Absent contractility of the esophagus; reflux disease and surgical treatment options

Thesis summary

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1 INTRODUCTION

Dysphagia, odynophagia and regurgitation are amongst the most prevalent primary complaints. Their presentation presumes the possibility of benign, malignant or functional disorders of the esophagus. The spectrum on clinical signs is overlapping between different clinical entities and as of today a broad scale of pathophysiological entities have been described as underlying factors. Thanks to this complexity, and the advancement of the diagnostic tools in esophageal physiology, the diagnosis and therapy of esophageal disorders have become a truly interdisciplinary challenge.

The development of investigation tools helped to explore phenomena that were previously associated with a single disease such as the absence of esophageal contractility.

Gastro-esophageal reflux disease is the most prevalent of benign esophageal disorders and gives the most work to functional esophageal testing laboratories worldwide.

A great sum of scientific literature and clinical experience is available regarding the diagnostic tools algorithms as well as clinical interventions in the treatment of this disease.

While surgical therapy is commonplace, optimal operative technique, patient selection and the achievable postoperative quality of life remain a matter of discussion.

2 OBJECTIVES

Chapter1.: Impact of antireflux surgery on gastroesophageal reflux-associated symptoms and quality of life

- To recognize the change of reflux associated complaints after laparoscopic hiatal reconstruction and antireflux plasty, and to reveal the predictors of patient satisfaction.

Chapter 2.: Clinical spectrum and presentation of patients with absent contractility

- To reveal the common characteristics and the clinical features of patients presenting with absent contractility on high resolution esophageal manometry.

Chapter3.: Remedial bypass or antrectomy and Roux-en-Y after failed fundoplication

- To summarize the approach to failed antireflux surgery. Review the selection criteria of operative approaches, techniques and literature of Roux-en-Y reconstruction as an antireflux measure.

Chapter 1.
Impact of antireflux surgery on gastroesophageal reflux-associated symptoms and quality of life

Introduction

Reflux disease is an endemic disease of affluence in the developed world. Plethorea of studies confirm that the properly executed reconstruction of the esophageal hiatus, along with a simultaneous anti-reflux plasty, is an exceptionally effective therapeutic option in its treatment. With surgery, we can permanently alleviate the symptoms, acid secretory medication can often be discontinued, and the rate of side effects and complications from the disease decreases.

The antireflux effect reconstructed by surgery can be measured in several ways. The most accepted objective parameters are the degree of esophagitis associated with reflux and the results of the ambulatory esophageal pH measurement, while subjective parameters are most often evaluated with the help of quality-of-life questionnaires.

Since the aim of surgical intervention is primarily to improve the quality of life, and secondarily to prevent complications, the evaluation of changes in subjective complaints is of paramount importance when applying this type of surgery.

Methods

We analyzed the quality of life associated with reflux disease in patients who underwent hiatal reconstruction and antireflux plasty in association with reflux disease between 01.12.2015 and 31.12.2020. in a tertiary referral center. Outcomes were measured based on the result of quality-of-life questioners. In our department, all patients undergoing hiatal reconstruction and antireflux plasty are required to fill out a quality-of-life questionnaire during their preoperative examination (on the day of preoperative manometric examination), this is undertaken to assess the burden of reflux disease on our patients and the severity of their complaints. The questionnaire applied is based on a certified translation of the questionnaire developed by the Functional Esophageal Surgery Workgroup at Creighton University, Omaha.

This questionnaire is filled out repeatedly by our patients during the follow-up visit (at least 6 months after the operation), and they are asked to subjectively evaluate the success of the operation in terms of the improvement of their quality of life on a scale of 1-10, and alsoto

consider whether they would recommend the intervention to their relatives and acquaintances with similar complaints. Follow up, unless there are other complaints that warrant earlier examinations is usually scheduled 6-8 months after the operation.

In accordance with the above, data collection is prospective. Data was continuously recorded in an electronic table accessible only to researchers, which was deprived of patient identifiers before the subsequent analysis. Together with the quality of life parameters, the following parameters were recorded: Age, Gender, Esophageal motility according to Chicago classification before surgery, Esophageal motility according to Chicago classification after surgery (if tested), DCI value before surgery, DCI value after surgery (if tested). Extent of the following complaints before and after surgery: heartburn, dysphagia, chest pain, nausea/vomiting, bloating. Medication used to treat reflux disease before and after surgery. Body weight before and after surgery. The number of months spent with reflux disease before the operation. The number of months until the follow-up examination, Postoperative patient satisfaction, willingness to recommend the operation.

Statistical methods: In addition to descriptive statistics, a paired t-tests and chi-squares tests were used to evaluate the results. The significance level was chosen at $p<0.05$.

A multivariate linear regression was performed to assess the relation between patient satisfaction and its potential cofounding factors. Data were checked for multicollinearity with the Belsley-Kuh-Welsch technique. Heteroskedasticity and normality of residuals were assessed respectively by the Breusch-Pagan test and the Shapiro-Wilk test. A p-value of less than 0.05 was considered statistically significant. Patients with missing data were excluded from the analysis. Statistical analysis was performed with EasyMedStat (version 3.39; www.easymedstat.com).

Results

143 patients underwent hiatal reconstruction and antireflux plasty in the study period. In 92 of these cases the indication was reflux disease. In the remaining 52 cases the indication was Type II and IV hiatal hernias, or chronic anemia caused by Cameron erosions. From the 92 patients complete pre an postoperative workup including quality of life metrics were available for 65 patients, they form the cohort of this study. The remaining 27 patients had incomplete or no follow-up. There were 34 women and 31 men. Average age was 50,6(±17,1) years at the time of the operation. Average years spent with reflux disease before the intervention was 6,5(±7,4). Follow-up visit was organized after an average duration of 9,7 (±7,6) months after intervention.

On preoperative motility testing, 47.7% (31) of the patients had normal and 40% had ineffective (26) esophageal motility, while 12.3% (8) had absent esophageal motility.

Heartburn decreased from a preoperative average of 1.7 (±1.15) to 0.26 (±0.59) points by the time of the postoperative assessment ($p<0.0001$).

Difficulty swallowing (dysphagia) decreased from 0.48 (±0.75) to 0.31 (±0.58) points after surgery ($p=0.155$).

Rregurgitation decreased from 2.22 (±0.89) to 0.32 (±0.62) points after the procedure ($p<0.0001$).

Chest pain associated with reflux has reduced from 1.03 (±1.02) to 0.17 (±0.42) points by the time of the follow-up examination. ($p<0.0001$).

Complaints of nausea and vomiting decreased from 0.79 (±0.91) to 0.31 (±0.64) points ($p<0.0008$). (See Figure 1).

