that does not extend between the tops of two mucosal folds
B	One (or more) mucosal break more than 5 mm long that does not extend between the tops of two mucosal folds
C	One (or more) mucosal break that is continuous between the tops of two or more mucosal folds but which involves less than 75% of the circumference
D	One (or more) mucosal break which involves at least 75% of the oesophageal circumference

GERD can result in serious complications, including esophagitis and Barrett's esophagus which can vary widely in severity with severe cases resulting into gastrointestinal (GI) bleeding or potential to progress Barrett's esophagus to esophageal adenocarcinoma.[8]

The treatment gastroesophageal reflux disease included lifestyle modifications like weight loss, avoid smoking, chocolate, carbonated beverages, spicy food, fatty food, alcohol, and large meals.[9] Elevating the head of the bed and sleeping in the left decubitus position, has positive effect too.[10] Pharmacologic management of esophageal reflux is classified into five major categories: acid neutralizing medications, alginate-based barriers, sucralfate, adjunctive therapies and acid-suppressive medications. However, the efficacy of this intervention is often hampered by adherence, costs, and the risks of long-term PPI use.

In the case of treatment failure several surgical techniques are currently available for the treatment of GERD. We include among them Nissen funoplication, antireflux surgery, magnetic sphincter augmentation and Roux-en-Y gastric bypass. Studies show only minimal long-term symptomatic improvements with anti-reflux surgery over PPI therapy, paired with an increased incidence of dysphagia and dyspepsia.[7-11]

Researchers in last years have focused on the development of endoscopic therapies for the management of GERD, which are less invasive and safer than surgical treatment. The original endoluminal therapies have been broadly categorized to four different types; (1) fixation, (2) ablation, (3) injection, (4) mucosal excision and suturing.[11,12] These therapies include injectable agents, electrical stimulation of the lower esophageal sphincter, antireflux mucosectomy, radiofrequency ablation, and endoscopic suturing devices designed to create a fundoplication. The most popular endoscopic antireflux devices include the following: radiofrequency ablation (RFA), transoral incisionless fundoplication (TIF),endoscopic full-thickness plication and Medigus Ultrasonic Surgical Endostapler (MUSE).[13,14]

There are currently two approved endoscopic GERD therapies: Stretta - radiofrequency therapy for GERD uses low-energy radiofrequency ablation of the submucosal tissue and transient lower esophageal sphincter relaxation.

Stretta's four-channel RF generator and catheter system delivers pure sine-wave energy (465 kHz, 2 to 5 watts per channel, 80 volts maximum at 100 to 800 ohms). Each needle tip incorporates a thermocouple that automatically adjusts the power obtup to a desired target temperature in the muscle layer. Maintaining target temperatures below 100° minimizes any adjacent tissue damage due to vaporization and high impedance values. Temperature is similarly monitored with a thermocouple at each needle base abutting the mucosa and the power delivery ceases if such mucosal temperature exceeds 47°. A recent meta-analysis of 18 studies and 1441 patients concluded that: (1) Stretta is very effective in GERD symptom relief; (2) Is safe and well-tolerated; and (3) Stretta significantly reduces acid exposure to the esophagus, but does not consistently normalize pH. On this last point it is important to note that even PPIs do not normalize pH in up to 50% of symptomatically controlled GERD patients treated with PPIs.[12-15] Stretta is an outpatient endoscopic option with unique mech-

