



A Historical and Scientific Review of Anti-Reflux Surgery: Evolution, Evidence, and Future Directions

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Abstract

Purpose of Review Gastroesophageal Reflux Disease (GERD) is a condition, which is frequently encountered by gastroenterologists, otorhinolaryngologists, surgeons and general physicians and requires a multidisciplinary treatment when there is a high symptom burden in patients. Besides lower oesophageal sphincter (LES) dysfunction there are several other risk factors that contribute to the development and symptoms (worsening) of GERD. While these lifestyle modifications and pharmacological therapies, particularly proton pump inhibitors (PPIs), are first-line treatments, a subset of patients requires surgical intervention due to refractory symptoms or complications. This review traces the evolution of anti-reflux surgery, examining its historical milestones, advancements, and future prospects.

Recent Findings This review discusses the epidemiology of GERD, its pathophysiology, but also the development of Anti-Reflux Surgery (ARS). We will discuss the available evidence regarding different ARS procedures and will focus on individualised treatment for patients with GERD.

Summary In the treatment of patients with GERD we have to take into account that it might be challenging to personalise treatment and therefore optimise results. In this instance special considerations need to be taken for patients with GERD and obesity, patients with Barretts oesophagus, patients after bariatric and metabolic surgery (BMS) and patients with oesophageal motility disorders.

Article Highlights

- Gastroesophageal Reflux Disease (GERD) is a condition, which is frequently encountered and requires a multidisciplinary treatment.
- Lifestyle modifications and pharmacological therapies are first-line treatments.
- Surgery is often required due to refractory symptoms or complications.
- In the treatment of patients with GERD we have to take into account that it might be challenging to personalise treatment and therefore optimise results.
- Special considerations need to be taken for patients with GERD and obesity, patients with Barretts oesophagus, patients after bariatric and metabolic surgery (BMS) and patients with oesophageal motility disorders.

Keywords Anti-reflux surgery · Nissen fundoplication · Dorr fundoplication · Magnetic sphincter augmentation · GERD · Gastro-Oesophageal reflux disease · Robotic surgery · Minimally invasive surgery

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Abbreviations

IBS Irritable Bowel Syndrome
NERD Non-Erosive Reflux Disease

Introduction

Gastroesophageal Reflux Disease (GERD) is a condition, which is frequently encountered by gastroenterologists, otorhinolaryngologists, surgeons and general physicians and requires a multidisciplinary treatment when there is a high symptom burden in patients [1, 2]. Besides lower oesophageal sphincter (LES) dysfunction there are several other risk factors that contribute to the development and symptoms (worsening) of GERD [1, 3]. Age older than 50 years, smoking, chronic use of non-steroidal anti-inflammatory drugs, obesity and lower social economic status (SES) are significantly associated with the incidence and prevalence of GERD [3, 4]. When GERD is left untreated it can lead to a variety of complications like erosive oesophagitis, bleeding, peptic ulcers and strictures, which can eventually lead to Barrett's oesophagus and finally oesophageal cancer [5].

Regarding the treatment of GERD, it can be stated that approximately 60–70% of the patients with GERD have relief of their symptoms with proton pump inhibitors (PPI), although a significant portion do not achieve adequate improvement of their symptoms. This indicates that in terms of its pathophysiology there are more factors that may play a role, like pepsin, bile acids and trypsin. In addition, factors like low treatment adherence and functional heartburn should also be taken into account [6–8]. These pathophysiological complexities made that these non-pharmacological approaches, like dietary and nutritional interventions have gained more attention over the years. This is partly due to the observation in several studies that mucosal irritants in gastroduodenal contents are secreted in response to food intake and this could be altered changes in nutrition and diet (Please see Fig. 1 [8–10]).

While these lifestyle modifications and pharmacological therapies, particularly proton pump inhibitors (PPIs), are first-line treatments, a subset of patients requires surgical intervention due to refractory symptoms or complications. This review traces the evolution of anti-reflux surgery, examining its historical milestones, advancements, and future prospects. We will specifically focus on the history and the evolution of ARS and the changes in surgical perspective in this regard.