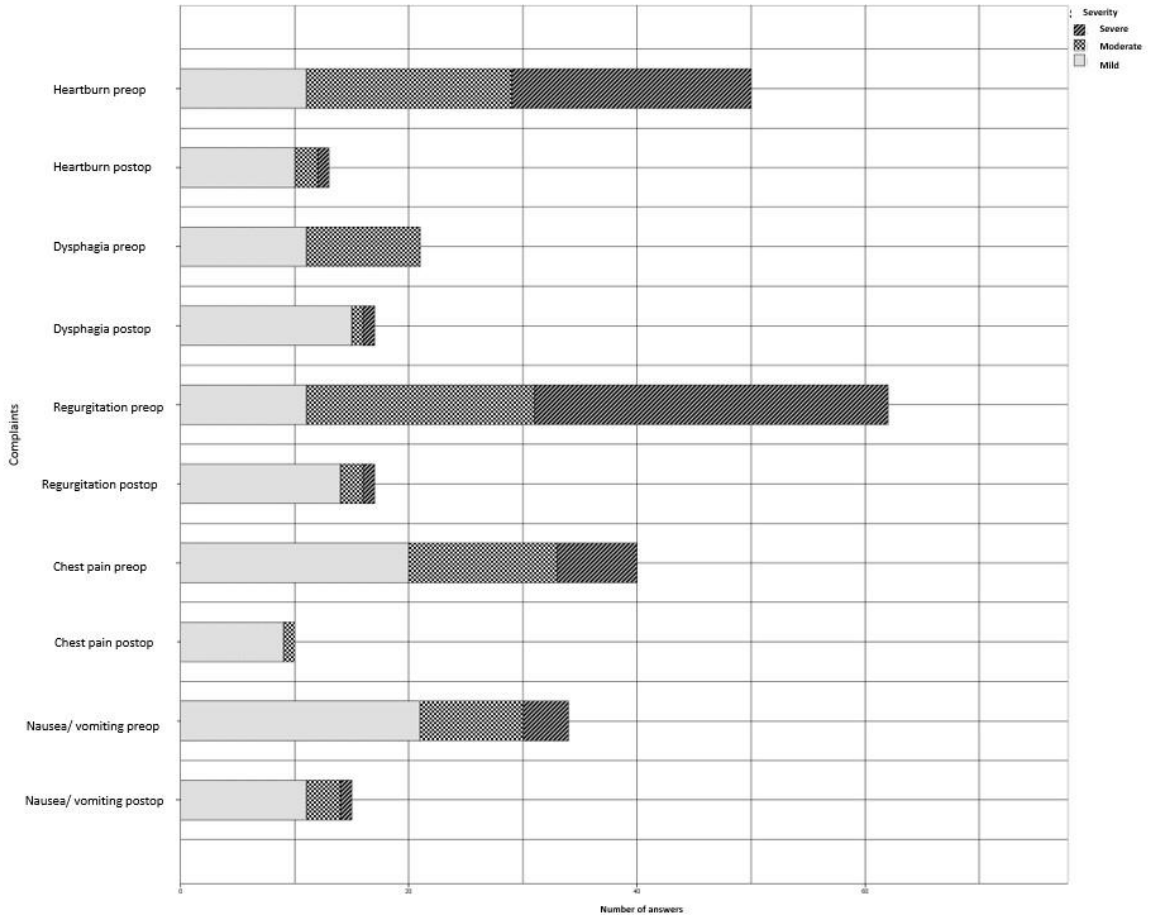


Figure 1.: Frequency of complaints before and after surgery in the cohort© Kovacs et al. (2023) -translated from Hungarian.

The mean preoperative body weight of the patient population was 77.55 (±15.4) kg, while the mean weight loss was 2.08 kg postoperatively. (See Figure 2).

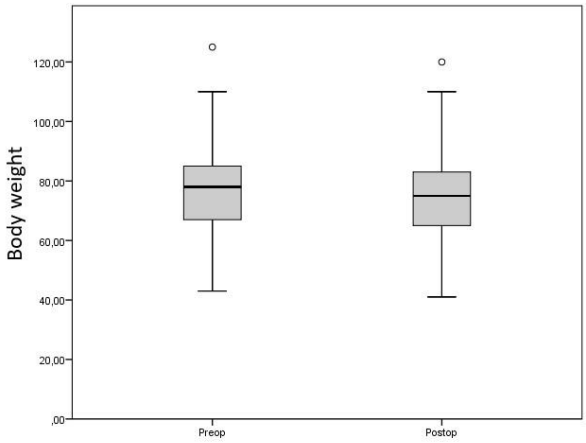


Figure 2: Change in the body weight of the cohort after surgery © Kovacs et al. (2023) - translated from Hungarian.

Subjective complaints of bloating were present in 32 (49.2%) patients before surgery, while 55.38% (36/65) reported these complaints after surgery. (p=0.4824)

Prior to surgery, 57 (87.7%) patients were on acid secretory medication (H2 receptor blockers or proton pump inhibitors), and this number decreased to 17 (26.2%) by the time of the postoperative examination.

The average satisfaction with the surgical intervention and the subsequent course of the disease was 8.73 (±1.83) on a scale of 10 among our patients.

Of the examined patients, 58 (89.2%) would recommend the surgical solution to their relatives or acquaintances with similar complaints.

On multiple regression analysis, age (β=0.02, [-0.01 ; 0.04], p= 0.2537), sex (β=0.11, [-0.96 ; 1.18], p= 0.839) and preoperative body weight did not affect postoperative patient satisfaction.

Presence of preoperative regurgitation (β=0.57, [-0.36 ; 1.5], p= 0.2223), presence of preoperative heartburn (β=0.73, [-0.41 ; 1.88], p= 0.203), presence of preoperative dysphagia (β=-0.91, [-1.93 ; 0.11], p= 0.079), presence of preoperative chest pain (β=-0.6, [-1.63 ; 0.43], p= 0.2503), preoperative bloating (β=0.38, [-0.56 ; 1.33], p=0.4194), and the presence of preoperative complaints regarding nausea and vomiting (β=0.39, [-0.54 ; 1.32], p=0.4035 did not affect postoperative patient satisfaction.

Based on a multivariate regression study, only postoperative heartburn (β=-1.3, [-2.46 ; -0.15], p= 0.0277) showed a clear correlation with patient satisfaction from the complaint profile. While the presence of regurgitation (β=-0.82, [-1.81 ; 0.17], p= 0.1029), chest pain (β=-0.81, [-2.03 ; 0.41], p= 0.1876), or bloating (β=-0.16, [-1.04 ; 0.73], p= 0.7265) could not be directly associated with the degree of patient satisfaction.

Postoperative need for H2 blocker or PPI use was clearly associated with lower patient satisfaction (β=-1.32, [-2.34 ; -0.31], p=0.0116), while preoperative use of the previous medications (β=0.15, [-0.89 ; 1.19], p=0.7694) did not affect it.

Neither preoperative esophageal contractility - quantified as numerical value of DCI - (β=0.0, [-0.0 ; 0.0], p= 0.2732) on high resolution esophageal manometry, nor the diagnostic category according to the Chicago classification (β=-0.52, [-1.76 ; 0.71], p= 0.4014) affected satisfaction.

The number of elements was insufficient for the regression analysis of the appearance of postoperative dysphagia, but when examined with a paired t-test, the score of dysphagia decreased after surgery in case of normal and ineffective esophageal motility parameters, but not in a statistically significant (0.45 vs 0.26 p=0.14 and 0.54 vs 0.31 p=0.217, respectively) amount. In the group diagnosed with absent esophageal contractility before surgery, dysphagia increased minimally, but this was also not statistically significant (0.38 vs. 0.63 p= 0.6).

There were no complications requiring urgent reoperation in the study cohort. There was no mortality either peri-operative or during the study period. Pyloric botulinum toxin injection was performed for delayed gastric emptying in two cases (3%). In two other cases, reoperation was performed for pronounced symptomatic recurrence (3%), in one case conversion to Nissen fundoplication was undertaken, and in one case Roux-Y gastric bypass was performed.

Discussion

In this study, we assessed the change in the quality of life of patients underwent antireflux surgery at our department. During the study, we paid special attention to the assessment of

patients' subjective complaints related to reflux disease during the postoperative follow-up period.

