Multidisciplinary Management of Gastroesophageal Reflux Disease

Sebastian F. Schoppmann
Martin Riegler
Editors

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“Not for nothing rivers
Flow in dryness.”

Friedrich Hölderlin; *The Ister*

"This book is dedicated to our families, friends, and teachers and to all our patients, from whom we are allowed to learn and borrow a better understanding to improve the management of the disease."

Meeting the Qualities of the Tube: Be Rapid, Essential, and Effective

Dear reader,

Welcome to this book entitled *Multidisciplinary Management of Gastroesophageal Reflux Disease (GERD)*.

It deals with one of the most important and most frequent lifestyle diseases of our modern world, i.e., GERD. In addition, the book aims to meet and synchronize the most essential demands of our modern time. It will offer *rapid* retrieval of *essential* information required for *effective* disease management.

The book summarizes our novel understanding of GERD and how this novel understanding translates into modern disease management and cancer prevention. Due to the unique anatomical, histopathological, and pathophysiological qualities and characteristics of the esophagus, the book offers a *multidisciplinary management* of GERD, including histology, physiology, radiology, ENT, pulmonology, gastroenterology, endoscopy, surgery, palliation, and interventional medicine.

We hope that the book will foster a cause-directed GERD management, which seeks to outbalance the failure of the function of the antireflux mechanism within the lower end of the esophagus. Conceptually novel GERD diagnosis aims to assess the extent of the failure of the lower esophageal sphincter (LES) and the grade of dys-geometry of the anchorage of the lower esophagus within the diaphragmatic hole. Multidisciplinary therapy aims to restore esophageal function and to compensate or eliminate multiple somatic manifestations of reflux, including premalignant *Barrett's esophagus*. Thus, the spectrum of therapies for symptom control and cancer prevention includes lifestyle, medical, and interventional measures (novel endoscopic and surgical therapies, oncological surgery, and palliation of esophageal cancer).

In addition, the book presents fascinating novel tools for the diagnosis and therapy of GERD including endoscopic techniques (mucosal resection, EMR; radio frequency ablation, RFA), novel antireflux surgery (endostim, magnetic sphincter augmentation LINX, radio frequency STRETTA, etc.). Special attention is focused on the management of Barrett's esophagus (BE), where reflux induces the formation of a *precancerous tissue* in the lower end of the esophagus.

The multidisciplinary approach uniquely allows to orchestrate an *individually tailored therapy* including different specialties involved in the management of GERD and BE (ENT, gastroenterology, pathology, radiology, pathophysiology, surgery, etc.).

We thank the outstanding panel of expert authors for their exceptional contributions and Springer for giving us the opportunity to publish the book and thus being allowed to bring it to the attention of the reader.

Taken together, we hope that the book helps you to have more fun and success in managing your GERD and BE patients and to gain a better understanding for the causes underlying this modern lifestyle disease.

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1 Pathophysiology of Lower Esophageal Sphincter Damage: A New Method of Diagnosis of Gastroesophageal Reflux Disease

Parakrama Chandrasoma

Pathology has no clinical value at the present time in the diagnosis and management of early gastroesophageal reflux disease (GERD). Biopsies are not recommended for establishing the diagnosis of GERD. Their only value is in the diagnosis of intestinal metaplasia in the patient with visible columnar-lined esophagus (vCLE), which establishes the diagnosis of Barrett esophagus. It is also necessary for the diagnosis of increasing dysplasia and adenocarcinoma in surveillance biopsies taken from patients with Barrett esophagus.

Barrett esophagus is a late complication of GERD. Its presence indicates that the patient has entered the neoplastic cascade which ends in adenocarcinoma in a small minority of patients. At the present time, there is no ability to prevent progression to neoplasia in Barrett esophagus. The only available course is early diagnosis of significant dysplasia and early adenocarcinoma followed by endotherapy directed as eradicating the neoplastic lesion.

We will only consider GERD in this chapter. We will explore the pathophysiology of GERD through its entire progression from the normal state to severe GERD. This will lead to the proposal of a new pathologic test for lower esophageal sphincter (LES) damage that is based on mucosal changes defined by histology. The new ability to measure LES damage has the potential to open the door to a new method of diagnosis and management of GERD that has the potential to eradicate GERD-induced esophageal adenocarcinoma.

