Before and after Esophageal Surgery: Which Information Is Needed from the Functional Laboratory?

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Keywords

Functional esophageal assessment ·
Surgery for benign esophageal disease ·
High-resolution impedance manometry ·
24-h pH-monitoring · Timed barium esophagogram ·
Functional outcome · Quality of life

Summary

Background: Indications for benign esophageal surgery and postoperative follow-up need to be highly elaborated with differentiated and structured algorithms, based on objective functional workup in the esophageal laboratory. Functional outcome is of utmost interest and has to be driven by the need for comprehensive but purposeful diagnostic methods. **Methods:** Preoperative diagnostic workup procedures by the functional laboratory include 24-h pH-monitoring, impedance testing, and high-resolution manometry (HRM) – in addition to upper gastrointestinal endoscopy and barium swallow/timed barium esophagogram. **Results:** The most frequent indications for benign esophageal surgery are gastroesophageal reflux disease and achalasia; quite rare indications are esophageal diverticula and benign tumors. Esophageal motility testing in addition to 24-h pH-monitoring is crucial before antireflux surgery (ARS) in order to rule out ineffective esophageal motility and to tailor the wrap. With respect to achalasia surgery, the exact type of achalasia (I–III) has to be labeled according to the Chicago classification, and other motility disorders have to be excluded. The postoperative functional evaluation in the early phase (6 months) after either ARS or Heller's myotomy serves as the new baseline motility testing in case of later occurring disturbances in the follow-up.

Conclusion: A complete and proper preoperative esophageal function assessment is crucial in order to rule out a primary motility disorder and to avoid postoperative functional complications.

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Introduction

Surgery for benign esophageal disease is sophisticated and demanding at the same time. Thus, indications for surgery need to be highly elaborated with differentiated and structured algorithms, based on objective functional workup in the esophageal laboratory – always in combination with the patient's history and respective symptom scores. Not only short- and long-term complications or adverse effects following functional esophageal surgery but also false indications and inadequate technical follow-up may lead to a deteriorating quality of life.

Functional outcome is of utmost interest and has to be driven by the need for comprehensive but purposeful diagnostic methods. Selection from the diagnostic 'toolbox' before and after esophageal surgery becomes more difficult in the context of economic pressure, as e.g. the German DRG (Diagnosis Related Groups) system does not adequately mirror the personal efforts, time resources, and materials used for the esophageal laboratory in the ambulatory setting. As not each patient can be offered the complete 'toolbox' of functional investigations, proper selection is the clue to successful therapy and long-term clinical course. Unfortunately, apart from the German S2k guideline 'Gastroesophageal Reflux Disease' [1], there are no guidelines regarding the use and algorithms of func-

tional methods for other benign esophageal diseases evaluated before surgery and during follow-up.

Diagnostic prerequisites *before* functional testing in the esophageal laboratory are i) upper gastrointestinal (GI) endoscopy to exclude malignant disease or other pathologic findings; and – in complex anatomic situations (e.g. previous esophageal surgery) – ii) barium swallow/timed barium esophagogram to depict patient-specific anatomic features and transport dynamics of the contrast medium, especially in selected cases with unclear endoscopic findings.

In addition to these, preoperative diagnostic workup procedures by the functional laboratory include 24-h pH-monitoring, impedance testing, and high-resolution manometry (HRM). The most frequent indications for benign esophageal surgery are gastroesophageal reflux disease (GERD) (including peptic strictures) and achalasia. Less frequent are esophageal diverticula (Zenker's and epiphrenic diverticula only, as there are no surgical indications for bifurcal or 'traction' diverticula), benign tumors of the esophagus, and surgery for Barrett's dysplasia. The latter indications of benign neoplasia have become fairly rare due to the wide spectrum of successful less-invasive endoscopic treatment options being applied nowadays. For this reason, we will focus on 'pure' functional esophageal diseases in this article, such as GERD and the most frequent esophageal motility disorder, i.e. achalasia.