Personalised Management and Importance of the Disease Phenotype before Anti-Reflux Surgery

Surgical therapy should ideally be the next step, when conservative treatment fails. In case of patients with GERD, Anti-Reflux Surgery (ARS) should be considered when conservative treatment with for example PPIs and/or nutritional and/or lifestyle changes give no symptom relief. Speaking for a technical point of view several aspects need to be addressed; (1) reducing a potential hiatal hernia; (2) restoring the intra-abdominal oesophagus; (3) repairing the remaining crural defect and (4) reinforcing or augmenting the antireflux barrier through a fundoplication [2, 11, 12]. Additionally, current literature also mentioned the anti-reflux effect of the 'so-called' gastroesophageal flap valve, which is a mucosal-muscular fold visible on retroflexed endoscopic view [11]. The American Foregut Society updated its endoscopic classification and also included the presence of an axial hiatal hernia (including its properties, like length, aperture diameter and the presence (or absence) of the earlier mentioned gastroesophageal flap valve) as one of the main anatomical characteristics that should be reported during an endoscopy when assessing patients with GERD [13]. These anatomical concepts and their presence can give important information, which can influence ARS procedure selection and tailor the surgical therapy. It also can help understand when procedures fail [13, 14].

Another important factor in tailoring ARS to patients needs is the determination of the GERD phenotype. It should be taken into account that historically most of the patients were treated in the same way (with mostly PPI's as medical therapy). When conservative treatment failed, the ARS procedure was mostly the choice of the treating surgeon [2, 12, 15]. Before proceeding to surgical therapy, adequate diagnostic tests are pivotal to objectively assess the burden of the disease. Historically, surgery was reserved for patients with refractory GERD and/or partial no response to PPI therapy. This created a gap in the spectrum of patients that fill in between these indications, and nowadays-increasing efforts are made to reduce this gap and provide personalised treatment approaches [2, 12, 15]. Tailoring treatment encompasses three crucial steps (1) objective testing, (2) identifying the disease its Phenotype and (3) adherence/optimisation of lifestyle and nutritional changes. In all these steps, shared-decision making with the patient regarding treatment options is of the utmost importance [16]. Fig. 2 gives an overview of the physiological and psychological aspects in GERD and its relation to disease phenotypes.