The evidence base in support of the new test is solid, albeit small. Its acceptance requires the removal of two long held and powerful dogmas that presently preclude acceptance of the new method: (a) that cardiac epithelium normally lines the proximal stomach and (b) that the gastroesophageal junction (GEJ) is accurately defined

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by the proximal limit of rugal folds and/or the end of the tubular esophagus. The evidence shows clearly that these are both false even as they continue to be accepted.

What is being proposed is revolutionary.

1.1 The Present Status of GERD and Its Management

Gastroesophageal reflux disease (GERD) is regarded as a chronic progressive disease. When defined by the presence of symptoms that reach a point where they are considered troublesome [1], 20–40% of the population has GERD. Approximately 70% of these patients are well controlled throughout life with proton pump inhibitors (PPIs). Their disease does not seem to be progressive although some dose escalation may be needed for control.

From this perspective, progression of GERD is limited to the approximately 30% of GERD patients in whom PPI therapy fails to control symptoms (Fig. 1.1). There is no ability or attempt to prevent the progression of this 30% of GERD patients into the stage of refractory GERD defined by treatment failure. Patients who fail to be controlled with PPIs live a life whose quality is compromised to varying degrees by their symptoms. It is only when they reach this stage, defined by failure of PPIs to control symptoms or when they develop alarm symptoms such as dysphagia, that endoscopy is indicated [2].

From the different perspective of endoscopy, GERD progresses from no visible endoscopic change to erosive esophagitis of increasing severity (Los Angeles grade A to D), visible columnar-lined esophagus (vCLE), Barrett esophagus (defined as vCLE with intestinal metaplasia in the USA), and through increasing dysplasia to adenocarcinoma.

Biopsy is not recommended in patients who do not have an endoscopic abnormality [2]. Biopsy of the endoscopically normal squamous epithelium may show histologic changes of reflux, but these are not sufficiently sensitive or specific to have practical value.

Biopsy of the "normal" squamocolumnar junction (SCJ) is not recommended in patients without vCLE, although it is known that a small but significant number of patients will have intestinal metaplasia if biopsies are taken [3].

Endoscopy in the patient who has failed PPI therapy changes management only in the patient with Barrett esophagus, who enters an endoscopic surveillance program aimed at detecting early neoplastic changes (Fig. 1.1). In patients without Barrett esophagus, endoscopy provides little, if any, useful information that impacts symptom control with PPIs. Barrett esophagus has no effective medical treatment. Progression to dysplasia and adenocarcinoma cannot be effectively prevented [4].

Symptoms of GERD and endoscopic findings are not concordant. A person without symptoms of GERD can have long segment Barrett esophagus or present with an advanced GERD-induced adenocarcinoma. Conversely, a patient with symptoms of GERD can be endoscopically normal (nonerosive reflux disease). Treatment of GERD with PPIs can heal erosive esophagitis without completely resolving GERD symptoms [2]. Patients with NERD are more resistant to symptom control with PPI than those with erosive esophagitis [2].