Gastroesophageal Reflux Disease

Indications for antireflux surgery (ARS) have been pointed out clearly in the guidelines of the American Gastroenterologic Association (AGA).

Besides medical therapy of GERD with proton pump inhibitors (PPI), weighing up the potential benefit of surgery versus its side effects, laparoscopic ARS should be offered to patients with i) good response but intolerance to PPI and ii) to patients with persistent or impairing reflux symptoms, especially regurgitation, in spite of PPI therapy [2].

Lack of PPI response might be due to the following differential diagnoses in which the indication for surgery has to be very restrictive or even completely rejected [3], while functional testing is mandatory:

- 1) Refractory reflux symptoms (symptoms not responding to double PPI dose during therapy of at least 12 months).
- 2) Non-erosive reflux disease (NERD) (no mucosal changes endoscopically *and* pathologic acid exposure during pH-monitoring).
- 3) Acid-hypersensitive esophagus (endoscopically no erosions, normal pH-monitoring, but a positive symptom score (symptom index (SI)) > 50%).
- 4) Functional heartburn (A + B + C *and* a negative symptom score (SI < 50%).

Surgery for GERD includes laparoscopic hiatoplasty and fundoplication (partial posterior 270° fundoplication according to Toupet or 360° Nissen with its modifications according to Rossetti

Fig. 1. Combined measurement of the esophageal pressure topography and impedance (purple). **A** Normal bolus clearance. **B** Bolus escape in the mid esophagus. **C** Ineffective motility with bolus escape in the upper third of the esophagus as well as right above the esophagogastric junction.

and DeMeester ('Floppy Nissen')). The anterior 180° wrap according to Dor/Thal/Watson is less frequently used. In patients with preoperatively reduced esophageal motility, partial fundoplication is the preferred procedure due to expected dysphagia following laparoscopic Nissen fundoplication in this cohort. Further side-effects, such as revisional surgery, gas bloating, and the inability to belch are significantly more frequent following Nissen fundoplication in contrast to the Toupet partial 270° wrap [4]. 'Tailored hiatoplasty' refers to the adoption of the type of wrap with respect to the extent of preoperative dysmotility [5].

Physiological Testing of Esophageal Function Prior to Antireflux Surgery

Beside an upper GI endoscopy, esophageal motility testing is crucial. Chan et al. [6] evaluated about 1,000 patients referred to an antireflux procedure, of which 1% and 4.5% were diagnosed with achalasia and severe motility disorders, respectively, contraindicating ARS. This study highlights the significance of preoperative motility evaluation. Whether disturbed esophageal body motility alters the surgical approach or not, is still highly controversial. Niebisch and Peters [7] clearly comment on this topic: Although the definition of ineffective esophageal motility (IEM) varies between studies, it is clear that patients with motility disorders and frequently failed peristalsis tend to suffer more from new-onset dysphagia following ARS. However, the lack of definition of IEM using HRM and that of focused studies on combined high resolution with impedance manometry demands further research in order to identify patients with IEM and coexisting conditions to tailor the potential surgical approach. Catheters with combined pressure and impedance sensors are impressively able to investigate the synergy of lower esophageal sphincter (LES) relaxation and esophageal body motility to evaluate the effectiveness of bolus clearance (fig. 1). Figure 2 demonstrates the HRM study of a patient with IEM referred for ARS. Being aware of new-onset dysphagia in these patients postoperatively, a partial wrap was recommended.

Fig. 2. High-resolution manometry demonstrating ineffective esophageal motility in a patient referred to antireflux surgery.

Fig. 3. High-resolution manometry in patients with giant hiatal hernia. **A** Shortened esophageal body and premature contraction. **B** Fastened wave propagation. **C** Elevated intrabolus pressure. **D** Signs of functional outflow obstruction.