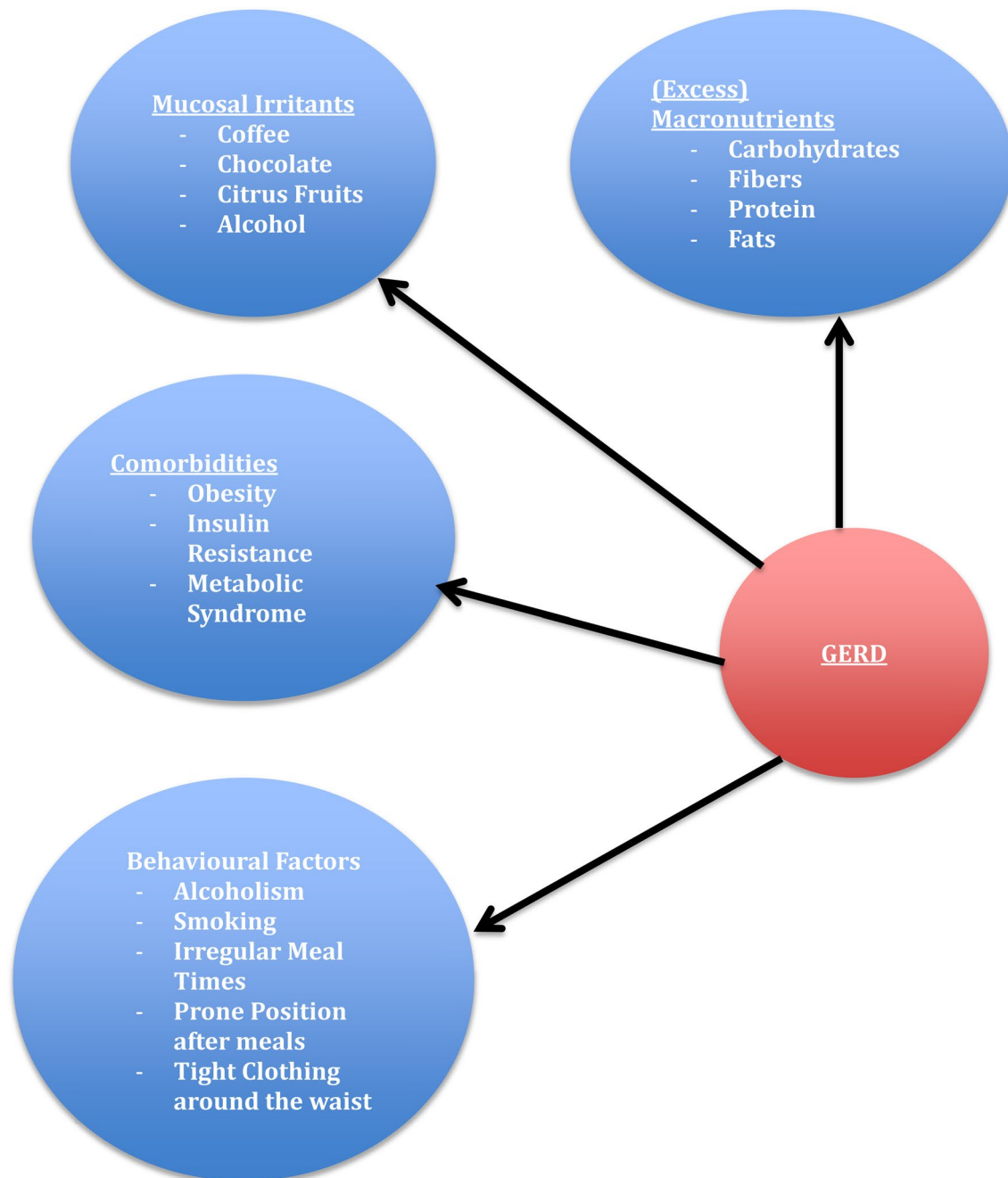


Fig. 1 Nutritional and lifestyle factors associated with Gastro Esophageal Reflux Disease (GERD)

Patient Selection for Surgical Therapy and Preoperative Work-up

Before surgical interventions, GERD management focused on lifestyle changes and rudimentary pharmacological approaches. The understanding of the lower oesophageal sphincter (LES) function and its role in preventing reflux was limited, and hiatal hernias were often

misdiagnosed or untreated. The lack of effective medical therapies highlighted the need for surgical solutions. All patients that are potential candidates for surgery need to undergo a thorough and detailed preoperative assessment to determine any anatomical and/or physiological substrates, which could explain their symptoms. This of course includes symptom evaluation, but also an appropriate preoperative diagnostic work-up, which

