

# Endoscopic alternatives to classic surgical fundoplication in the treatment of gastroesophageal reflux disease

## Alternatywne metody endoskopowe dla klasycznej chirurgicznej fundoplikacji w leczeniu choroby refluksowej przełyku

Michał Miciak<sup>1</sup> , Krzysztof Jurkiewicz<sup>1</sup> , Mariusz Chabowski<sup>2, 3, 4</sup> 

<sup>1</sup>Student Research Club No. 180, Faculty of Medicine, Wrocław Medical University, Wrocław, Poland

(Studenckie Koło Naukowe nr 180, Wydział Lekarski, Uniwersytet Medyczny we Wrocławiu, Wrocław, Polska)

<sup>2</sup>Department of Nursing and Obstetrics, Faculty of Health Science, Wrocław Medical University, Wrocław, Poland

(Katedra Pielęgniarstwa i Położnictwa, Wydział Nauk o Zdrowiu, Uniwersytet Medyczny we Wrocławiu, Wrocław, Polska)

<sup>3</sup>Department of Surgery, 4th Military Teaching Hospital, Wrocław, Poland (Klinika Chirurgiczna, 4 Wojskowy Szpital Kliniczny, Wrocław, Polska)

<sup>4</sup>Department of Clinical Surgical Sciences, Faculty of Medicine, Wrocław University of Science and Technology, Wrocław, Poland

(Katedra Nauk Klinicznych Zabiegowych, Wydział Medyczny, Politechnika Wroclawska, Wrocław, Polska)

### Abstract

Gastroesophageal reflux disease (GERD) is one of the most common gastrointestinal disorders in the modern world. Its onset is predisposed by factors related to poor lifestyle. Treatment of GERD consists of pharmacotherapy or surgery. The classic procedure is Nissen fundoplication. The development of endoscopy has enabled the use of new treatment methods that provide faster patient recovery with efficacy comparable to fundoplication. These methods include TIF (transoral incisionless fundoplication), the Stretta procedure (use of radiofrequency energy), injection of strengthening polymers and implantation of prostheses or anti-reflux stimulators. The TIF procedure is an endoscopic mirroring of fundoplication, the Stretta procedure is designed to reduce the relaxation of the lower oesophageal sphincter. Some polymers and prostheses have had promising therapeutic results but have been withdrawn due to complications, while others are expected to be used in the future. Endoscopic methods are constantly being improved based on the results of clinical trials. This study aims to present selected examples.

**Key words:** gastroesophageal reflux disease; fundoplication; endoscopy; gastroplasty; gastroesophageal junction

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### Streszczenie

Choroba refluksowa przełyku (GERD) jest jednym z najczęstszych zaburzeń żołądkowo-jelitowych we współczesnym świecie. Jej początek jest predysponowany przez czynniki związane ze złym stylem życia. Leczenie GERD polega na farmakoterapii lub zabiegu chirurgicznym. Klasyczną procedurą jest fundoplikacja Nissena. Rozwój endoskopii umożliwił zastosowanie nowych metod leczenia, które zapewniają szybszy powrót pacjenta do zdrowia ze skutecznością porównywalną z fundoplikacją. Metody te obejmują gastroplastykę endoskopową (TIF), procedurę Stretta (wykorzystanie energii o częstotliwości radiowej), wstrzykiwanie polimerów wzmacniających i implantację protez lub stymulatorów antyrefluksowych. Procedura TIF jest endoskopowym lustrzanym odbiciem fundoplikacji, a procedura Stretta ma na celu zmniejszenie rozluźnienia dolnego zwieracza przełyku. Niektóre polimery i protezy miały obiecujące wyniki terapeutyczne, ale zostały wycofane z powodu powikłań, podczas gdy oczekuje się, że inne będą stosowane w przyszłości. Metody endoskopowe są stale udoskonalane na podstawie wyników badań klinicznych. Niniejsze opracowanie ma na celu przedstawienie wybranych przykładów.