Table 1. Normal thresholds of ambulatory pH-testing (according to [9])

Component	Mean and S.D. Group I Control	p-value	Normal value	% Incidence Group II Abnormal
Supine period	0.286% ± 0.467	0.001	<1.2%	81.5% (31/38)
Total period	1.478% ± 1.381	0.001	<4.2%	79% (30/38)
# Episodes >5 min	0.6 ± 1.241	0.001	3 or less	73.6% (28/38)
Longest episode	3.866 min ± 2.689	0.001	<9.2 min	73.6% (28/38)
Upright period	2.33% ± 1.975	0.01	<6.3%	63.1% (24/38)
# Total episodes	20.6 ± 14.773	0.01	<50	50% (19/38)

When considering sphincter augmentation with the LINX® system ('magnetic sphincter'), preoperative motility evaluation is mandatory, as proper contractility in the light of postoperative temporary dysphagia is necessary to overcome this phase. In fact, dysmotility is a contraindication for magnetic sphincter augmentation.

When interpreting esophageal function tests in patients with large hiatal hernia including giant hernia, paraesophageal hernia, and upside-down stomach, physicians have to be aware of certain facts:

- 1) Proper placement of the manometry catheter is applicable in only 25% of the cases for sphincter assessment.
- 2) 55% have altered esophageal motility according to the current Chicago classification; however, this is not conclusive to alter the approach [8] (fig. 3).

Ambulatory pH-monitoring objectifies increased acid exposure of the distal esophagus. Depending on the raised question and the patient's symptoms, we either use the wireless capsule- or the catheter-based system. The only available capsule-based system is the Bravo™ probe (Given Imaging, Shoreview, MN, USA). By means of upper endoscopy, the capsule is placed 6 cm above the Z-line and wirelessly transmits pH data to the receiver for up to 96 h. The

catheter-based system is multifunctional. These catheters can be used with dual pH probes and/or combined with impedance channels. Therefore, assessment of proximal esophageal acid exposure and retrograde bolus movement as well as bolus quality can be analyzed. This makes it the perfect tool especially to evaluate laryngopharyngeal reflux symptoms. Esophageal acid exposure is measured in the upright and supine position. The number of total reflux episodes, episodes lasting longer than 5 min, and the longest reflux episode are assessed. These items are combined into an overall score, the DeMeester score, with <14.7 being the physiological value. Table 1 illustrates the normal threshold according to Johnson and DeMeester [9].

Revisional Antireflux Surgery

Revisional surgery following laparoscopic fundoplication becomes necessary due to recurrent reflux in most of the patients (42%), dysphagia (17%) (tight wrap or scarring of the wrap), the combination of both (4%), anatomical abnormalities (2.5%), and gas bloat syndrome (0.7%) as the result of an underlying combined denervation of the vagal nerve with delayed gastric empty-

ing (functional pyloric obstruction) and abnormal aerophagia [10]. According to Hatch et al. [11], there are three types of wrap dysfunctions/dislocations, all necessitating redo ARS. Type I matches cranial dislocation of the esophagogastric junction through the hiatus, type II is a secondary paraesophageal hernia ('slipped fundoplication'), and type III is a primary malposition of the wrap below the cardia [11]. If they are symptomatic, all types require redo fundoplication (with or without re-hioplasty) with a highly differentiated perioperative re-workup in the functional laboratory.

As symptoms after ARS occur mostly due to anatomical disturbances, as mentioned above, pH-monitoring is not groundbreaking in most cases but also necessary in order to evaluate an insufficient postoperative reflux barrier when upper GI endoscopy reveals a normal anatomy. Esophageal motility testing before revisional surgery, however, is important in order i) to compare new-onset motility disorders with preoperative manometry and ii) to determine whether pathological obstruction leads to those symptoms [12].

Generally, it is recommended to go through the entire preoperative workup prior to each redo procedure. As it is known to experts, however, most of the patients with postoperative persistent or new-onset symptoms did not receive the entire diagnostic workup in the first place.