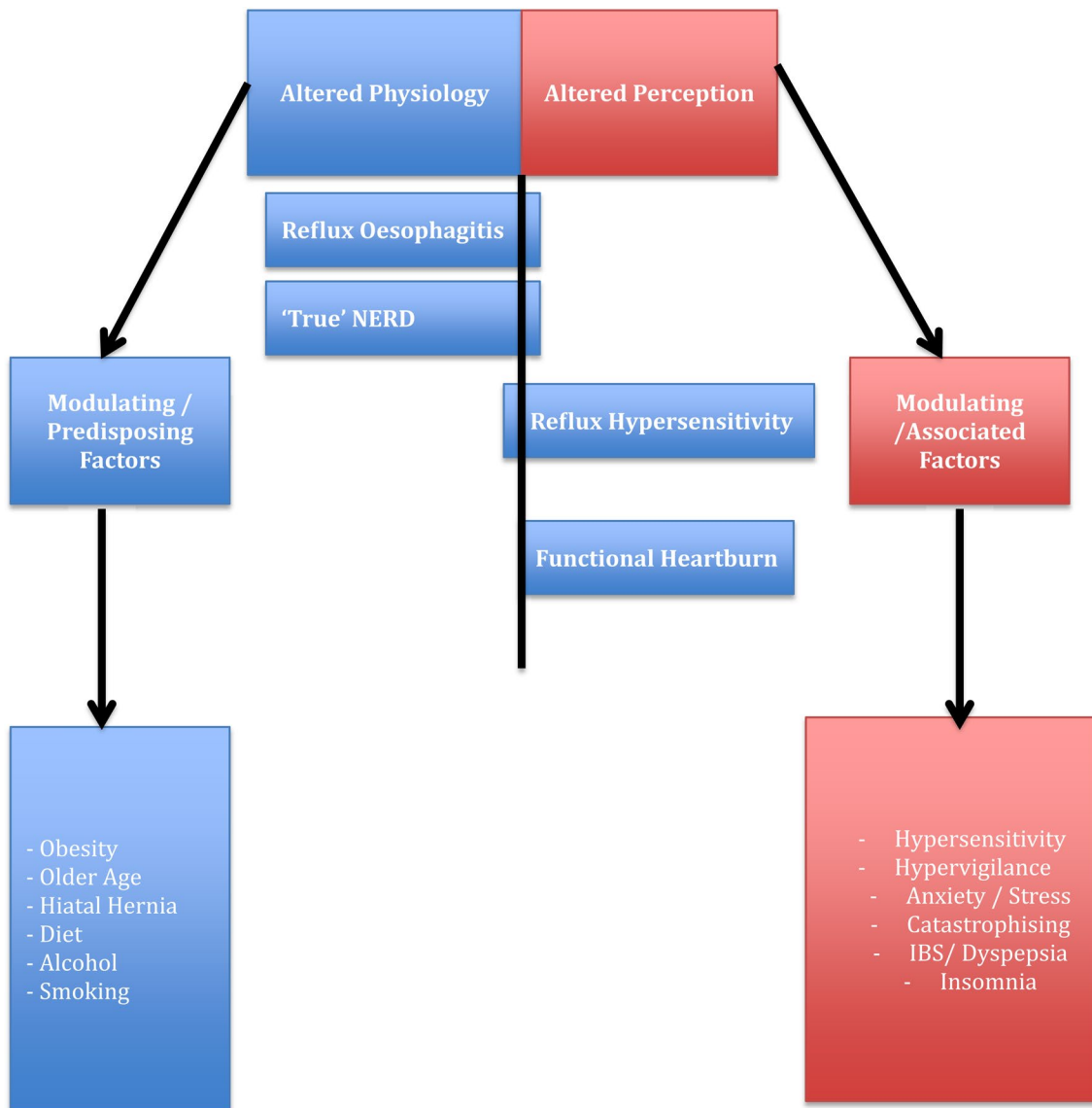


Fig. 2 Physiological and psychological aspects in Gastro Esophageal Reflux Disease (GERD) and its relation to disease phenotypes

could consist of at least an esophagogram, oesophageal manometry, and ambulatory pH/impedance monitoring [2, 17]. Based on symptom profile and initial diagnostics, a gastric emptying scintigraphy could be of additional value. This is especially the case in selected patients with a suspicion of ineffective peristalsis or delayed gastric emptying [17]. Finally these diagnostic tests should confirm the presence of pathologic (acid) GERD, exclude achalasia and should contain an assessment of oesophageal peristaltic function [17]. Table 1 gives an overview of the essential components of the earlier discussed personalised treatment. Well-established preoperative predictors of success of laparoscopic ARS are the presence of typical symptoms, an abnormal 24-h pH score off PPI,

and a good clinical response to acid suppression therapy with PPI [18].

Birth of Anti-Reflux Surgery

The inception of anti-reflux surgery can be attributed to Dr. Rudolph Nissen and his partner Philip Allison, who, in 1955, performed the first fundoplication procedure, wrapping the gastric fundus around the oesophagus to reinforce the LES [19]. Published in 1956, this technique, initially termed “gastroplication,” gained recognition as “Nissen fundoplication” and became the cornerstone of surgical GERD management [19, 20]. In the years after surgical

Table 1 Essential components of multimodal and personalised treatment of patients with GERD