In our institute, we prefer partial, Toupet fundoplications. Several recent studies have shown that the antireflux effect of partial fundoplication is the same as that of Nissen fundoplication, but the frequency of postoperative dysphagia is significantly lower in the case of partial fundoplications. Our results confirm this. Postoperative dysphagia was not significantly higher, and in fact, preoperative swallowing complaints decreased by the time of the control examination (although not statistically significant). The symptoms associated with reflux also decreased significantly, regurgitation, heartburn, and chest pain associated with reflux were also significantly reduced in the postoperative period. Toupet fundoplicaiton is repeatedly criticized for its allegedly higher symptomatic recurrence rate, which varies from one publication to another, but is often higher than that of Nissen reconstruction. Despite this, due to the high proportion of ineffective, often borderline absent, or absent esophageal motility observed in our patient population, and the related risk of postoperative dysphagia, our working group uses the Toupet fundoplication as a first line procedure.

As seen above, patient satisfaction and improvement in quality of life mimicks the statistics of other centers specializing in the care of these patients. The value of 87.3% present in our srudy can be considered fair. 89.2% of our patients would recommend the surgery to a relative or acquaintance with similar complaints, which also confirms our patients' satisfaction with the procedure.

The demographics of the cohort showed similarities with other publications in the literature, both in terms of age and duration of complaints. Due to the low average age of the patient group, one of the relative indications for surgery may also be the patient's refusal of lifelong use of acid secretory medications. The use of proton pump inhibitors and H2 receptor blockers was significantly reduced in the postoperative period (from 87.7% to 26.2%). Subjective b complaints of bloating did not increase significantly, we account this favorable result as a yield of the partial fundoplication used.

Other research has shown that the results of postoperative quality of life can be influenced by the gender of patients. This difference was not significant in our study, although there was a difference in median satisfaction in favor of men (8 vs 9). Several studies have shown that laparoscopic antireflux surgery can achieve a significant improvement in quality of life even in patients with reduced esophageal motility described by esophageal manometry. There was no

difference in patient satisfaction in our study, neither as a function of the DCI before surgery, nor based on the diagnosis according to the Chicago classification.

The most widely supported quality of life improving effect of antireflux surgery is the reduction of typical reflux complaints, such as regurgitation and heartburn. Our study clearly showed that if heartburn is still present after surgery, it significantly affects patient satisfaction. It was also clear that the need for postoperative acid suppressing medications (which, among other indications, can be necessary due to inadequate symptom control) also reduces patient satisfaction.

Limitations: Our study was conducted with prospective data collection, but the questionnaires were not anonymized. The number of elements was sufficient to show fundamental differences, but it only provided limited opportunity to evaluate the predictors of change. Keeping in mind that most of the measured parameters are subjective, the fundamental aim of the intervention is to improve the quality of life, so the reduction of subjective complaints alone supports the efficacy of surgical therapy. The evaluation of objective output parameters is the subject of another study. With the adaptation of the ICARUS guideline, the requirements for the indication of surgery have become stricter, and in our subjective opinion, the satisfaction of patients undergoing surgery did further improve.

In summary surgical intervention is an important and highly effective modality in the treatment of reflux disease. It improves the quality of life and can significantly reduces the symptom burden associated with reflux disease, even in the case of imapired esophageal motility. Further prospective research with the involvement of objective disease measurements are needed.

Chapter 2.

Clinical spectrum and presentation of patients with absent contractility

Introduction

Primary absent contractility is an uncommon finding on high-resolution manometry (HRM), and this condition has been associated with autoimmune disorders. An aperistaltic esophagus was first described in the conventional manometric era, with somewhat different characteristics. The classification of absent contractility has had multiple iterations as esophageal motility studies have evolved, and the currently accepted definition of absent contractility is described

by the Chicago Classification v.3.0. For HRM, the first version of the Chicago classification defined absent contractility as “no continuous pressure domain above an isobaric contour of 30 mmHg in the distal esophageal segment in any swallow; and scleroderma pattern: no continuous pressure domain above an isobaric contour of 30 mmHg in the distal esophageal segment in any swallow and a mean lower esophageal sphincter (LES) pressure (LESP) <10 mmHg”. The second version of the Chicago classification defined it as “normal mean integrated relaxation pressure (IRP), 100% of swallows with failed peristalsis”, similar to the final version of Chicago classification v.3.0. However, the third version (i.e., the current version) changed the definition of failed peristalsis, from “minimal (<3 cm) integrity of the 20mmHg isobaric contour in the distal esophagus” to “distal contractile integral (DCI) <100,” which is easier to interpret. Each update reflects stricter, more specific criteria. However, this means that comparisons and discussions of patients deemed “aperistaltic” by different classifications might be fraught with errors, but given the sparse literature of this topic, there is no alternative. An aperistaltic esophagus noted in type I achalasia is a very different clinical entity than primary absent contractility. The causative and associated factors of this condition are not well understood, and absent contractility is associated with challenging clinical scenarios.

Some have pointed out a possible association between absent contractility and systemic sclerosis (SSc), dysphagia, and severe gastroesophageal reflux disease (GERD). Recently, some have reported on the association of absent contractility with systemic disorders other than SSc and GERD. The goal of this study was to describe and explore the clinical spectrum and presentation of patients diagnosed with absent contractility at a tertiary referral center.

The study was approved by InstitutionalReviewBoard. Number: PHXA-17-0172-71-18. InstitutionalReview Board Approval Date: 06. July 2017.

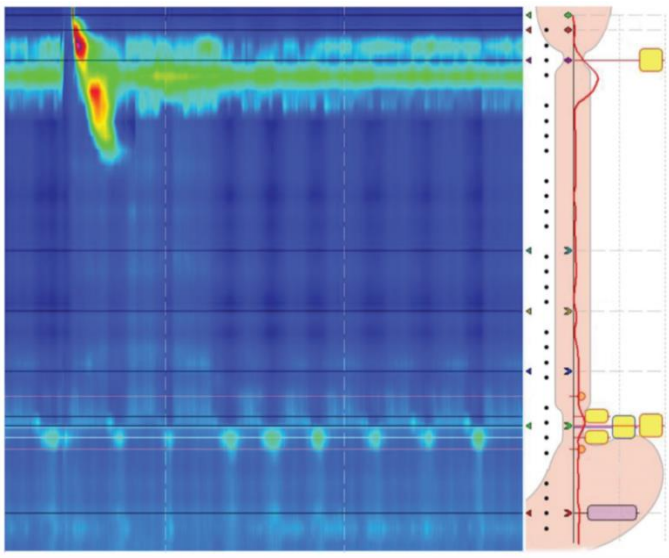
Methods

Patient Population

At our center, we enter all patients who undergo esophageal function testing into a prospectively maintained database. For this study, we queried the database to identify those who underwent HRM between August 2016 and September 2018 and were diagnosed with absent contractility. We excluded patients who had: (1) previous foregut surgery or endoscopic intervention, (2) poor HRM study or missing medical information, or (3) other clinical testing consistent with achalasia or history of achalasia.

High-resolution Manometry

High-resolution manometry was performed with a 36-channel probe with circumferential solid-state pressure transducers at 1-cm intervals (Medtronic, Minneapolis, MN). HRM studies were reanalyzed using Manoview software version 3.0.1 (Medtronic) by a single author (BK), who was blinded to the outcomes of other testing results and clinical findings. The pressure topography of ten 5-mL water swallows was assessed using Chicago Classification v3.0 [1]. According to this classification, “absent peristalsis” (ie, absent contractility) was defined as 100% failed water swallows, distal contractile integral (DCI) <100, and integrated relaxation pressure (IRP4s) <15 mm Hg. DCI and IRP4s were collected and calculated by Manoview software version 3.0.1 in concordance with Chicago classification v.3.0.[1] LESP was calculated as the average pressure during both inspiration and expiration in the eSleeve window (respiratory mean) referred to gastric pressure by software [5]. Figure 3 shows the appearance of absent contractility on HRM. No provocative maneuvers (eg, Multiple Rapid Swallows) were conducted.