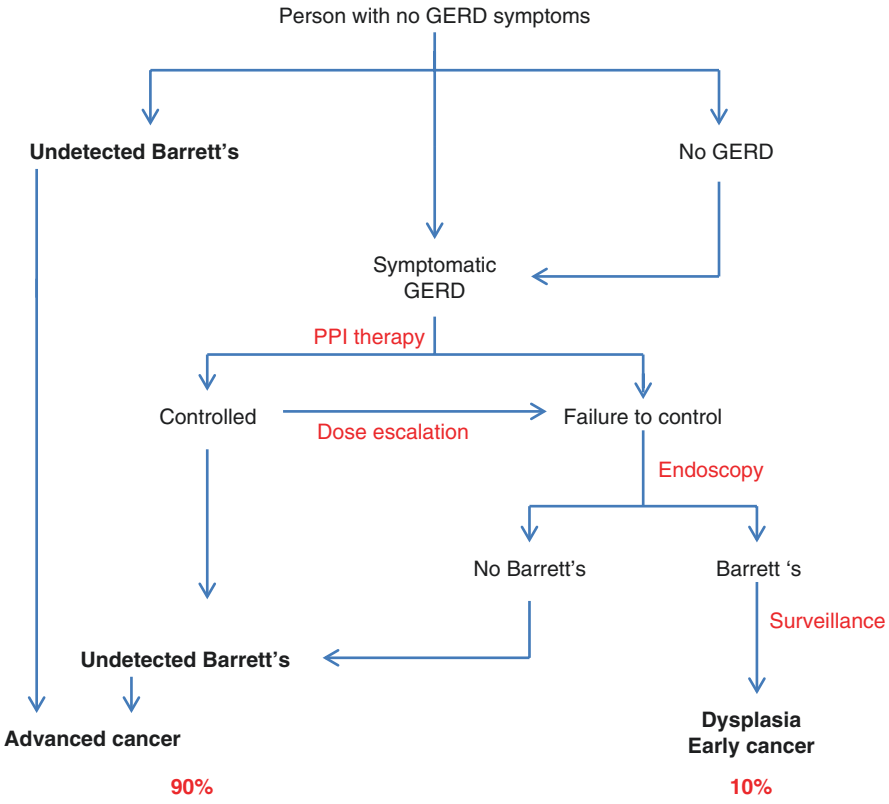


Fig. 1.1 The failure of the present treatment algorithm of GERD to prevent mortality from esophageal adenocarcinoma. Endoscopy is limited to patients who fail medical therapy, and surveillance is limited to those patients who have Barrett esophagus at endoscopy. Ninety percent of adenocarcinomas occur in asymptomatic people, patients well controlled by PPI, and people that do not have Barrett esophagus at endoscopy. Only 10% are found in early stages of cancer and can be treated effectively with a mortality of <30% compared to 90% for advanced cancer

There is no practically effective method of diagnosis of GERD in a patient presenting with symptoms that are suspected to be the result of GERD. As a result, all patients receive empiric acid suppressive treatment with the sole objective of symptom control. A positive empiric test of PPI therapy is commonly used to confirm the symptom-based diagnosis of GERD [2].

There is no symptom complex or test at present that can accurately predict which GERD patient under empiric treatment will progress to failure of PPI therapy in the future. Failure is recognized only when maximum PPI therapy fails to control symptoms.

There is no symptom complex or endoscopic finding short of Barrett esophagus that can predict with sufficient accuracy to warrant screening that a GERD patient will develop adenocarcinoma in the future. Screening for Barrett esophagus is not recommended [3].

This treatment algorithm therefore precludes any method that can prevent the progression of GERD to its severe end points of treatment failure and adenocarcinoma. When the end point of severe GERD is compromised quality of life, surgical sphincter augmentation and fundoplication offers the only hope of control. However, surgery has its own problems and is performed relatively rarely. Many patients who opt to not have surgery continue to live a life that is disrupted by fear of eating, sleep deprivation, and loss of productivity at work [5].

When the end point is advanced adenocarcinoma, hope exists for very few patients and too commonly for a very short period of time (Fig. 1.1). Only 10% of patients developing adenocarcinoma have ever had a diagnosis of Barrett esophagus. These patients are detected with early stage cancer that is amenable to endoscopic therapy, which is often curative and obviates the need for esophagectomy, chemotherapy, and radiation. The other 90% of patients have a dismal outcome with a 5-year survival of around 15%.

This is a sad commentary of our present management of GERD. We have abandoned the hallowed principles of early diagnosis and prevention in favor of an illogical and unrealized hope that PPIs will cure the disease. We simply permit the development of severe GERD and then struggle with few good answers to prevent the inevitable impaired quality of life and progression to adenocarcinoma in a highly significant minority of patients with GERD.

There is no attempt to control progression of GERD. There is no attempt to prevent adenocarcinoma or its premalignant state, Barrett esophagus. There is no attempt to prevent the state of misery associated with GERD that becomes refractory to PPI therapy.

A revolution is essential if there is to be any control of the ever-increasing incidence of adenocarcinoma [6]. This is the first attempt at such a revolution.

1.2 Progression of GERD with Empiric PPI Therapy

The best available scientific prospective study of long-term outcomes associated with treating symptomatic GERD with acid suppressive medical therapy is the ProGERD study [7]. Six thousand two hundred fifteen patients over 18 years old with the primary symptom of heartburn were enrolled into this prospective multicenter open cohort study in Europe. The study was largely conducted under the auspices of AstraZeneca, makers of esomeprazole, which makes any result that suggests a negative effect of PPI therapy highly credible.