**Słowa kluczowe:** choroba refluksowa przełyku; fundoplikacja; endoskopia; gastroplastyka; połączenie żołądkowo-przełykowe

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## Introduction

The essence of gastroesophageal reflux disease (GERD), one of the most common gastrointestinal disorders, is the pathological dumping of food content mixed with hydrochloric acid and enzymes from the stomach back into the oesophagus. This condition is caused by, among other things, delayed gastric emptying (primarily in obesity), oesophageal motility disorders, or a dysfunction of the lower oesophageal sphincter [1, 2]. It occurs in approximately 20% of the adult population, with an increase in incidence in recent years, most likely due to lifestyle (eating in a hurry, shortly before bedtime, in too large a volume at one time) or comorbidities (e.g., diabetes) [3]. Transient GERD can be seen in pregnant women, in whom pressure from the developing fetus on abdominal organs causes unwanted symptoms. Symptoms of the reflux disease can be both oesophageal — heartburn as well as extraoesophageal — cough, hoarseness and retrosternal pain of a non-cardiac origin. Special attention should be paid to patients with persistent vomiting, especially if the vomit contains blood. Other alarming symptoms include recent unintentional weight loss, abdominal pain that awakens a person from sleep, and difficulty swallowing. Long-term, untreated GERD leads to several complications. Chronic irritation of the oesophageal epithelium, which is not resistant to the acidic environment, initially results in the narrowing of the oesophagus, loss of muscular motor function, and Barrett's neoplastic dysplasia [4–6].

## The management of GERD

A patient with the symptoms must follow a diagnostic pathway, the purpose of which is not only to confirm the presence of the condition but more importantly to determine its extent and severity to select the most favourable treatment method. Patients with GERD symptoms but without the alarming ones are instructed to make lifestyle changes and receive PPI pharmacotherapy (1 × daily in the morning) for 8 weeks. When symptoms do not subside after this time, or immediately in patients with alarming symptoms, the gold standard is to perform an endoscopic examination — a gastroscopy. During this procedure, it is possible to take a tissue specimen for histopathological examination, which is particularly important for the diagnosis of GERD complications but is not routinely used [7, 8]. Secondary methods include 24-hour oesophageal pH-metre to determine the extent of the condition and the presence of acidity of gastric origin. It is used especially in the qualification of patients for surgery, and in patients without improvement after a drug treatment. Nowadays, a rarely used diagnostic method is an X-ray of the oesophagus after administration of a contrast agent. The effectiveness of this method is the greatest for the diagnosis of oesophageal hiatal hernia or oesophageal stenosis [9–11]. The classic surgical procedure used in GERD is Nissen fundoplication (Fig. 1). The primary aim of this procedure is to strengthen and improve the func-

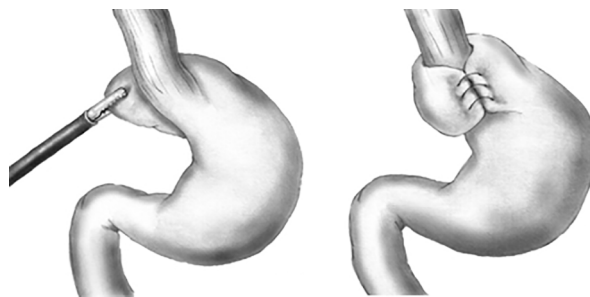


Figure 1. Nissen fundoplication. Based on [17]

tion of the lower oesophageal sphincter. The procedure is most often performed laparoscopically and involves suturing the anterior and posterior walls of the stomach fundus around the oesophagus (after discharging the hiatal hernia, if present). The stomach is then stabilized below the diaphragm, which prevents the recurrence of the hernia and accumulation of acidic food content [12–14]. Like any surgical intervention, fundoplication can also be followed by complications. Most of them are mild and include a feeling of stomach distension, nausea, and transient postoperative dysphagia. The primary surgical anastomosis site may develop a haematoma or perioesophageal abscess at a later time. About 10% of patients present recurrent GERD symptoms despite fundoplication, in which case diagnostic imaging studies like oesophagogastroduodenoscopy and pharmacotherapy are indicated. Reoperation may be necessary if the patient is resistant to PPI or in the case of complications due to technical errors during the procedure. Incomplete release of the abdominal segment of the oesophagus, or unfixing of the manufactured gastric band to the diaphragm, can cause it to slip and retract the gastric body. This leads to increased reflux or severe complications like oesophagitis, ulceration, or perforation. However, such situations do not occur frequently [13, 15]. However, modern surgery offers several other, often more effective, treatments performed endoscopically to treat GERD. The implementation of such methods aims to effectively control disease symptoms with a lower risk of surgical complications and faster patient recovery [16].