Figue 3. Absent contractility on esophageal high-resolution manometry. The examined patient had no history of autoimmune or myopathic disorders neither idiopathic pulmonary fibrosis.

Ambulatory pH Testing

Ambulatory pH testing was carried out with either a dual-channel catheter pH testing system (Digitrapper 400pH, Medtronic) or a wireless single-channel pH testing probe (Bravo, Medtronic). The catheter-based pH probe was passed transnasally and positioned 5 cm above

the upper border of the manometrically defined lower esophageal sphincter (LES). The capsule-based system was passed transorally and positioned 6 cm above the gastroesophageal junction under endoscopic guidance. In accordance with the Lyon consensus [6], the distal esophageal acid exposure time (AET) was calculated as percentage of time pH less than 4.0, measured over the course of 2 days, for the capsule-based system. For the catheter-based system, distal esophageal AET was calculated as percent time pH less than 4.0, measured on the distal esophageal pH probe, 5 cm above the LES. All patients were required to keep track of supine periods, eating, drinking, and gastrointestinal symptoms; these logs were compared to the electronic diary, and the diagrams were corrected if necessary. All measurements had an analysis time of at least 18 hours. All pH testing was conducted while the patients were not taking any acid suppression medications.

Symptom Questionnaire

All patients who underwent functional esophageal testing were asked to complete a standardized foregut symptom questionnaire. The questionnaire assesses to the severity of foregut symptoms a patient may experience, such as heartburn, dysphagia, chest pain, regurgitation, and abdominal bloating. Each symptom is to be scored on a scale of 0 to 4 (Grade 0: none; Grade 1: mild, less than once a week; Grade 2: moderate, several times a week; Grade 3: severe, daily, affecting the patient's lifestyle; Grade 4: very severe, always present, markedly affecting the patient's lifestyle).

Patients' detailed medical history was retrieved from electronic medical records, as well as clinical results of gastroduodenoscopy, histopathology, and barium swallow tests. Descriptive statistics were applied to the data retrieved. Continuous variables were described as mean ± standard variation or median (interquartile range [IQR]).

Results

In total, 2068 patients underwent HRM at our institution between August 2016 and September 2018. Of these, 112 (5.4%) were diagnosed with absent esophageal contractility. 46 patients were excluded: 25 patients were referred from an outside facility solely for testing or because they had poor-quality studies in which proper gastric reference pressure could not be obtained due to artifact or suspected coiling; 11 were excluded because they had undergone previous foregut surgery; and 10 were excluded due to a history of achalasia or findings consistent with achalasia on clinical testing other than HRM. This left 66 patients who met inclusion criteria

and formed the cohort of this study. 38 patients (57.6%) were women, and the mean age of the cohort was 56.6±13.86 years. The mean body mass index was 26.37±5.7 kg/m^2.

The primary complaint indicating a diagnostic workup was heartburn or regurgitation in 54.5% (36/66) of the patients. Nearly half of the patients in this study (29/66, 43.9%) underwent HRM as part of evaluation for lung transplant. 59 patients had a detailed medical history available, and 22/59 patients (37.3%) had history of autoimmune, immune-mediated, or myopathic diseases, while 29/59 patients (49.2%) had some form of interstitial lung disease (Table 1).

Disorder	**n (%)**
Not available	7 (10.6)
No history of ILD, AI or MP	13 (19.7)
Interstitial lung disease	
Unspecified ILD	8 (12.1)
Idiopathic pulmonary fibrosis	9 (13.6)
IPF with autoimmune features	5 (7.6)
NSIP	3 (4.5)
Other rare lung disease*	4 (6.1)
Autoimmune and myopathic diseases	
Scleroderma	11 (16.7)
Fibromyalgia	3 (4.5)
Muscular dystrophy	1 (1.5)
Mixed connective tissue disease	2 (3.0)

Table 1. Autoimmune and myopathic diseases and interstitial lung disease in 66 patients. © Kovacs et al. (2021)

*Combined pulmonary fibrosis and emphysema, cystic fibrosis, alveolar microlithiasis, hypersensitivity pneumonitis

Of the patients with a history of autoimmune disease, 11 had scleroderma (10 scleroderma with SSc), and 5 patients had idiopathic pulmonary fibrosis (IPF) with signs of a localized or systemic autoimmune problem. There were no cases of obstructive lung disease in the cohort. 14/66 patients had diabetes mellitus, and all but 1 of these 14 was in the lung transplant evaluation subgroup.

In addition to the HRM studies, 51/66 patients completed the symptom questionnaire. 42/51 patients (82.4%) reported some degree of heartburn, and 17/51 patients (33.3%) reported experiencing severe heartburn (Grade 3 or higher). 24/51 patients (47.1%) reported dysphagia; 11/51 patients (21.6%) reported experiencing severe dysphagia (Grade 3 or higher). 23/51 patients (45.1%) reported both heartburn and dysphagia, and 9/51 patients (17.6%) reported experiencing severe levels of each. Figure 4 contains additional detail on some of the more commonly reported symptoms. 42/51 patients reported additional symptoms, including change of voice (25/51, 49.0%), recurrent cough (25/51, 49.0%), night cough (21/51, 41.2%), nausea and vomiting (17/51, 33.3%), and recurrent pneumonia or bronchitis (9/51, 17.6%). Reported symptom characteristics did not differ in the lung transplant evaluation subgroup.