All patients underwent an index endoscopy done in selected centers by endoscopists who received special training. Endoscopic findings were recorded and the patients were given 4–8 weeks of PPI therapy with assessment of symptoms control and repeat endoscopy to assess healing. They were then sent back to their primary care physicians for continuation of empiric acid suppressive treatment at their discretion. Treatment used during follow up and symptom control was monitored by questionnaires. 2721 of this cohort of patients reported to the study centers for repeat endoscopic assessment at 5 years.

At the initial endoscopy, the distribution of endoscopic changes of these 2721 patients was as follows: nonerosive disease, 1224; erosive disease LA A/B, 1044; erosive disease LA C/D, 213; 240 (8.8%) patients had vCLE. (Note: vCLE was reported as "Barrett esophagus, endoscopic" and "Barrett esophagus with histologic confirmation," the latter with intestinal metaplasia). The patients with vCLE at the initial endoscopy were not included in this study.

Reversal and prevention of progression of erosive esophagitis at 5 years was impressive. Of the1041 patients with nonerosive disease at baseline, 784 remained nonerosive, 248 progressed to LA A/B, and 9 to LA C/D erosive disease. Of the 918 patients with LA A/B erosive disease at baseline, 578 had reversed to nonerosive disease, 331 remained LA A/B, and 9 had progressed to LA C/D erosive disease. Of the 188 patients with LA C/D erosive disease at baseline, 94 now had nonerosive disease, 78 had LA A/B, and 16 stayed at LA C/D erosive disease. Over a period of 5 years, the number of patients with severe erosive esophagitis had decreased from 188 to 34. Regular intake of PPI reduced the likelihood of progression compared with on-demand PPI or other therapy. The severity of symptoms at baseline was not a predictor of progression to severe erosive esophagitis. It could reasonably be concluded that PPI therapy was highly effective in healing erosive esophagitis.

In contrast, 241 (9.7%) patients who did not have vCLE initially had developed this at 5 years. These patients who progressed included 72/1224 (5.9%) who originally had NERD, 127/1044 (12.1%) with LA grade A/B, and 42/213 (19.7%) with LA grade C/D erosive esophagitis. The factors significantly associated with progression to vCLE at 5 years were: (a) female gender, which had a negative association ($p = 0.041$); (b) alcohol intake ($p = 0.033$); (c) erosive esophagitis compared with NERD ($p < 0.001$); and (d) regular PPI use ($p = 0.019$).

This data shows that empiric PPI therapy titrated to control symptoms in the primary care setting heals erosive esophagitis effectively, but simultaneously results in an endoscopic progression to vCLE with and without intestinal metaplasia. Whether PPI therapy causes this conversion is unproven. However, the study data proves that nearly 10% of the GERD population under empiric acid reducing treatment will progress from not having vCLE to vCLE within 5 years. A patient without vCLE is not considered at present to be at risk for GERD. This means that 10% of patients being treated by standard treatment for GERD in the community progress from a state that is not considered at risk for malignancy (i.e., no vCLE) to a premalignant state (i.e., Barrett esophagus).

When one considers that 20–40% of the population have symptomatic GERD, 10% translates to an absolute number that easily explains why GERD-induced adenocarcinoma has increased sevenfold in the past four decades [6].

1.3 Value of Pathology in the Diagnosis of GERD

Pathologic criteria for diagnosis of GERD are presently limited to changes in the squamous epithelium of the esophagus that result from exposure to gastric contents. Reflux esophagitis is characterized by intercellular edema (dilated intercellular

spaces), basal cell hyperplasia, papillary elongation, and infiltration by eosinophils and neutrophils. These changes do not have the necessary sensitivity or specificity for the diagnosis of GERD. As such, histologic examination of biopsies has no practical value in the diagnosis of GERD.

Pathologic criteria do not exist at present for assessment of the lower esophageal sphincter (LES). In this chapter, we will develop a new set of pathologic criteria that can define the presence and extent of damage to the abdominal segment of the LES (a-LES). We will also explore how this simple histologic test for a-LES damage can transform the future management of GERD.