## Endoscopic gastroplasty

The procedure of endoscopic suture placement in the area of the gastroesophageal junction is now possible as a result of the development of appropriate devices. These include EndoCinch, Plicator, ESD (Endoscopic Suturing Device), Syntheon ARD Plicator, MUSE (Medigus Ultrasonic Surgical Endostapler), His-Wiz, or EsophyX® [18, 19]. The procedure called Transoral Incisionless Fundoplication (TIF) is performed using the EsophyX® (Endo-Gastric Solutions, Redmond, WA, United States) device, it is the best known and tested device in treating patients with the TIF method [20]. The TIF procedure was introduced in 2006 and has evolved over time to achieve the

best possible therapeutic results. Currently, there are three variants of the device, EsophyX®, EsophyX2®, and EsophyXZ®, which allow several modifications of the TIF procedure to be performed, depending on anatomical conditions or the need for additional oesophageal hiatal hernia repair [21]. During the TIF procedure, the hiatal hernia is reduced, the lower oesophageal sphincter pressure is increased, the gastric cardia is narrowed and the gastric angle (His angle) is reconstructed [22]. The device is composed of a body containing an endoscope that visualizes the operated tissues and a conduit with a spiral retractor that allows the tissue plane to be retracted and held. The distal part of the mentioned conduit folds proximally causing approximation and compression of the tissues of the gastric fundus. Polypropylene connectors, equivalent in strength to 3–0 sutures, are then snapped between the two tissue parts [21–23]. In the version currently performed (TIF 2.0), the procedure mirrors the classic surgical Nissen fundoplication [24]. However, not every patient has the opportunity to undergo the TIF procedure. Certain elements of the anatomy of the area of the gastroesophageal junction need to be assessed, such as the size of the hiatal hernia, the condition of the diaphragmatic crura (especially the right side, as this is the side used in the procedure), and the condition of the lower oesophageal sphincter muscle. Patients who require reconstruction of the diaphragmatic crura or those who have very low sphincter tension will not benefit from the described procedure. Also, those who have a hernia > 2 cm in diameter or longer axially > 2 cm (2 × 2 rule) should not be qualified for TIF but for classic Nissen fundoplication [24, 25]. The long-term results of the TIF procedure appear to be satisfactory. A study by Reginald C. et al. included 151 patients receiving PPIs for the treatment of GERD. All underwent the TIF procedure using the EsophyX2® device. The effects of the procedure were shown to be maintained for nine years after the procedure, with 80% of patients reporting an increase in quality of life in HQLR questionnaires. The procedure had complications with the need for a laparoscopic revision in 23% of patients, in one case due to an iatrogenic injury during the procedure, in one case due to a developed oesophageal abscess, while the rest of the patients had either loosened connectors or developed a hernia at another site. The revisions did not affect the claimed quality of life, which places TIF in an advantageous position due to less patient burden [26, 27]. A study by Bomman S. et al. included 30 patients after a TIF procedure. It was technically successful in 29 patients (97%), and only three patients (10%) underwent a laparoscopic revision due to complications. As many as 70.9% of patients had their PPI doses discontinued or reduced due to a significant improvement in GERD [28]. This is important because studies indicate disease progression during long-term PPI therapy and a higher rate of developing oesophageal adenocarcinoma in this case. It is believed that the TIF procedure should be implemented after a maximum of six months of ineffective PPI pharmacotherapy. Despite the occasional need for laparoscopic revisions after the

TIF procedure, it still offers greater safety and equivalent durability to classic Nissen fundoplication [21, 29].