Treatment Component	Explanation
<i>Definition of GERD</i>	<ul style="list-style-type: none"> - Symptoms - Endoscopic Findings - Reaction to PPIs - Functional Definition - Other
<i>Patient Identification</i>	<ul style="list-style-type: none"> - Symptom Evaluation using Questionnaires - Presence of Esophagitis in Endoscopy - Presence of (features of) pathologic acid exposure (by measuring Refluxate) - Other
<i>(Preoperative) Diagnostics</i>	<ul style="list-style-type: none"> - Endoscopy - Radiography - High-resolution Manometry - Impedance – 24 h pH Monitoring - Scintigraphy - Other
<i>Defining Disease Phenotype</i>	<p>Phenotyping based on symptoms:</p> <ul style="list-style-type: none"> - Reflux-type: Heartburn, Esophagitis - NERD-type: Functional Heartburn, Esophageal hypersensitivity - Regurgitation-type: weak EGJ, hiatal hernia - Chest pain-type: Hiatal hernia - Extra-oesophageal symptoms type: cough, hoarseness
<i>Special cases/Personalised Approach</i>	<ul style="list-style-type: none"> - Psychological evaluation - Evaluation of Oesophageal Motor Diseases - Gastric-Emptying Studies
<i>Defining and starting multimodal treatment</i>	<ul style="list-style-type: none"> - Lifestyle modifications - Medical Therapy - Interventional Endoscopic Therapy - Surgery
<i>Anti-Reflux Surgery</i>	<ul style="list-style-type: none"> - Explaining a differentiated surgical treatment concept - Explaining technical details and success predictors for surgery procedures
<i>Long-term Management</i>	<ul style="list-style-type: none"> - Follow-up concept - Management of complications and treatment failures

techniques for treating patients with GERD advanced and lead to a better understanding of the LES and its contribution to the pathophysiology of GERD [19, 20]. Therefore the Nissen Fundoplication became the gold standard in the surgical treatment of patients with GERD [2, 19, 20]. In the 1960s the ARS was further developed by the introduction of the partial posterior (Toupet) and anterior (Dor) fundoplication [2, 19–21]. This was mainly a reaction because a lot of patients developed postoperative dysphagia after a Nissen Fundoplication, so both techniques were an attempt to reduce these complications [2, 19, 20]. With the rise of laparoscopy, ARS of course became also minimally invasive and an attractive therapeutic surgical option for patients with GERD. However, due to the higher failure rate in the early stages of laparoscopic surgery and the subsequent rise of more variants of PPIs there was a significant decrease in the utilisation of ARS seen [21]. Over the years this changed, because there was still a high rate of patient dissatisfaction with PPIs, increasing safety concerns regarding the long-term use of PPIs, rising numbers of patients with obesity, and a higher prevalence of GERD among the younger generation [22]. The Global Burden of Disease Study showed

that in present day, GERD remains a very debilitating disease with a significant amount of patients with persistent and/or refractory symptoms despite treatment with PPIs. This is approximately forty per cent of the patients with GERD, which could be candidates for ARS and multimodal treatment [22].

Early Surgical History, Surgical Strategies and Outcomes

In terms of history and surgical approaches, we can state that there have been three major eras in ARS: a Crural Centered Approach, an LES Centric Approach and eventually back to a Crural Centered surgical approach [23].

Crural centered surgical approach

With the discovery of hiatal hernias at the early 20th Century, the initial surgical focus lied in the correction of the hernia, reposition of the content of hiatal hernia and the concomitant closing of the defect in the diaphragm. Soresi et al.

[24] were the first that performed these elective hiatal hernia repairs back in 1919. This was followed by Harrington et al. [25] who used the same technique as Soresi and they concluded that the anatomical closure of such hiatal hernia defects were one of the essential components of symptom relief. With this new techniques and first results, several surgeons tried to adapt e.g. optimise the surgical repair of hiatal hernias. Back in the 1950's Sweet introduced a trans-thoracic approach in which the primary closure of the crural opening was done with a heavy type of silk. The goal was to reduce the diaphragmatic crural opening to a size that only an index finger could be admitted [23]. Whether that was anatomically correct, remains a question until today. The nowadays known connection between hiatal hernias and reflux symptoms was not made until the second half of the 20th century. Allison [26] was the first that described a clear connection between the technical repair of the hiatal hernia and reflux symptomatology, but also laid the basis for the fact that surgery could prevent sequelae associated with repeated exposure of acid to the lower part of the oesophagus [26]. Important parts of his research focused on the crural sling fibers as the cause of reflux related changes. His seminal work laid the basis for our current more detailed understanding of the complex interplay between anatomical changes in the hiatal region, LES and stomach and the occurrence of reflux and its accompanying clinical sequelae. However, the mentioned crural centered approach was a dominant surgical strategy for many years, despite the increased awareness that the anatomical changes due to acid reflux were not addressed adequately [23]. This was supported by a 20 years follow-up study done by Allison himself and it showed a 33% recurrence of paraoesophageal hernias and a 49% recurrence of sliding hernias [27]. These recurrence rates were accompanied by a wide variety of clinical 'reflux' symptoms, which only partially correlated with radiographic diagnostics done at that time. This was especially a great challenge since (medical) anti-acid therapy was very minimal [19, 26, 27].