1.4 A Proposed New Objective in the Management of GERD

The present treatment algorithm for GERD (Fig. 1.1) can be described as totally reactive. There is no defined objective aimed at detecting or preventing any cellular change that may be a harbinger of adenocarcinoma. We simply wait for symptoms that are "troublesome" to begin empiric PPI therapy [1]; then wait for failure of PPI therapy to perform endoscopy [2]; and then wait for the occurrence of high-grade dysplasia and adenocarcinoma. The only proactive event in this algorithm that improves outcomes is Barrett esophagus surveillance, results in earlier detection of adenocarcinoma.

Even worse, most physicians convince themselves that PPI therapy is a wonderful method of treating GERD that brings comfort to millions of GERD sufferers. This is true. However, we hide and ignore the greatest increase of a specific cancer type in the history of medicine that has concurrently occurred while patients are being treated with increasingly effective acid reducing drugs [6].

In this chapter, we will attempt to change the present outcomes of GERD with a new approach based on the development of a new understanding of GERD based on the pathogenesis of progression of a-LES damage.

It is well known that GERD is the result of LES damage. As such, focus on LES damage attacks the problem at its root. The primary objective of the new approach is to turn the curve of increasing incidence of adenocarcinoma downward all the way to zero. A secondary objective is to prevent failure of medical therapy.

1.4.1 Defining a Criterion of Irreversibility: vCLE

The first step in preventing adenocarcinoma is to recognize the point of irreversibility that signals the inability to prevent progression to adenocarcinoma. In GERD, at this point in time, that point of irreversibility is the occurrence of vCLE. In the United Kingdom, vCLE defines Barrett oesophagus [8]. In the USA and Europe, intestinal metaplasia is required for the diagnosis of Barrett esophagus.

Medical treatment does not reverse vCLE or prevent its progression to intestinal metaplasia, increasing dysplasia and adenocarcinoma. Present medical treatment of GERD therefore commits 10% of all patients to irreversibility every 5 years [7].

The advantage with defining irreversibility in GERD by the presence of vCLE is that there is no evidence that any patient who does not have vCLE progresses to adenocarcinoma. If we prevent vCLE, we will prevent adenocarcinoma.

It can be reasonably argued that the person who is endoscopically normal with intestinal metaplasia at the normal SCJ is at risk for adenocarcinoma of the "gastric cardia." However, present management guidelines recommend that such patients with GERD should not undergo biopsies because the risk of cancer in patients who have intestinal metaplasia is unknown [2]. The argument, therefore, has no practical merit at this time. It may change in the future if an increased cancer risk is defined in this group. If and when that happens, preventing intestinal metaplasia at the SCJ in the endoscopically normal person will become necessary.

The detection of vCLE requires endoscopy. The present management guidelines delay endoscopy to the point of treatment failure. At this point a significant number of patients will already have vCLE. If endoscopy is performed proactively without waiting for treatment failure, as was done in the Pro-GERD study, 240/2721 (8.8%) patients would already have vCLE [7]. In addition, the following endoscopic findings were predictive of progression to vCLE in the next 5 years: (a) presence of erosive esophagitis with risk increasing to 19.7% in patients with severe erosive esophagitis [7] and (b) presence of intestinal metaplasia in a biopsy taken from the SCJ of an endoscopically normal patient; such patients had a 25% risk of progression to vCLE within 5 years [9]. The patients in the Pro-GERD study had well-established GERD, often with severe symptoms and a long duration [7]. It is probable that endoscopy performed at the onset of GERD would have a lower prevalence of vCLE.

In the Pro-GERD study, the non-endoscopic findings that were significantly associated with progression to vCLE in GERD patients under medical therapy were male gender, alcohol use, and regular PPI use.

None of the non-endoscopic criteria that are predictive for development of vCLE within 5 years listed above are indications for endoscopy in the GERD patient. The indication remains the occurrence of treatment failure. The main reason for this is the lack of any desire to prevent vCLE in the minds of the medical community. To them, vCLE is simply another inevitable event in the course of GERD that occurs in a minority of GERD patients. The fact that it is a cellular change whose end point is a lethal malignancy is ignored.