anisms of action, is effective, safe and durable. Stretta therapy has been shown to acid and volume reflux. Side effects are extremly rare and included fever, superficial mucosal injury, chest pain requiring opioid analgesic use, transient dysphagia, sedation-related hypotension and submental swelling related to topical analgesia allergy, serious complications are including esophageal perforation and aspiration pneumonia.[14,15] Transoral fundoplication uses polypropylene H fasteners to create a serosa-to-serosa fusion to create a fundoplication, it reconfigures the tissue to obtain a full-thickness gastro-esophageal valve from inside the stomach, by serosa-to-serosa plications which include the muscle layers; the new valve boosts the barrier function of the LES with potentially fewer procedure-related side effects than surgery. The device body is composed of the following: fasteners cartridge; retractor lock; vacuum connection; fastener pushers and helix retractor control; tissue mold knob. The device chassis and tissue mold provide fundic tissue rotation and compression during fastener firing. Fasteners over a stylet: the spear-like stylet penetrates approximated tissue planes, and fasteners ensure adequate tissue alignment and compression during the healing period. Helical retractor provides tissue retraction, anchoring of the GEJ during the creation of fundoplication. This retractor is stored inside the tissue mold during EsophyX-Z insertion into the stomach and during its withdrawal. The invaginator allows circumferential tissue retraction and reduction of small hiatal hernias, and ensures adequate localization of the fundoplication.[16,17]

New endoscopic methods for PPI-resistant GERD are in constant demand. For example Inouone et al. conducted a new method of treatment for gastroesophageal reflux - ARMA - minimally invasive anti-reflux mucosal ablation (Tab. 2). At first stomach was insufflated with CO_2 to visualize the cardia in retroflex view. Next they marked placed using the triangle-tip knife J connected to an electrocautery generator in spray coagulation mode (50W). Mucosal ablation was planned around the cardia on the gastric side in a butterfly shape with width of approximately 1.5 scope diameter, leaving two contralateral areas of normal cardia mucosa with approximately one scope diameter, to avoid stenosis. Saline with indigo carmine dye was injected into the submucosal layer along the markings using a 25-gauge needle. A submucosal cushion reduces thermal injury and the risk of perforation during ablation. Mucosal ablation was performed using the triangle-tip knife J in spray coagulation mode (50W). Adequate ablation depth was defined as reaching the submucosal layer, which could be confirmed by observation of the indigo carmine dye during ablation.[18]

In new study Mondragón used new ablative technique named antireflux ablation therapy - ARAT - for control of GERD in patients without hiatal hernia, the novel treatment using argon plasma coagulation, combined with a submucosal bleb creation (Tab. 2). Process started after marking two lines composed of 5 to 6 dots were placed at EGJ in retroflex view over the greater curvature, using soft coagulation (effect 2, 40W) with 1 to 1.5cm of distance between. Next submucosal bleb was created with the injection of saline solution combined with methylene blue all along the EGJ in retroflex position. High-power coagulation (forced coagulation effect 3, 100w) was applied all along the EGJ starting at z-line up to 3cms below this point in circumference direction, except for the marking lines previously performed, in order to make 270 to 320 degrees of ablation.[19]

Table 2. Comparision of new methods

Short-cut	ARMA	ARAT
Name	anti-reflux mucosal minimally invasive ablation	antireflux ablation therapy
Method	Mucosal ablation around the cardia on the gastric side, next injected aaline with indigo carmine dye into the submucosal layer along the markings and finally mucosal ablation.	Marking two lines dots placed at EGJ in retroflex view over the greater curvature, using soft coagulation. Next created submucosal bleb with the injection of saline solution combined with methylene blue all along the EGJ in retroflex position. In the end high-power coagulation applied all along the EGJ
Study patients	GERD in patients without sliding hiatal hernia >3cm	GERD in patients without hiatal hernia

Conclusion

Endoscopic therapies for the management of GERD have made significant advances in the past 20 years. However, more studies are needed to define optimal techniques and most appropriate patient selection criteria and to further evaluate device and technique safety.

Declarations

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Author contributions

Conceptualization, A.S., D.B.A., A.K.K.,W.L. and G.C.; Formal Analysis, A.S., D.B.A., A.K.K.,W.L. and G.C.; Writing – Review & Editing, A.S., D.B.A., A.K.K.,W.L. and G.C.

Conflicts of interest

The authors declare no conflict of interest.

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