### Stimulation of the gastroesophageal junction (Stretta procedure)

The Stretta (Curon Medical, Sunnyvale, CA, USA) procedure uses radiofrequency energy to stimulate and neurolize muscles of the gastroesophageal junction. The procedure is designed to thicken and reduce the relaxation capacity of the lower oesophageal sphincter, allowing GERD symptoms to subside. The Stretta procedure was developed and implemented in 2000 and is considered a safe and effective endoscopic alternative to surgery [31]. The device consists of a guiding catheter, a balloon anchoring at the gastroesophageal junction, and a stabilizing basket. Radiofrequency energy is delivered to the myometrium via nickel-titanium needle electrodes. To prevent thermal burns, the oesophageal mucosa is constantly moistened by the device. The procedure, performed with the Stretta device, is intended for patients suffering from GERD symptoms for a minimum of six months, who have responded to drug treatment but have refused to undergo a classic fundoplication [31, 32]. The procedure is performed under general anaesthesia, and after the endoscope is inserted and the device is properly positioned, four electrodes are placed at the appropriate length and energy delivery is initiated. Each electrode reaches a target temperature of 85°C and, during the procedure, several circular constrictions of the musculature above and below the oesophageal hiatus are produced. The temperature is controlled by the device's internal trigger (47°C measured on the mucosa), which prevents iatrogenic injury [33]. The Stretta device can be used even in patients who have undergone surgery in this area or with difficult anatomical conditions, as it requires minimal operative space [34]. The exact mechanism of tissue response to the device's energy has not been clearly described. It was believed that tissue exposed to radiofrequency energy initially undergoes coagulative necrosis and then heals through fibrosis which immobilizes the gastroesophageal junction. However, this theory is unlikely due to the excessively low temperature that Stretta heats the tissue to. What seems the most probable is a reversible change in the neuromuscular function of the oesophageal hiatus. In one study, patients receiving sildenafil after undergoing the Stretta procedure showed a return of myofascial compliance to pre-Stretta levels, suggesting a more complex mechanism of action for the procedure [35, 36]. Multiple clinical studies have shown the safety of the Stretta procedure and its good tolerance by patients, reported complications were also low [33]. Ma L. et al. conducted a study where 230 patients underwent a therapeutic procedure for GERD. 142 of them underwent classic fundoplication and 88 underwent the Stretta procedure. Patients were measured for oesophageal pressure, muscular tension, and pH as prognostic factors in GERD therapy. The results were not statistically different between the procedures, suggesting

identical treatment success with no surgical risk to the patient (in the Stretta procedure) [37]. This was noted in a study conducted by Richards WO. *et al.* They treated 140 patients (65 — the Stretta procedure, 75 — classic fundoplication). There were seven major postoperative complications in the fundoplication group with none in the Stretta procedure group. Despite this, the patients' satisfaction with the results of the procedure was not affected (about 90% satisfaction in both groups) [38]. The Stretta procedure is also more effective in controlling GERD symptoms than PPI pharmacotherapy. He S. *et al.* compared two groups of patients, 28 following the Stretta procedure and 21 using PPIs alone. The improvement in the symptoms and quality of life was significant in the group of patients after the Stretta procedure [39]. Its major advantage is also no lost opportunity for future anti-reflux procedures. Fanous M. *et al.* described the case of a 56-year-old female patient who required the previously discussed TIF procedure because of inadequate control of GERD symptoms after the Stretta procedure. Due to multiple comorbidities and the patient's own decision, the Stretta procedure was implemented. After attempting to discontinue the PPI, GERD symptoms returned and the patient had to undergo a TIF procedure, which was finally successful. Therefore, there are cases of failure even in such a novel method, not due to its inadequacies but usually due to too late a referral of patients with GERD for the procedure. The described patient had been struggling with a reflux disease for 25 years, which is a factor that makes the procedure less likely to succeed. In addition, patients are often afraid of the side effects of long-term PPI use (dementia, kidney failure, osteoporosis), which also does not predict success in the treatment of GERD. Thus, comprehensive care and cooperation between the gastroenterologist and the surgeon performing the anti-reflux procedures is required [40, 41].

### Implementation of substances strengthening the gastroesophageal junction area (polymers)

Substances implemented in the area of the gastroesophageal junction are designed to strengthen the muscular tone and constrict the junction, making it possible to control the symptoms of GERD. They are called "bulking agents". A substance called Enteryx® (Boston Scientific, Natick, Massachusetts, USA) has been used for this purpose in the past. It is a biopolymer consisting of 8% vinyl ethyl alcohol and tantalum (a radiopaque contrast agent) dissolved in dimethyl sulfide. The liquid substance was injected peripherally into the gastroesophageal junction under fluoroscopic guidance. After contact with the tissue, it increased its density and filled the tissue adding volume to the sphincter [43–45]. Kushner BS. *et al.* conducted a study administering Enteryx® to 144 patients with GERD. They achieved a complete PPI withdrawal in 67% of patients over 24 months [46]. A study by Devière J. *et al.* included 64 patients suffering from GERD. Half received Enteryx® and half underwent sham upper gastro-