Achalasia

Idiopathic achalasia as a primary esophageal motility disorder is rare with an incidence of 1–3/100,000 per year. Primary achalasia is a neurodegenerative disease of the esophagus, characterized by a lack of or insufficient swallowing reflex relaxation of the LES and an impaired propulsive peristalsis of the tubular esophagus due to loss of inhibitory innervation of the myenteric plexus (Auerbach's plexus) [13]. Its exact etiopathogenesis is largely unknown [14]. It only affects the smooth muscle fibers of the esophagus; thus, the pathologic motility findings are mainly concentrated within the distal third of the esophagus. Classical clinical symptoms, as depicted by the Eckardt Score (composite score, summing up the frequency/intensity of dysphagia, regurgitation, retrosternal pain, and the extent of weight loss), lead to further functional testing [15]. When talking about upper GI surgery focusing on preoperative esophageal function, however, achalasia certainly is *the* motility disorder which has to be ruled out before performing surgery. Functionally, non-relaxing LES as well as non-propagating motility of the esophageal body are associated phenotypes of achalasia.

Laparoscopic Heller myotomy in combination with a partial antireflux plasty is the gold standard of surgical treatment for achalasia [16–18]. Due to the minimally invasive division of the longitudinal and circular muscle fibers of the LES down to the submucosal layer, Heller myotomy aims at a significant reduction of the LES resting and residual pressure alongside with the consecutive improvement of food passage from the esophagus into the stomach.

Physiological Testing of Esophageal Function Prior to Heller Myotomy

Upper GI endoscopy and radiological esophagogram suggest the diagnosis of achalasia in only 33% and 66%, respectively [19]. Endoscopy is the first step of the diagnostic algorithm, especially in order to rule out secondary or 'pseudoachalasia', caused by adenocarcinoma of the esophagogastric junction or other diseases, mimicking achalasia by infiltration or destruction of the esophageal wall and/or the neurons of Auerbach's plexus (e.g. systemic storage diseases, inflammatory processes of the GI tract, nerve tumors). Usually, the clinical picture of 'pseudoachalasia' is reversible if the underlying cause is removed [20]. However, upper GI endoscopy can be 'normal' in a respectable proportion of patients, often resulting in an unnecessary long way to diagnosis and therapy [21]. Barium swallow shows the classical 'bird-beak sign' of the esophagogastric junction in the early stages of achalasia. The esophageal clearance or dynamics of esophageal emptying can best be represented radiologically by timed barium swallow, especially in patients with end-stage disease or with megaesophagus. PH-monitoring in achalasia is insignificant in the preoperative setting, although some patients might be wrongly diagnosed with GERD due to 'heartburn' by acid fermentation in the esophagus as a consequence of food stasis. In the follow-up of achalasia treatment, however, pH-monitoring can become more important as peroral endoscopic myotomy (POEM) has been recently reported to cause significant gastroesophageal reflux in the long run [22, 23].

The role of HRM is essential in the correct diagnosis, exclusion of differential diagnoses, and follow-up of achalasia [21]. Moreover, HRM is the designated gold standard in diagnosing achalasia and related unspecific or pre-achalasic motility disorders, a significant proportion of which shows progression or transition into manifest achalasia [24].

In 2008, the Chicago group defined three distinguished phenotypes of achalasia using HRM [25, 26] (fig. 4):

- Type I: 'Classic achalasia' with complete aperistalsis of the esophageal body.
- Type II: Achalasia with panesophageal compression.
- Type III: Achalasia with spastic (hyper-)contractions of the esophagus.

With the introduction of HRM, tailoring of the length of myotomy can now be better estimated. Especially in patients with type III achalasia, the laparoscopic myotomy can be extended more upwards if the manometric high-pressure zone extends to the distal third of the esophagus. However, it is important to know that the myotomy of the entire esophageal body cannot be achieved by the laparoscopic approach.