LES centered surgical approach

Due to various scientific advances that happened more or less parallel to each other, ARS transitioned to a more LES centered approach. This was mainly due to the resurrection of the oesophageal manometry in combination with 24 h pH measurements. The core surgical focus of the LES centered approach was deemed to be the reconstruction of the Angle of His [23]. One of the most pivotal figures in the surgical development of ARS was Nissen and his initial experience with the techniques of both Harrington and Allison's (e.g. transabdominal and transthoracic repair) was not great. Nissen reported approximately 50% failure rates.

Secondly he found out that patients with hiatal hernia and/or reflux esophagitis had a blunting of the Angle of His [28, 29]. Reason enough for Nissen to start innovating and optimising ARS. Nissen approach could be divided into three substages: (1) reduction of the sliding hiatal hernia with a gastropexy at the lesser curvature of the stomach; (2) for paraoesophageal hernias he added a pexy suture to the abdominal wall and (3) with regards to the reflux he created a Witzel Tunnel around the distal part of the oesophagus (which was later named a fundoplication). Because of the good results described by Nissen, his technique became the (golden) standard [28, 29].

As an attempt to further optimise and improve ARS, some surgeons began focussing on the cardiophrenic angle. Skinner and Belsey [30] developed a technique in which there was a need for extensive mobilisation of the oesophagus, which they thought could only be done by a transthoracic approach. Their surgical philosophy was that only with sufficient length of the (intra-abdominal) oesophagus the crural angle could be adequately restored [30]. Over the years these procedures were further optimised. Hill described a posterior gastropexy in his cadaver study and he demonstrated that the posterior part of the phreno-oesophageal membrane was the strongest to restore the angle of His. Logically he did not believe in studies advocating for the cardiophrenic angle as maintainer of the reflux barrier [31].

During the same time period the results of the DeMeester his manometry and 24-hour pH studies were published, which provided a physiological understanding of GERD and demonstrated the importance of the high-pressure zone when focussing on the LES and its potential surgical reconstruction [32]. Follow-up studies showed that the LES is influenced by the degree of reflux and by the presence of a hiatal hernia [33]. Moreover further studies showed the complex function of the LES and the influence of the Nissen Fundoplication [34–37]. The seminal works coming from the research group of DeMeester layed the foundation for the current ARS and physiological understanding of GERD in general.

Back to the crural centered surgical approach

In the last few years the surgical approach in ARS regained its focus on the LES and this is probably due to the failure rates of funduplications, which is commonly due to crural failure [38–40]. But also the recurrence rates of paraoesophageal hernias (up to 50%) were a reason to research the pivotal aspects of crural reconstructions [41]. The evolution of ARS in the last few years lies within the fact of combining surgical steps e.g. technical aspects. Louie et al. [42], randomised patients to either crural closure followed by fundoplication, or fundoplication followed by crural closure, with

intraoperative high-resolution manometry after each part of the repair. Crural closure was documented to contribute to esophageal sphincter length and increased pressure at the EGJ, highlighting the importance of this step in the surgical management of GERD [42].

Technical Aspects, Development and Evolution of Surgical Techniques

The 1990s marked a paradigm shift with the advent of laparoscopic techniques. The laparoscopic Nissen Fundoplication was first introduced by Dallemagne et al. [43] in 1991. This approach replicated the open procedure with reduced morbidity. Benefits included shorter hospital stays, decreased postoperative pain, and faster recovery [43]. In the initial report by Dallemagne et al. [43], it was shown that the transition to laparoscopy necessitated training and adaptation.