intestinal endoscopy. The results were found to be strongly in favour of the group that received Enteryx® (81% reduction in the PPI dose, 67% improvement in quality of life) than the other group (53% reduction in the PPI dose, 22% improvement in quality of life) [47]. De Moura EGH. *et al.* used Enteryx® in 21 patients, while endoscopic gastroplasty procedures were used in 26 patients. Compared to gastroplasty, Enteryx® implementation showed identical results, but was associated with a higher rate of short-term complications (dysphagia, vomiting); however, lower rates of oesophagitis were observed in this group of patients in the long term [48]. Despite the promising results, the substance was withdrawn from the market in 2005 due to several cases of death and vascular complications following its use. There was a described substance migration into the visceral trunk and renal arteries, which was the cause of the patient's chronic haematuria [49]. Another agent, Durasphere® (Carbon Medical Technologies, St. Paul, MN, USA), is a polymer of graphite, carbon-coated beads that contain zirconium oxide and are suspended in a polysaccharide gel carrier. Like Enteryx®, Durasphere® also swells demonstrating a similar mechanism of anti-reflux action. The substance is registered for the treatment of urinary incontinence in functional disorders of the bladder sphincter. A trial of the use of Durasphere® in the treatment of GERD was conducted by Ganz RA. *et al.*, with 10 patients suffering from GERD, using PPIs and demonstrating the presence of an oesophageal hiatal hernia. 70% of patients completely discontinued PPIs, and no erosions, oesophagitis, or migration of polymeric material was reported. The results have been positive but the necessity for studies with larger samples and the lack of registration in the treatment of GERD makes the use of Durasphere® an off-label procedure [43, 44, 50]. A promising "bulking agent" administered via endoscopy for the treatment of GERD may be polymethylmethacrylate (PMMA), also known as Plexiglas. This substance, in the form of round microspheres (125 µm in diameter), is suspended in a collagen carrier that prevents the microspheres from moving during the remodelling of the gastroesophageal sphincter muscle layer. The combination of PMMA along with the collagen scaffold was named the G125 implant [51]. The substance is administered submucosally using a 23G needle placed on an endoscopic device. Human collagen at the gastroesophageal junction is stimulated and fibrous tissues and vessels grow into the G125 implant. This results in an autologous thickening of the submucosal layer of the area, which prevents acidic contents from being thrown into the oesophagus [52]. The substance, like Durasphere®, can also be used to strengthen the sphincters of other areas, such as the urogenital area in the treatment of urinary incontinence [53]. The use of G125 will not succeed in patients with a large oesophageal hiatal hernia (> 3 cm), nor is it recommended when oesophageal stenosis or extensive Barrett's metaplasia are identified [52, 54]. Currently, there are not many clinical studies conducted on patients after using this method. Feretis C. *et al.* performed the procedure on 10 patients suffering

from PPI-resistant GERD. They reported a significant reduction in the severity of symptoms in all patients, and seven of them completely discontinued PPIs. Thus, the PMMA implementation method seems promising for the future [43, 55]. Animal studies have also been conducted using Dextranomer-Hyaluronic Acid polymer (DxHA). This agent has proven efficacy in the treatment of vesicoureteral reflux. A study by Martin K. et al. involved the administration of Deflux (the above-mentioned substance) into the area of the gastroesophageal junction in rabbits. They observed the formation of a specific autologous implant with infiltration of foreign body-type giant cells and fibroblasts, and collagen deposition without mucosal or vascular damage. There were no significant differences in sphincter tension concerning the control group, but the histological picture and oesophageal thickening were satisfactory results giving DxHA a chance in the future. It is currently under further study and if it proves to be a therapeutic agent, it will be necessary to develop suitable endoscopic methods for its delivery into the region of the gastroesophageal junction [56, 57].