This is a nihilistic attitude that permits conversion of the patient without risk to one whose progression to adenocarcinoma becomes inevitable. The only excuse for this attitude is that cancer is rare in GERD patients. With the sevenfold increase in the incidence of GERD-induced adenocarcinoma over the past four decades [6], this excuse has become increasingly lame and unacceptable.

If the presence of vCLE is recognized as the point of irreversibility in GERD, there can be a new objective of management of the GERD patient: *the prevention of progression to vCLE.*

This would then provide an incentive and demand for earlier endoscopy before failure with empiric treatment with PPI in the patient with GERD. Early endoscopy presently has the ability only to recognize the presence of vCLE and predict its

occurrence within the next 5 years by the presence of severe erosive esophagitis (19.7%) and intestinal metaplasia at the normal SCJ (25%). Successful repair of the damaged lower esophageal sphincter (LES) in the patient with a high risk of vCLE in 5 years has a high probability of preventing vCLE.

These reasons for early endoscopy are presently not justified because of the cost associated with increasing the number of endoscopies. However, it emphasizes the fact that any push to prevent adenocarcinoma must change the indications for endoscopy to an earlier stage in the progression of GERD. This will only happen if a new and more accurate method of predicting progression of GERD to vCLE becomes available. The new histologic measure of LES damage that we propose can be that test.

1.4.2 The Cause of vCLE

To be effective in preventing vCLE, we must identify its cause. It is certain that vCLE is the result of exposure of the esophagus above the endoscopic GEJ to gastric contents as a result of reflux. As such, it is also certain that if reflux can be prevented, vCLE will not occur.

There is strong evidence that the risk of vCLE increases with increasing severity of reflux (demonstrated by objective evidence of acid exposure by a pH test), increasing duration of reflux, male gender, regular PPI therapy, and possibly alcoholism and smoking. Nason et al. [10], showed that the prevalence of Barrett esophagus was higher in patients whose symptoms were controlled with PPI therapy. They suggested that the present practice of waiting for treatment failure was irrational if the objective for endoscopy was the detection of Barrett esophagus.

The most dominant factors in the etiology of vCLE are the severity and duration of reflux. Patients with Barrett esophagus are known to have a higher prevalence of an abnormal pH test than any other category of GERD. There is no specifically defined level of abnormality in the pH test or a specific number of years of reflux that correlates with the occurrence of vCLE. If the objective is preventing vCLE, success will demand intervention at the earliest practical time after the onset of reflux. For prevention of vCLE to be certain, intervention must occur before any significant reflux occurs into the thoracic esophagus.

From a practical standpoint, it is necessary that we can identify criteria that separate very low and high risk of impending and future vCLE by some defined severity and/or duration of reflux. This is not possible by presently available tests. We will propose that the new test of LES damage provides accurate criteria for predicting future vCLE.

It is certain that the severity of reflux into the thoracic esophagus correlates with the frequency of LES failure, which in turn correlates with the severity of LES damage. In relation to our objective of preventing vCLE, this recognition establishes a new more practical objective: *prevention of reflux into the thoracic esophagus that is severe enough to cause vCLE.*

1.5 The Lower Esophageal Sphincter

One of the great obstacles to the study of GERD is the absence of a pathologic method of assessing the LES by pathology at autopsy and resection specimens. Careful study of the region has identified complicated arrangement of the muscle fibers that may represent the LES [11], but these cannot be translated into routine pathology practice. The LES can only be defined and measured by manometry (Fig. 1.2).

The LES acts as a beautifully designed barrier that prevents reflux of gastric contents into the esophagus [12, 13]. The LES pressure is normally >15 mmHg, exceeding the baseline luminal pressure in the esophagus (normally around—5 mmHg) proximally and the baseline luminal pressure in the stomach (normally around +5 mmHg) distally. The LES therefore acts as a valve that effectively prevents reflux along the natural pressure gradient that exists from the stomach into the esophagus (Figs. 1.3 and 1.4).