It can be stated that besides the earlier mentioned patient-related factors, the technical factors are just as important for the success of ARS. Logically, surgeons need to have a clear understanding of GERD pathophysiology, and also need to have had a preferably structured training laparoscopic and/or robotic surgery. In ARS there are a few steps within the surgery that need to be done carefully: (1) Dissection of the Esophageal Gastric Junction (EGJ) to avoid damage to the oesophageal wall and to preserve the vagal nerves; and (2) A lower mediastinal dissection is necessary to obtain a tension-free, intra-abdominal oesophageal segment (which is mostly in between 3 cm and 5 cm) [38, 44]. Patients that have medium-large hiatal hernias need to receive a posterior or composite crural repair including the anterior and left-lateral aspect of the hiatus. For technically the most optimal results, the anatomical interplay between the hiatus, EGJ and the fundus of the stomach needs to be geometrically correct [38, 44]. To mobilise the gastric fundus it is necessary to dissect the short gastric vessels and the gastrophrenic ligament, but also removal of the fat pad at the angle of His might be necessary [38, 44]. When constructing the wrap and wrapping it around the distal part of the oesophagus, we need to make sure that the fundoplication is tension-free and symmetrical. In some instances the measurement of the cross-sectional area and distensibility of the EGJ might be useful. For these intraoperative measurements an endoluminal functional lumen-imaging probe (EndoFLIP) can be used [45].

Comparative Studies and Evidence Base

Subsequent decades saw refinements in surgical techniques, of which a few aspects have been pivotal for current ARS:

- *Partial Fundoplications*: To mitigate postoperative complications like dysphagia and gas-bloat syndrome associated with complete wraps, partial fundoplications were introduced. The Toupet (posterior 270°) and Dor (anterior 180°) procedures offered alternatives tailored to patient-specific oesophageal motility profiles [2, 46, 47].
- *Hiatal Hernia Repair*: Recognizing the role of hiatal hernias in GERD pathophysiology, concurrent repair during fundoplication became standard, enhancing surgical outcomes [2, 46, 47].

Basically it can be stated that ARS is safe, effective and has good long-term effects when performed in hospitals that have been specialised in ARS. In the multicentre study done by Zimmermann et al. [48] it was shown that when medical therapy and surgical therapy have had similar remission rates after five-years of follow-up (85% vs. 92%). However, ARS is still underused despite good long-term outcomes [2, 12, 43, 46, 47]. This might be due to the perceived risk of long-term side effects as stated in the study of Richter and colleagues [40].

As stated earlier technical and patient-related factors determine the success of ARS and in the current treatment it is of the utmost importance to determine the clinical phenotype of the patients scheduled for surgery (Please see Table 1). In the past there have been inconsistencies in reported outcome date of studies, due to the heterogeneity of the GERD patient group. For example in patients with GERD and a medium-to-large hiatal hernia, a wrap that is too tight, too long or twisted can cause persistent symptoms like dysphagia postoperatively. Markar et al. [49] showed that this leads to revisional surgery in approximately 9% of patients.

In general it can be stated that the Nissen Fundoplication has better efficacy in controlling reflux compared to partial fundoplications [45, 46, 49, 50]. However it should be stated that guidelines suggest that the procedure of choice in ARS should be discussed with the patient with an emphasis in symptom improvement of minimisation of postoperative side effects [50]. The Toupet fundoplication is mostly offered to patients that have nonspecific oesophageal motility disorders to reduce the incidence of postoperative complications like dysphagia [51]. Several studies have also shown that the Toupet fundoplication is effective in reducing dysphagia and bloating with a similar reflux control to its counterpart the Nissen Fundoplication [49, 50, 52, 53]. The Dor fundoplication also reduces the risk of dysphagia postoperatively, since the abdominal oesophagus is not angulated by a posterior wrap [50, 54].

Watson et al. [55] studied two variations of the fundoplication (a modified version with no dissection of the short gastric vessels with 180-degree fundoplication versus the Nissen fundoplication) and found no significant differences in outcomes measures. Both procedures had no significant

differences in reflux symptoms, and overall patient satisfaction at 10 years postoperatively. Over the course of 10 years it was shown that the anterior fundoplication had a lower reoperation rate, which was probably due to less frequent dysphagia and hiatal hernias [55].