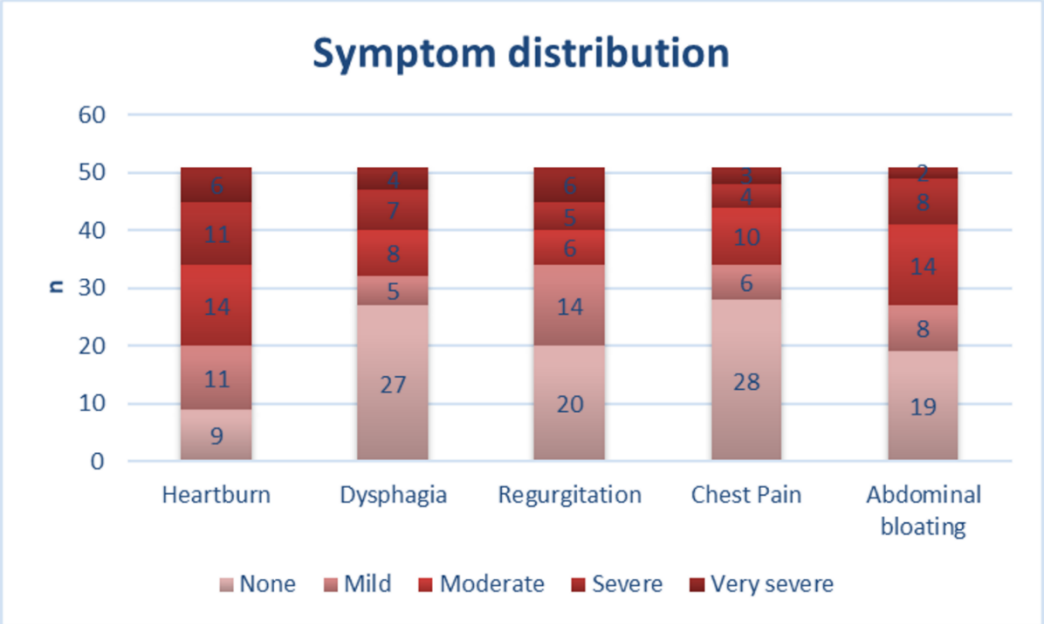
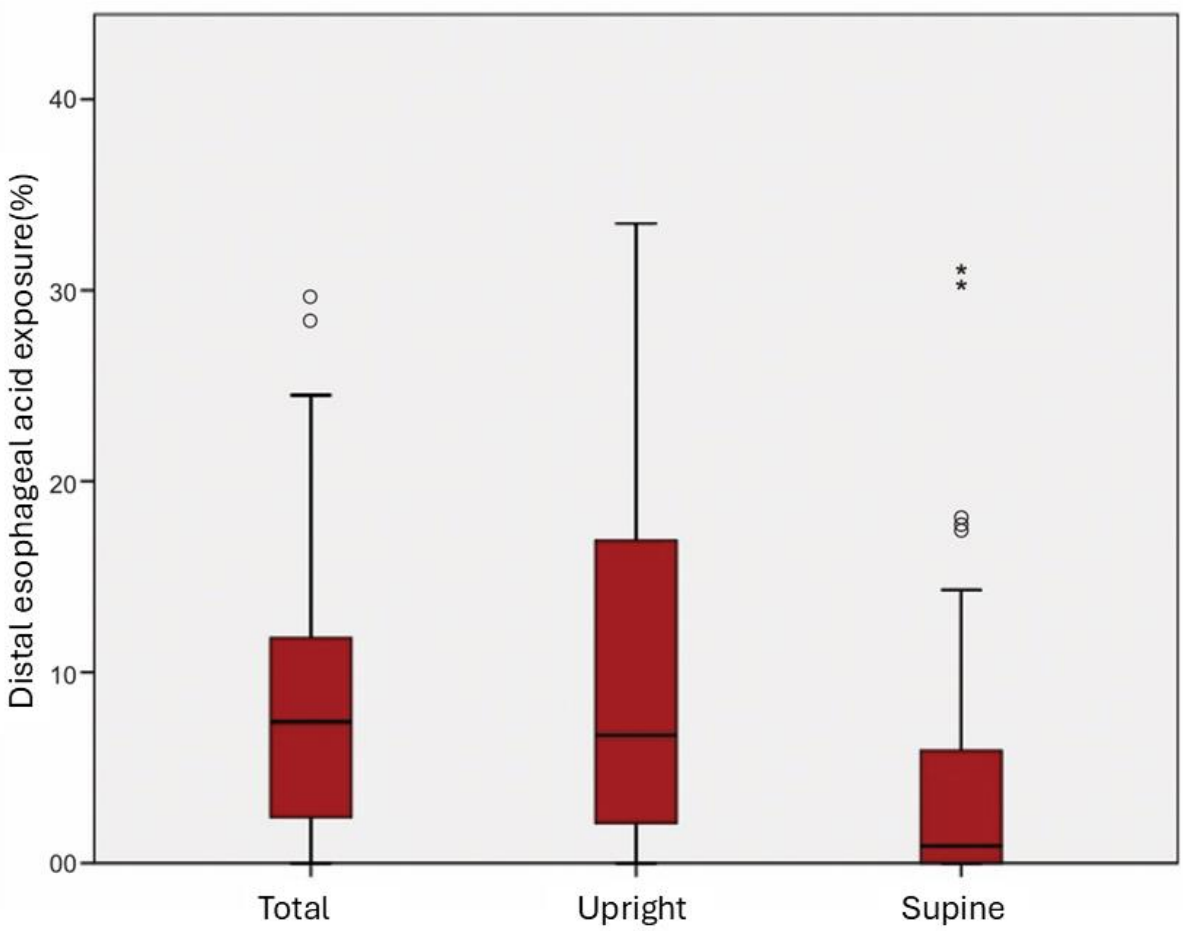


Figure 4. Summar of quality of life questioner results © Kovacs et al. (2021)

In terms of HRM findings, 12/66 patients (18.2%) had hiatal hernia on HRM. The median IRP at 4s was 4.8 mmHg, and the average LES pressure (LESP) was 21 mmHg. Thirty-seven patients underwent ambulatory pH monitoring within two weeks of HRM (6 with wireless testing method); of these, 23 patients (62.2%) had pathological distal esophageal exposure

(AET >6%). The mean distal esophageal AET was 8.7% ± 7.4%; the median distal AET was 7.4% (IQR, 9.9%). The mean reflux time was much more pronounced in the upright position



than in the supine position (10.4% ± 10% upright vs 5.3% ± 8.3% supine; Figure 5). Total number of reflux events were also compared, and no difference was found.

Figure 5. The proportion of distal esophageal exposure regarding position. © Kovacs et al. (2021)

Fifty patients had 50 EGD results available, 45 of which also had biopsies. Esophageal candidiasis was confirmed in 4/45 patients (8.8%). Pathologically confirmed esophagitis was present in 26/45 patients (57.7%).

Fifty-two patients had an esophagram available. 17 of these patients (32.7%) had delayed esophageal emptying, 11 (21.2%) were noted to have dilation of the esophagus (IRP in this

subgroup was under 11 mmHg; none of these patients showed characteristics of achalasia on HRM), and 2 patients (3.8%) were also diagnosed with Zenker diverticulum.

Discussion

Absent contractility on esophageal manometry was first associated with scleroderma, which is known to affect esophageal contractility. The prevalence of absent contractility in patients with systemic sclerosis is reported to be as high as 55%. However, as HRM is becoming more commonly used as a diagnostic tool in patients with functional esophageal diseases, we are facing more cases of absent contractility in patients without a clinical history of scleroderma. Although only a few publications address absence of contractility outside the scope of scleroderma, it seems that a number of other autoimmune disorders, myopathic diseases, and non-immunologic factors may be linked to absent contractility. 37.3% of patients in our cohort had a history of autoimmune, immune-mediated, or myopathic diseases of various origin; meanwhile, only 15.2% had scleroderma. This indicates that a wider array of systemic processes could have a causative association with absent contractility. Laique et al reported that as high as 80% of their patient populations were affected by systemic autoimmune rheumatologic disease.

Gasper et al noted that esophageal dysmotility, including absent contractility, is common in lung transplant candidates diagnosed with connective tissue disease. Dysmotility-associated reflux and aspiration have since been found to drastically affect long-term outcomes of lung transplant. Esophageal dysmotility might also play a role in the evolution of some lung diseases. In our cohort, 29 of 66 patients were tested while being evaluated for potential lung transplantation, and we plan further follow-up of these patients in another study. We have previously reported that esophageal motility improves in a subset of patients with interstitial lung disease posttransplant. This would indicate that esophageal dysmotility in patients with interstitial lung disease is at least partly due to lateral traction from fibrosis and deranged pulmonary dynamics.

Similar to our observations, most reports agree that GERD is a primary problem of patients with absent contractility, and GERD symptoms such as heartburn and regurgitation are experienced by many patients with absent contractility. Smout et al observed a high prevalence of reflux and Barrett esophagus in this patient population. Dysphagia is present in a number of patients who do not have objective signs of outflow problems or bolus-clearance issues.

Denaxas hypothesizes that some of this dysphagia might be a result of *Candida* esophagitis, which is also more prevalent in patients with absent contractility.

As demonstrated in our cohort, dilated esophagus is seen in advanced-stage esophageal disease even without outflow obstruction such as in “burned out” reflux and scleroderma.

No definitive therapy is available for patients diagnosed with absent contractility. However, our experience with lung transplant patients suggests that restoration of normal intrathoracic aerodynamics improves esophageal motility in certain patients with restrictive pulmonary disease. For medical treatment, both metoclopramide and erythromycin may increase LESP, while cisapride seems to increase LESP and distal esophageal body peristalsis. All three of these medications have been used in clinical practice, but their effectiveness is not clearly reported. A study of 22 patients with symptomatic SSc (who were taking proton pump inhibitors), found that buspirone effectively ameliorated symptoms and significantly improved objective parameters such as LESP.