## Use of antireflux prostheses and stimulators

Another way to create an anti-reflux barrier in the course of GERD can be the use of submucosal implantable components in the area of the gastroesophageal junction. These can include hydrogel prostheses or modern stimulating electronic devices that also offer diagnostic functions. The Gatekeeper™ system offers the implantation of hydrogel prostheses. The device is constructed of a 16 mm diameter sheath for the endoscope, a 2.4 mm diameter prosthesis delivery system, a guide wire, and the Gatekeeper™ prosthesis itself. The prosthesis is composed of polyacrylonitrile and does not exhibit immunogenicity or tissue migration. Its additional tantalum covering provides radiopacity. The procedure is performed under general anaesthesia or conscious analgesia. After insertion of the guide wire and endoscope, the device aspirates a mucosal fold of the gastroesophageal junction, then saline is injected to create a suitable tissue pocket. A dry hydrogel prosthesis is inserted into the area prepared in this way and expands to the desired size after 24 hours due to its hygroscopicity and water drawing from the tissues [58–60]. A pilot study was conducted to evaluate the performance of the Gatekeeper™ system. Fockens P. et al. included an observation of 67 patients prosthesised with the Gatekeeper™ device. A total of 270 prostheses were implanted (an average of 4.3 per patient). The prostheses were maintained at 70% after six months. Lower oesophageal sphincter pressure and quality of life scores increased significantly in patients. Two patients experienced adverse events (nausea requiring endoscopic removal of the prosthesis and an iatrogenic pharyngeal perforation during the procedure). The Gatekeeper™ system was judged to be safe and to improve the outcomes in patients with GERD [61]. Fockens P. et al. continued

their study of the Gatekeeper™ procedure by conducting a comparative trial between patients with the procedure and a sham procedure on a total of 143 patients. The trial was terminated due to a lack of convincing evidence of efficacy and reported adverse events (perforations in two patients, pulmonary infiltration in one patient, and severe chest pain in one patient). The device was withdrawn from the commercial market due to the negative aspects cited above [44, 60]. The literature also describes the application of the device in the treatment of faecal incontinence. Also, in this case, complications were observed. After inter-urethral placement of the prosthesis, migration of the prosthesis and the formation of a perianal abscess occurred. This was a single case, but there are no other larger studies available on this use of the Gatekeeper™ device to evaluate it correctly [62]. A relatively new concept in the treatment of patients suffering from GERD is electrostimulation of the lower oesophageal sphincter. This method is safe and effective, has no side effects, and has been proven to reduce the symptoms of gastroesophageal reflux disease. The method uses anti-reflux stimulators, of which implantation was only possible surgically until recently. The Enterra II and EndoStim devices were based on placing electrodes in the gastroesophageal junction muscles and supplying them through a battery-operated device located subcutaneously in the abdominal wall, which was quite bulky. Thus, the aim was to create a neurostimulator implanted in the gastroesophageal junction that uses wireless communication [63–65]. Banerjee R. et al. conducted a study by implanting electrodes into the lower oesophageal sphincter muscle in seven patients. After the patients were electrically stimulated with an external energy source, there was a significant increase in the resting pressure of the lower oesophageal sphincter muscle with no major complications. It was considered a satisfactory result [66]. Hajer J et al. went a step further and conducted a study looking for a device internally powered by its battery. By implanting it into animal models, they obtained the preserved functionality of the device six months after the implantation. This was on the level of the value of the already known Enterra II device, which was the standard at that time [67]. In the latest research, they developed a novel method of coating such a device with biocompatible resin and also managed to reduce its weight to less than 1.22 g. The external device for wireless energy transfer was able to power the stimulating electrodes of the implanted receiver from a distance of 12 cm. Currently, there are plans to test it on live animal models and develop a feedback-controlled sensor that would adjust to the pH prevailing in the oesophagus and turn on neurostimulation only when the pH is too high. This would provide very high energy savings by keeping the device in a resting state [63]. It has also been noted that in the implantation of such devices, the size of the created submucosal pocket for the implant, is extremely important, and so is its hermeticity, which will prevent the implant from being destroyed and rejected by the

body. Thus, the importance of using specialized coatings and the potential future performance of such procedures only by experienced endoscopists is emphasized [68].