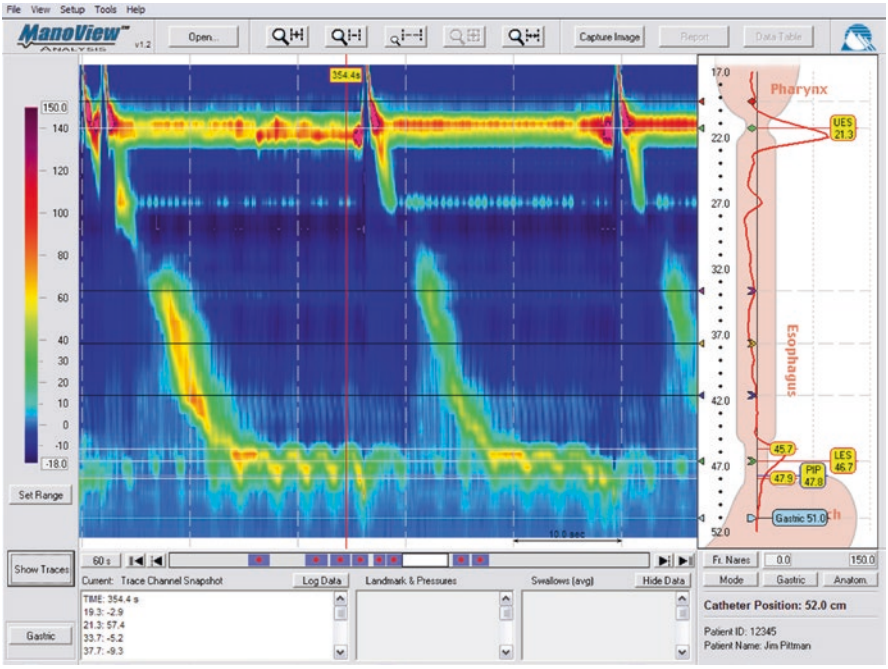


Fig. 1.2 High-resolution manometry showing the esophageal pressure tracing during three swallows. The LES is the high-pressure zone defined by an increase of 2 mm from baseline esophageal pressure at the proximal end and from baseline gastric pressure at the distal end. The LES relaxes during the swallow and regains its resting pressure between swallows

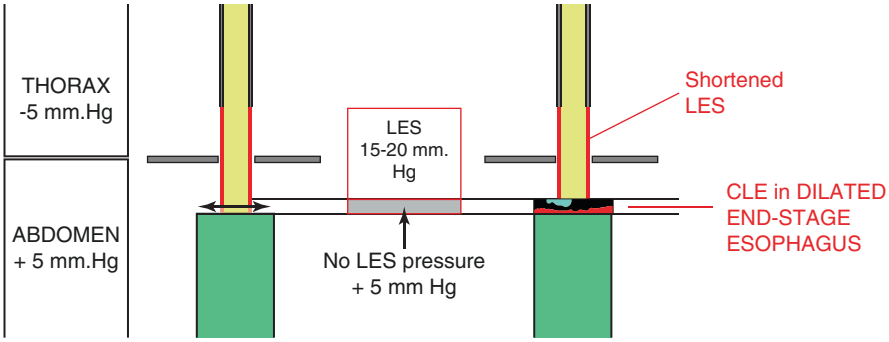
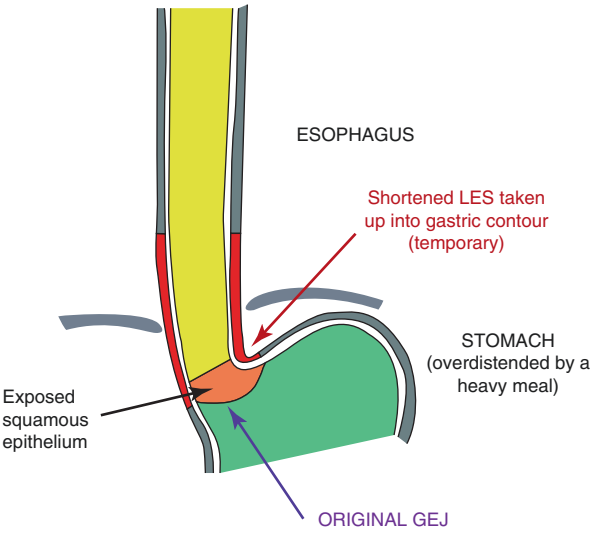


Fig. 1.3 Effect of loss of pressure in the abdominal segment of the LES. The normal resting pressure of the abdominal LES overcomes the positive intraluminal pressure in the abdominal esophagus and maintains the tubal shape of the esophagus. When the LES pressure is lost, the intraluminal pressure causes this part of the distal esophagus to dilate. (NOTE: dilated end stage esophagus was the older term for dilated distal esophagus)