Watson et al proposed that partial fundoplication for GERD control in patients with absent contractility might be adequate and does not pose as high a threat of dysphagia; however, most centers do not perform fundoplication in patients who have absent peristalsis. Hiatal hernia repair might also improve dysphagia in patients who have both hiatal hernia and absent contractility. Kent reported that Roux-en-Y gastric bypass as an antireflux measure is superior to partial fundoplication and has less morbidity than esophageal resection for symptom control in patients with scleroderma.

Although most of our data were collected prospectively, our study was limited by its retrospective design. A longitudinal study and direct comparison with a healthy control group would greatly benefit our understanding of this rare clinical entity. Even though the results of conventional and wireless pH metrics were combined, the clearly pathological results (AET >6%) of patients tested with a wireless probe system mitigates the inaccuracies that may arise from the different normative values of these modalities.

Inclusion of provocative testing (eg, multiple rapid swallows or standardized solid test meal) to our HRM testing protocol might be beneficial in a subset of these patients, as normal IRP on standard testing might hide Achalasia-like disease. Further investigations, including impedance planimetry and solid bolus on timed barium swallow, should be considered for patients with absent contractility and pronounced dysphagia.

Absent contractility is rare and can occur concurrently with a wide array of diseases; the usual clinical presentation is reflux, dysphagia, or both. A large number of patients in our study were undergoing lung transplant evaluation; this could be due to a causative underlying disease process, or it may be reflective of the effects of deranged pulmonary dynamics on esophageal motility.

Chapter 3.:

Remedial bypass or antrectomy and Roux-en-Y after failed fundoplication

Introduction

Excellent outcomes have been reported with primary antireflux surgery; however, some patients require reoperation. Of the patients who undergo reoperation, a select few are at higher risk for poor outcomes after redo fundoplication. In this chapter, we summarize our approach for reoperative intervention after antireflux surgery has failed, and discuss criteria for patient selection, operative technique, and outcomes of RNY reconstruction as a remedial antireflux procedure.

Discussion

Risk factors associated with redo fundoplication

Several large series and meta-analyses have shown that redo fundoplication is associated with significantly worse patient reported outcomes than primary anti-reflux surgery. Redo fundoplication also carries greater perioperative morbidity and mortality (18). The subsequent sections detail factors that may contribute to worse outcomes after redo fundoplication.

Obesity

Patients with an elevated body mass index (BMI) also have higher intraabdominal pressure, which puts stress on the crus closure and fundoplication sutures. Morbid obesity (i.e., BMI >35 kg/m2) has reportedly been associated with poorer outcomes after primary and redo fundoplication; however, RNY with gastric bypass is often carried out in morbidly obese patients due to its secondary benefits of weight loss and its tendency to be reimbursed by health insurance providers (at least in some western countries). Interestingly, several papers have

shown equivalent outcomes between patients with higher BMI (up to 40 kg/m2) and patients with BMI within the reference range.

Akimoto et al. previously reported that patterns of failure after fundoplication were associated with BMI and found similar patterns of failure for patients with BMI 30–35 kg/m2 and patients with BMI 35 kg/m2. These patterns were distinct from patients with BMI <30 kg/m2, indicating that similar physiological forces were at play at BMI >30 kg/m2 rather than >35 kg/m2. In a separate retrospective analysis, Olson et al. graphed patient-reported outcomes along a linear BMI scale rather than comparing categorical groups. Patients with BMI >32 kg/m2 had significantly worse outcomes after redo fundoplication. Regardless of absolute value, increasing BMI seems to be associated with poorer outcomes after redo fundoplication; therefore, an alternative antireflux procedure (e.g., RNY reconstruction) should be considered for obese patients.

Multiple previous fundoplication

As mentioned above, redo fundoplication is associated with higher morbidity and mortality, along with poorer patient-reported outcomes. Negative outcomes of redo fundoplication may include greater prevalence of short esophagus, esophageal dysmotility, delayed gastric emptying compounded by increased inherent risk of vagal nerve injury, and damage to the fundus. The likelihood of these undesirable conditions increases with each reoperation. When a patient has undergone 3 or more fundoplications, they may be at increased risk for vagal injury and poor outcomes. We also found similar results. It is probably prudent to consider RNY reconstruction as the preferred option for the 2nd reoperation, especially if the initial procedure was performed at a center of expertise.

Short esophagus

A successful fundoplication mandates partial or complete wrap of the fundus around the distal esophagus, which must lie tension-free below the diaphragm. This requires 2 to 3 cm of intraabdominal esophageal length; absence of this length after esophageal mobilization is called short esophagus. Collis gastroplasty with fundoplication is the preferred procedure for a patient with a short esophagus. Perhaps no other topic in foregut surgery evokes a more visceral argument than the enigmatic short esophagus; in fact, some experts deny its very existence. However, most surgeons agree that short esophagus not only exists, but it also must be addressed for successful outcomes after fundoplication. Short esophagus is more prevalent in reoperations, implying a missed diagnosis at the time of the previous procedure. Short

esophagus results in undue tension and, ultimately, failure of the fundoplication. However, Collis gastroplasty with fundoplication has less-than ideal outcomes. This is especially the case in patients with esophageal dysmotility. In our opinion, in the reoperative setting, an RNY reconstruction should be strongly considered if a short esophagus is identified, especially if preoperative symptoms included dysphagia or if preoperative testing showed ineffective esophageal motility.

Additionally, if a previous fundoplication involved a Collis procedure, a redo fundoplication is likely already doomed to have poor outcomes, and an RNY conversion is the most viable option.

Esophageal dysmotility

Severe esophageal dysmotility with recalcitrant GERD is noted in a subset of patients, especially those with scleroderma. It has been reported that an RNY reconstruction is a better option than partial fundoplication; RNY also carries lower morbidity than an esophagectomy for control of reflux in scleroderma patients. There is a higher prevalence of moderate or severe dysmotility in these patients, especially those with a short esophagus or those who have undergone more than one previous fundoplication. Such patients should instead be considered for RNY reconstruction. Additionally, because dysmotility may worsen over time and ultimately require an esophagectomy, it is imperative that the distal stomach be left in situ.

Damaged GEJ or fundus

Reoperation requires complete takedown of the previous fundoplication and distal esophageal mobilization before either redo fundoplication or RNY conversion. Not infrequently, patients undergoing reoperation have dense adhesions, and the takedown portion of the procedure results in full thickness or seromuscular damage of the GEJ, the fundus, or both. Although smaller defects (especially in the fundus) can be managed with primary repair, larger defects preclude proper fundoplication. In this situation, it is preferable to proceed with RNY, even if the RNY requires an esophagojejunal anastomosis. The use of mesh, including absorbable biosynthetic mesh, in earlier procedures increases the risk of damage to the GEJ and/or the fundus during takedown; in fact, there is a high need for conversion to RNY in such cases.

Delayed gastric emptying

In most patients with delayed gastric emptying, RNY conversion for another reason (such as one of those listed above) would eliminate the need for gastrectomy. Patients who experience

delayed gastric emptying—especially if the condition is persistent after previous pyloroplasty—are patients best managed with RNY conversion. In patients who experience delayed gastric emptying but exhibit none of the other factors listed above, redo fundoplication with distal gastrectomy is an excellent choice for good outcomes.