## Other minimally invasive procedures

In addition to the classic fundoplication procedure and the endoscopic methods described above, minimally invasive surgical techniques performed laparoscopically are also used in the treatment of GERD. The MSA (Magnetic Sphincter Augmentation) procedure performed with the LINX® (Torax Medical, St. Paul, MN, USA) device has gained recognition. This is an implant constructed from a series of titanium spheres, connected by a wire. The spheres have a magnetic core which makes them attract each other. LINX® is inserted laparoscopically at the gastroesophageal junction from the peritoneal cavity side. In older generation devices, the wire was attached with sutures to the tissues, but today it is fastened with a clamp which further reduces tissue traumatization. The device causes a constriction of the gastroesophageal junction, and the fact that the spheres are magnetically attracted allows the implant to expand as the food bolus passes through [69, 70]. Ganz RA. *et al.* evaluated the effectiveness of the LINX® device on 100 patients. There was an increase in quality of life in HQRl questionnaires, PPI withdrawal by 85% of patients, and a decrease in symptoms typical of GERD: dysphagia, heartburn, and vomiting. The results included a five-year follow-up on the LINX® device and rated it as highly satisfactory and effective in the long-term treatment of GERD [71]. A publication by Lipham JC. *et al.* focused on a review of complications in more than 1,000 patients from multiple centres who received the LINX® procedure. The rate of adverse events in patients was insignificant (5.6% of implant expansions, 3.4% of reoperations due to the necessity of device removal, 0.1% of device-induced erosions), and the device was rated as safe. The much lower probability of oesophageal perforation compared to even the TIF procedure was highlighted [72]. The possibility of removing the implant from the patient's body in the case of increasing adverse symptoms has also been investigated. Bona D. *et al.* performed an explantation in five patients with an average implant lifetime of 46 months. The symptoms reported most frequently were epigastric pain, dysphagia, and heartburn. Intraoperatively, 40% of patients were found to have developed oesophageal hiatal hernia juxtaposing the pre-implant status. Each patient had the device explanted safely and underwent a fundoplication procedure. The implication is that the anti-reflux therapy must be tailored individually to the patient [73]. In the

case of a high probability of hiatal hernia, endoscopic gastroplasty or classic fundoplication seem to be a better therapeutic option. In such patients, repair of the hernia or strengthening of the gastroesophageal junction should be simultaneously included in the LINX® implantation procedure [69]. Another device implanted laparoscopically is the RefluxStop™. It is a cube-shaped implant with rounded tops that is implanted into a tissue pocket created from the folds of the gastric fundus. The procedure is designed to prevent the lower sphincter from moving through the implant, acting in this case like a restrictor. The device does not interfere with the area of the gastroesophageal junction, preserving its normal anatomy. Bjelović M. *et al.* performed the procedure on 50 patients, normal pH-metric values were observed in 98% of patients six months after the implantation, and improvement was also seen in quality of life [74]. Other implants placed laparoscopically at the gastroesophageal junction are also in trials (polyurethane implant), and those whose application had too high a rate of complications (Angelchik implant) — have been withdrawn. The main problem with the Angelchik implant was dysphagia in long-term studies. The implant also did not adhere very well to its target location [75, 76]. Thus, the use of mobile devices capable of expanding during the act of swallowing (LINX® described) appears to have the best long-term implantation results.

## Conclusions and future directions

Endoscopic techniques for the treatment of GERD have made significant progress in recent years and are constantly being refined and developed. Currently, classical fundoplication is the method of choice for later stages of treatment if less invasive methods do not work. Endoscopic methods are the option of choice for patients refractory to the PPI therapy or in those who have undergone classical fundoplication or bariatric surgery earlier. The development of novel devices and implants with lower complication rates should yield better patient outcomes in the future. It also seems possible to combine diagnostic and therapeutic methods (e.g., electronic sphincter stimulation devices capable of measuring pH), which may save physicians from performing multiple procedures on patients. The invention of other polymeric substances may also lead to a breakthrough in this field and the successful implantation of injectable materials. Larger clinical randomized trials, especially for the new methods, are needed to show their predictable greater effectiveness compared to classic surgical methods. Table I summarizes the surgical procedures for the treatment of GERD.

**Table I. Summary of treatment methods for GERD. Explanations in the text**

Procedure	Examples
Nissen fundoplication	Open method Laparoscopic method
Endoscopic gastroplasty Transoral incisionless fundoplication (TIF)	EsophyX® EndoCinch Plicator Syntheon ARD MUSE ESD
Radiofrequency stimulation	Stretta
"Bulking agents" implementation	Ertaryx® Durasphere® PMMA Plexiglas DxHA
Anti-reflux prostheses and stimulators	Gatekeeper™ Enterra II EndoStim Microstimulators
Other laparoscopic procedures	LINX® RefluxStop™ Angelchik Polyurethane implants

## Conflict of interest

None declared.

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**Adres do korespondencji:**

dr hab. n. med. Mariusz Chabowski, prof. UMW  
 Department of Surgery, 4<sup>th</sup> Military Teaching Hospital  
 Weigla 5, 50–981 Wrocław  
 e-mail: [mariusz.chabowski@gmail.com](mailto:mariusz.chabowski@gmail.com)

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