When comparing 90-degree and 120-degree anterior partial fundoplication the evidence is not that supportive, since reflux symptoms are quite prevalent 5-years postoperatively [50, 54–57]. Hoffsten and colleagues [58] attempted to investigate the effectiveness of laparoscopic anterior (90- and 180-degree) compared to Nissen (360-degree) fundoplication. In their systematic review and meta-analysis they included only for four studies, with 398 patients and showed that the risk of dysphagia for solid food was higher after a Nissen fundoplication at 5 years follow-up. However they reported a lower postoperative GERD medication use after Nissen compared to the anterior fundoplications [58]. They found no significant differences in outcomes like heartburn, reoperations or satisfaction rates [58].

New and Emerging Techniques

Over the course of the last decade, newer techniques have arisen to treat patients with GERD. One of them is Magnetic sphincter augmentation (MSA) or otherwise the LINX procedure [59, 60]. Studies have shown that this procedure is highly effective in reducing the symptom burden of GERD. Especially when combined with crural repair, MSA significantly reduces symptoms, PPI use, and improves quality of life drastically [59, 60]. The MSA is performed using the LINX device, which is a ring of magnets that will be placed around the EGJ laparoscopically. This procedure has the advantage that only limited surgical dissection with preservation of the phrenoesophageal ligament and no division of short gastric vessels is necessary in the absence of hiatal hernia [15, 61]. Feared device complications like erosion or migration have been rarely reported. Another advantage is that in case of treatment failure the LINX device can be easily removed laparoscopically and if necessary patients can be converted to a fundoplication or other surgical therapies [15, 61, 62]. The only technical limitation is that patients treated with a LINX device cannot undergo imaging in high-power Tesla magnetic resonance systems [15, 61, 62].

Regarding the long-term outcomes of patients treated with a LINX device, Ferrari et al. [63]. studied 124 patients and followed them for a median of 9 years. In this study they showed that the mean GERD-Health Related Quality of Life (HRQL) score decreased from 19.9 to 4.01, the prevalence of Grade 2–4 regurgitation decreased from 59.6% to 9.6%, and 79% of patients discontinued use of PPI [63]. Despite that implanting a LINX device does not compromise esophageal motility of

peristaltic body reserve, it should be noted that a small proportion of patients needs to get the LINX device removed, due to symptoms of dysphagia. Preoperative identification of manometric abnormalities would be useful to stratify patients with an increased risk of persistent dysphagia. Adequate peristaltic reserve after multiple rapid swallows correlates with decreased incidence of dysphagia following LINX implantation [64]. Baisson et al. [47]. showed in their study that independent risk factors for needing endoscopic dilation or LINX device removal (in patients with or without preoperative ineffective esophageal motility) are Age > 45 years, preoperative dysphagia, MSA size < 15 beads, and less than 40% intact swallows during the preoperative manometry [47].

Another new emerging procedure in ARS is the Refluxstop, which is specifically designed to optimise and stabilize the EGJ. Refluxstop is a small device, which is implanted in a pocket just behind the gastric fundus and above the level of the LES [65]. The Refluxstop therefore gives stability to the EGJ by blocking the upward movement of the LES, prevents unfolding or mediastinal herniation of the fundoplication, and maintains the anatomically correct position of the angle of His [65]. Harsanyi et al. [65]. showed promising results after following 50 patients for four years. They showed a significant improvement on the GERD-HRQL scale, no postoperative dysphagia, and a significant decrease of daily regurgitations [65]. Interestingly, the Refluxstop procedure seems feasible, safe and effective even in GERD patients with Ineffective Esophageal Motility (IEM) [49, 66, 67]. This procedure has the potential to be a reasonable trade-off between reflux control and risk of unwanted complications and/or side effects. However, current randomised studies and related evidence are lacking.

Conclusion

Over the course of 70 years, ARS has developed in a major way and nowadays we are more focused on individualising treatment for patients with GERD and concomitant diseases. Further research needs to be comparing different surgical and/or medical treatment strategies for different patient groups (with GERD and concomitant diseases).

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Declarations

Competing Interests The authors declare no competing interests.

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