How we do RNY conversion

Reoperative antireflux surgery with RNY conversion requires 3 distinct steps: (I) takedown of previous fundoplication, (II) restoration of the intraabdominal length of esophagus and crus closure, and (III) RNY reconstruction, with or without distal gastrectomy. After complete takedown of the previous fundoplication and mobilization of the esophagus, the hiatus is closed and an intraoperative esophagogastroduodenoscopy (EGD) is performed to assess complete takedown and to rule out injury to the GEJ or the fundus. If RNY conversion is the next step, there is no need for a Collis gastroplasty (in patients with a short esophagus). Additionally, mesh reinforcement of the hiatus is not as critical. Whether to proceed via laparotomy or laparoscopy is a matter of surgeon preference. For surgeons with sufficient experience, many cases can be performed laparoscopically, which has the benefits of decreased perioperative pain and shorter hospital stay. In rare cases, we have had to perform a left-sided transthoracic mobilization of a herniated stomach (the patient had a healed gastric perforation of a deep penetrating ulcer near vascular structures), followed by transabdominal RNY conversion.

An RNY conversion includes 3 critical steps: (I) selecting esophagojejunal vs. gastrojejunal anastomosis, including the size of the proximal gastric pouch; (II) determining the length of biliary and alimentary limbs of the RNY; and (III) assessing the state of the distal stomach and choosing whether to resect it or to leave it in situ. See Figure 5 for a schematic summary of procedural approaches.

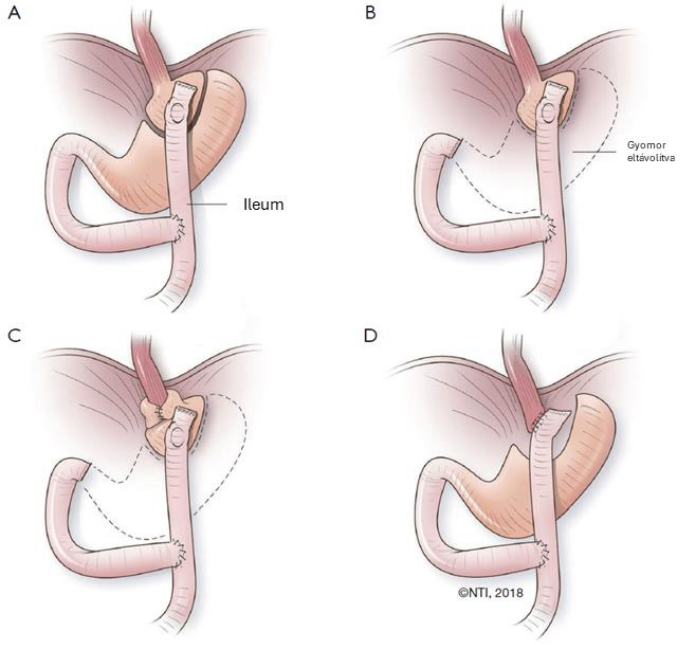


Figure 5. The most common proven surgical approaches for bypass. (A) Classic Roux-en-Y gastric bypass procedure (RNYGBP); (B) RNYGBP with resection of distal stomach; (C) RNYGBP with resection of the distal stomach and fundoplication; (D) RNY with esophagojejunostomy and resection of the gastroesophageal junction with cardia. © Kovacs et al (2018)

Selecting esophagojejunal vs. gastrojejunal anastomosis, including the size of the proximal gastric pouch

In patients with extensive damage to the GEJ from takedown or from recalcitrant stricture, there is no alternative but to proceed with esophagojejunal anastomosis. We recommend a proximal gastric pouch along the lesser curvature rather than transversely across the fundus. In traditional RNY for bariatric procedures, the proximal pouch is very small (i.e., 30 to 50 cc). However, it may be wiser to make a larger pouch in reoperations, due topotential devascularization of the proximal-most stomach below the GEJ during takedown. In addition, such a small pouch has been associated with postoperative dysphagia. We assess the vascularization of the lesser curvature and go at least 5 to 6 cm below that to start our pouch construction. At times, this may be even at the incisura angularis, if takedown of a slipped fundoplication has devascularized several centimeters of proximal lesser curvature. A defect is made in the lesser

mesentery, next to the chosen spot on the lesser curvature. A linear stapler is fired (45 mm) perpendicular to the lesser curvature. The serial loads of staplers are fired parallel to the lesser curvature, up to the angle of His. Care is taken to follow the arc of the lesser curvature, so as not to make the proximal-most section too narrow. The gastric pouch holds somewhere between 60 and 100 cc, allowing the patient to have a meal of a reasonable size. An EGD is carried out to check for air leaks in the pouch. The pouch is opened at the verge of the horizontal and vertical staple line, and the anvil of a 21mm circular stapler is fixed with a purse-string suture.

Determining the length of biliary and alimentary limbs of the RNY

For traditional bariatric RNY gastric bypass, a biliary limb of 50-100 cm and an alimentary limb between 100 and 150 cm are used. To prevent bile reflux, a minimum length of 40 cm for the alimentary limb has been proposed, and with a margin of error, a 60-cm limentary limb is most commonly used, even in malignant gastric resections. The length of the biliary limb does not affect bile reflux. We identify the ligament of Treitz and run the bowel distally to choose the first section, which will easily reach the location of the proximal anastomosis. This is generally about 15 to 20 cm long. Here the bowel is opened and the circular stapler is introduced. The alimentary limb is brought in an anti-colic fashion to the proximal gastric pouch/esophagus for anastomosis. About 1cm orally from the anastomosis the bowel is then cut with a 60mm linear stapler. About 60cm distally on the alimentary limb a 60mm linear stapler is used to create the Roux anastomosis. After anastomosis, a repeat EGD is performed to check for leaks.

Assessing the state of the distal stomach and choosing whether to resect it or leave it in situ

We leave the distal stomach in situ whenever possible to help decrease operative time and to lessen morbidity of distal gastrectomy, including the dreaded duodenal stump leak.The distal stomach can also be used for reconstruction if an esophagectomy is needed in the future, in case of malignant deterioration from Barrett's esophagus or progression of esophageal dysmotility. Additionally, the gastric remnant can be used for a perioperative gastrostomy tube for delivery of medications and nutrition in these often-complex and debilitated patients. Except in extreme circumstances (e.g., recalcitrant ulcers or peptic stricture of the distal stomach), there is no medical reason for distal gastrectomy. The greater curvature is occasionally so devascularized that the distal stomach is not amenable for use as future gastric conduit; in such situations, it may be prudent to proceed with gastrectomy. Figure 6 summarizes our decision-making process on selecting the tailored procedure for the patient.