HRM comes along with a sensitivity of 98% to diagnose achalasia, thus being the gold standard in esophageal function assessment in this motility disorder [27]. Unfortunately, it has to be pointed out that HRM is only utilized in two thirds of achalasia patients to make the correct diagnosis [21].

Various publications highlight the different postoperative and postinterventional outcomes of those distinct phenotypes of acha-

Fig. 4. High-resolution manometric phenotypes of achalasia and manometric patterns of differential diagnoses. **A** Type I – aperistaltic. **B** Type II – panesophageal pressurizations. **C** Type III – spastic contractions. **D** Hypocontractility – sclerodermatous. **E** Hypertensive poorly relaxing lower esophageal sphincter. **F** Hypercontractile esophagus (Jackhammer).

Table 2. High-resolution manometry parameters and reference threshold (according to [28]).

Parameter	Mean (SD)	Median (range)	5 th percentile	95 th percentile
End-expiratory length, cm	3 (0.8)	2.9 (1.3–4.8)	1.8	4.5
Intra-abdominal length, cm	1.5 (0.6)	1.4 (0–2.6)	0.3	2.3
Resting pressure (respiratory mean) – eSleeve, mm Hg	27.9 (11.5)	26.2 (10–58)	12.3	52.2
4 s-IRP (mm Hg) relaxation, %	9.3 (4.3)	9.4 (0–20)	3	16.7
DCI, mm Hg * cm * s	1,766 (1,074)	1,485 (232–5,066)	420	4,236
DCI max, mm Hg * cm * s	2,631 (1,787)	2,103 (442–9,186)	628	7,234
CFV, cm/s	4.8 (1.3)	4.6 (2.8–9.6)	3.2	7.5
DL, s	6.8 (0.9)	6.8 (5.1–8.9)	5.4	8.1

DCI = Distal contractile integral; CFV = contractile velocity; DL = distal latency.

lasia. Especially type III does not respond well to either laparoscopic myotomy or endoscopic dilatation with regard to persistent retrosternal spasms. POEM offers an entire myotomy of the esophageal body, which might resolve typical esophageal spasms in type III achalasia. However, randomized trials investigating exactly this issue are nonexistent so far.

Important differential diagnoses of achalasia include *hypercontractile* (hypertensive LES, diffuse esophageal spasm, Nutcracker and Jackhammer esophagus) as well as *hypocontractile* motility disorders of the esophagus, the etiology and pathogenesis of which are hardly understood [13]. As symptoms might be similar for GERD and achalasia, these phenomena have to be ruled out prior to surgery, too. Figure 4 compares the manometric pattern of achalasia to that of the above-mentioned differential diagnoses. As all of these are rather rare, the correct performance and conclusion of HRM are of utmost importance and should be carried out in experienced centers, since misinterpreted manometric findings might

lead to wrong diagnoses and surgical indications – with well-known devastating consequences.

Esophageal Function Testing Following Surgery

In our clinic, a postoperative follow-up including symptom assessment, upper GI endoscopy, and HRM are performed 6 months postoperatively. This evaluation in the early postoperative phase after either ARS or Heller’s myotomy serves as the current postoperative motility testing following surgery. We consider it as the new baseline in case of recurrent symptoms. In this context, the comparison of the postoperative motility pattern with the latest manometry might shed some light on further occurring disturbances in the follow-up. Being aware that normal thresholds following upper GI surgery do not exist, we refer postoperative manometry findings to our normal thresholds, as summarized in table 2.

Conclusion

A complete and proper preoperative esophageal function assessment is crucial in order to rule out a primary motility disorder and to avoid postoperative functional complications. To highlight the crucial necessity, we summarize with quotations from leading physicians treating esophageal diseases:

- 1) 'Manometry is critical in order to rule out achalasia or other motility disturbances which may predispose to dysphagia after surgery' [29].
- 2) 'The complete absence of motility on the other hand is widely considered a red flag and often an indication for a partial wrap' [30].

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Disclosure Statement

A conflict of interest does not exist.