Fig. 1.4 Mechanism of exposure of the squamous epithelium of the distal esophagus to acid. When the stomach overdistends with a heavy meal, the LES shortens, the distal LES becomes effaced, i.e., moves down into the contour of the gastric fundus and the squamous epithelium becomes exposed to gastric contents of the full stomach. There is, at the top of the food column, an acid pocket that meets the descending squamous epithelium



1.5.1 Defining the Normal and Defective LES by Manometry

The functional state of the LES can be defined manometrically by three separate components [12, 13]: its mean pressure, its total length, and the length of its abdominal segment. Manometric studies of asymptomatic subjects indicate that the LES pressure is >15 mmHg, and the total LES length is approximately 50 mm and the length of the abdominal segment (a-LES) is approximately 35 mm.

The criteria that define a defective LES that correlates with the presence of sufficient reflux into the esophagus to produce clinical GERD are [13]: (a) a decrease

in the mean LES pressure to <6 mmHg, (b) a decrease in total LES length to <20 mm, and (c) a decrease in a-LES length to <10 mm. At these levels of LES damage, sphincter failure occurs so frequently that it results in an abnormal pH test and significant exposure of the squamous epithelium in the body of the esophagus to reflux [13]. LES damage defined by these criteria correlate with an increased probability of symptoms of GERD, severe grades of erosive esophagitis, and vCLE.

There is a significant gap between the above criteria that define a normal LES and a defective LES that is associated with abnormal reflux into the esophagus as defined by an abnormal pH test and the presence of clinical GERD. The mean LES pressure must decrease from a normal of >15 to <6 mmHg; the total LES length must decrease from a normal of 50 to <20 mm; and the a-LES length must decrease from 35 to <10 mm before it becomes a criterion of LES failure.

At least part of this gap between a normal and defective LES represents the reserve capacity of the LES. As LES damage increases, its reserve capacity is progressively reduced. However, as long as it is not exhausted, the LES maintains its competence (green zone in Table 1.1).

Table 1.1 Length of a-LES damage (measured by the new test), length of the residual functional a-LES, and their correlation with LES failure and severity of reflux

a-LES damage	Residual a-LESlength	Postprandial a-LESlength	Probability of LES failure	Severity of reflux (% time pH < 4)
zero	35 mm	25 mm	Zero	Zero
> 0 to < 5 mm	30-35 mm	20-25 mm	Zero	Zero
5 - < 10 mm	25-30 mm	15-20 mm	Zero	Zero
10 - < 15 mm	20-25 mm	10-15 mm	Postprandial - rare	> zero to 4.5%
15 - < 20 mm	15-20 mm	5-10 mm	Postprandial - frequent	> zero to 4.5%
20 -25 mm	10-15 mm	0-5 mm	Postprandial – very frequent	> 4.5%
25 -30 mm	**5-10 mm**	**zero**	**Incessant**	**>> 4.5%**
30 -35 mm	**Zero to 5 mm**	**zero**	**Incessant**	**>>> 4.5%**

LES = lower esophageal sphincter; GERD = gastroesophageal reflux disease;
a-LES= abdominal segmentof the lower esophageal sphincterNOTE: Green areas: the LES is competent with damage that is within its reserve capacity.
Orange areas: clinical GERD from onset of symptoms topoint oftransition from postprandial reflux to incessant reflux and an increasing prevalence of vCLE. Red areas: the LES is incompetent with severe reflux and a high prevalence of vCLE;

We assume that the patient has an initial a-LES length of 35 mm, that a heavy meal causes 10 mm of dynamic shortening of the a-LES in the postprandial phase, and that LES failure occurs at an a-LES length of <10 mm

LES lower esophageal sphincter; *GERD* gastroesophageal reflux disease; *a-LES* abdominal segment of the lower esophageal sphincter

NOTE: Green areas: the LES is competent with damage that is within its reserve capacity. Orange areas: clinical GERD from onset of symptoms to point of transition from postprandial reflux to incessant reflux and an increasing prevalence of vCLE. Red areas: the LES is incompetent with severe reflux and a high prevalence of vCLE