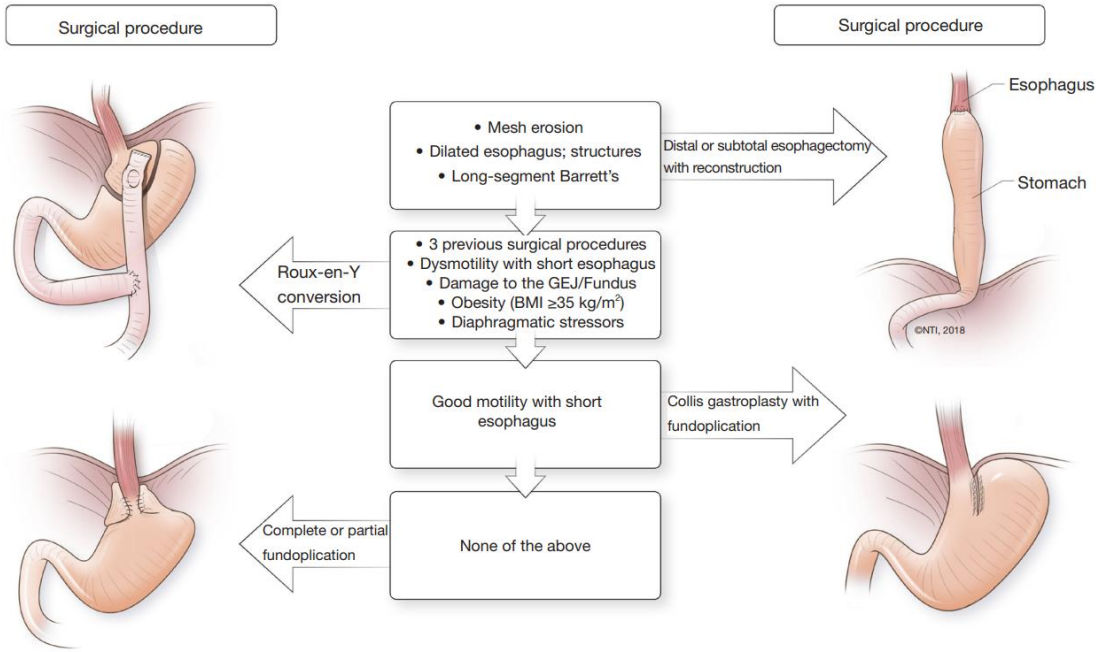


Figure 6. Decision-making process for antireflux intervention selection, taking into account the patient's comorbidities. © Kovacs et al (2018)

Postoperative care

After an RNY procedure, patients are managed in the same fashion as after any foregut surgery. We routinely do a radiographic swallow study on postoperative day 1 (or later, for patients who have undergone an open procedure) with water-soluble contrast. If no leak is identified, a bariatric liquid diet is initiated. We usually discharge the patient home on a liquid diet (with instructions on how to avoid foods with high sugar content) and ulcer prophylaxis (i.e., famotidine 20 mg twice daily) after passing flatus. Patients are advanced to a post-gastrectomy diet over the next 2 to 3 weeks. We also recommend that patients take a multivitamin each day and check the nutritional panel at 6 months after surgery as a precaution, even though we have yet to identify new nutritional deficiencies (other than any preexisting deficiencies). Occasionally, doses of medications generally absorbed in the duodenum or proximal small bowel (e.g., levothyroxine) need to be adjusted over time. In the long term, both the patient and the physician must be aware of closed-loop obstruction due to internal hernia.

Outcomes of RNY conversion for reoperative antireflux surgery

Few studies report exclusively on outcomes of RNY conversion as a reoperative intervention after previous antireflux surgery. Ellis et al. reported a small series of 33 patients; these researchers used an open approach and had an acceptable 27% morbidity rate as well as excellent symptom control (72% of patients) at a mean follow-up of 534 months. Awais et al. reported their outcomes of RNY conversion in 105 patients for whom antireflux operations had failed, describing a high number of previous Collis fundoplications (i.e., 26%). In this series, 46% of patients had 2 or more previous procedures; still, Awais et al. were able to complete 54% of the cases laparoscopically, with a major postoperative complication rate of 21%. Makris et al. reported a series of 72 patients who underwent RNY conversion, with up to 5-year follow-up. They reported significant improvement in heartburn, regurgitation, and dysphagia scores after the procedure. In their series, a subset of patients who were underweight before surgery actually gained weight after resolution of symptoms, whereas morbidly obese patients lost some weight. Mittal et al. previously reported a large series of 130 patients who underwent redo fundoplication and RNY conversion, and found equivalent symptom control and patient satisfaction in both groups, despite a significantly higher prevalence of risk factors for poor outcomes in the RNY group compared to the redo fundoplication group. Patients who underwent RNY had better outcomes than patients who underwent redo fundoplication for the 3rd time or more. Juhasz et al. reported better comes with RNY conversion than with redo fundoplication in patients undergoing reoperative procedures for a recurrent hiatal hernia measuring more than 5 cm. They attributed this to a higher possibility of short esophagus in this subgroup of patients. Singhal et al. reported a large series of primary and reoperative procedures, and described a significantly higher use of RNY conversion as the preferred reoperative strategy in patients undergoing their 2nd or more reoperation.

Conclusions

Overall, several factors are taken into account for reoperative antireflux surgery or when considering RNY conversion. We think of RNY as but one tool for amelioration of symptoms in patients who have undergone previous antireflux procedures. In some patients with mesh erosion, long-segment Barrett's esophagus (and young age), profound esophageal dysmotility with a dilated esophagus, and strictures that cannot be dilated, the only surgical option is a distal or subtotal esophagectomy with reconstruction.

Our operative planning and procedure loosely follow the diagram in the Figure 6. Overall, several options for reoperative interventions exist, and are tailored to the patient's symptoms, underlying physiology, and intraoperative findings. We believe that RNY conversion is a better alternative to redo fundoplication in patients who require reoperation, or for those who have a short esophagus (especially with poor motility); profound esophageal dysmotility; delayed gastric emptying; BMI >32 kg/m2 (definitely for patients with BMI >35 kg/m2); or large, recurrent hiatal hernia. RNY conversion is the only option when the GEJ or fundus has been damaged intraoperatively.

3 OBSERVATIONS:

Chapter1. Impact of antireflux surgery on gastroesophageal reflux-associated symptoms and quality of life

Based on my work we succesfully adapted the diagnostic and threapeutic algorithms to our settings. With adaquate patient selection laparoscopic hiatal reconstruction and Toupet fundoplication is a formidable tool in ameliorating reflux associated symptoms and improvins quality of life in the short term, Imparied esophageal motility before antireflux surgery does not hinder postoperative patient satisfaction. Redisdual heartburn and ongoing necessity of acid secretion medication use after surgery univocally reduces patient satisfaction.

Chapter 2.: Clinical spectrum and presentation of patients with absent contractility

Absent contractility is rare and can occur concurrently with a wide array of systemic diseases; the usual clinical presentation is reflux, dysphagia, or both.

Chapter3.: Remedial bypass or antrectomy and Roux-en-Y after failed fundoplication

Based on our review Roux-en-Y conversion is a better alternative to redo fundoplication in patients who require reoperation, or for those who have a short esophagus (especially with poor motility); profound esophageal dysmotility; delayed gastric emptying; BMI >32 kg/m2 (definitely for patients with BMI >35 kg/m2); or large, recurrent hiatal hernia. RNY conversion is the only option when the GEJ or fundus has been damaged intraoperatively.

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Page 5 - Kovács et al. Figure 1. (2023) Impact of antireflux surgery on gastroesophageal reflux-associated symptoms and quality of life.: Early experiences. *Orvosi Hetilap, 164*(2), 57-63. doi: 10.1556/650.2023.32672 Retrived:26.04.2025.Translated, used under CC BY 4.0

Page 6 - Kovács et al. Figure 1. (2023) Impact of antireflux surgery on gastroesophageal reflux-associated symptoms and quality of life.: Early experiences. *Orvosi Hetilap, 164*(2), 57-63. doi: 10.1556/650.2023.32672 Retrived:26.04.2025.Translated, used under CC BY 4.0

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Page 14 - Kovacs et al. Table 2. (2021) Clinical spectrum and presentation of patients with absent contractility. Ann Gastroenterol. 2021;34(3):331-336. doi: 10.20524/aog.2021.0583. Retrived:26.04.2025. used under CC BY-NC-SA 3.0

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Page 22 - Kovacs et al Figure 1. (2018). Remedial bypass or antrectomy and Roux-en-Y after failed fundoplication. Annals of Esophagus Vol 1 (September 2018) doi:10.21037/aoe.2018.08.02 used under CC BY-NC-ND 4.0 Retrived: 26.04.2025.

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Coauthored publications: 121

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