



# Secrets for a successful laparoscopic antireflux surgery: patients with extraesophageal symptoms

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**Abstract:** The outcomes for antireflux surgery in patients with extraesophageal symptoms of gastro esophageal reflux disease (GERD) are usually worse compared with patients with esophageal symptoms. This paper focuses on how to obtain a successful laparoscopic antireflux surgery in patients with extraesophageal symptoms. A successful laparoscopic antireflux surgery in patients with extraesophageal symptoms depends on: (I) an objective diagnosis for GERD. The diagnosis of pathological distal reflux is straightforward; however, the diagnosis of proximal reflux and to the target organs may be hard to be established; (II) the attribution of the symptoms to GERD. Extraesophageal symptoms may have a different cause than GERD even in the presence of GERD. A rational and complete workup is necessary to answer this question. A single test is not able to correlate symptoms to GERD. Judicious clinical decision based on a sum of different pieces of information is needed; and (III) the correct selection of patients based on predictors for good outcomes to show those who would benefit from surgery. Adequate surgical technical principles should be followed.

**Keywords:** Extraesophageal reflux syndrome; gastro esophageal reflux disease (GERD); fundoplication; outcomes

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## Introduction

The Montreal definition and classification of gastro esophageal reflux disease (GERD) defined GERD simply as a condition that develops when reflux of gastric contents causes troublesome symptoms or complications (1). This consensus pointed out extraesophageal manifestations of GERD, including cough, laryngitis, asthma and dental erosion (1).

Two mechanisms are proposed to explain extraesophageal GERD syndromes. The first is a direct reflux to the target organ with irritation or microaspiration and the second a reflex (2-4) inciting an esophagus-tracheobronchial reflex that is mediated by the vagus nerve and triggered by chemical stimulation of the esophagus (5,6).

The same Montreal consensus pointed that “medical and surgical treatment trials aimed at improving presumed reflux cough, reflux laryngitis, and reflux asthma syndromes by treating GERD are associated with uncertain and inconsistent treatment effect”. Indeed, some studies showed worse outcomes for patients with extra compared to esophageal symptoms after surgical therapy (7,8). This may be explained by the fact that a cause-and-effect relationship between GERD and extra esophageal symptoms is often difficult to establish since other disorders of the lung and upper respiratory tract can produce similar symptoms. That situation brings greater difficulty in selecting those who effectively have GERD and can benefit from surgery, which requires a more careful preoperative workup (8), as well as the participation of other specialists to decide for the best

treatment for each patient.

This paper focuses on how to obtain a successful laparoscopic antireflux surgery in patients with extraesophageal symptoms.

## Workup

A panel of expert gastroenterologists and surgeons suggested that every patient who will undergo an antireflux surgery should perform a symptomatic evaluation, barium swallow, upper endoscopy, esophageal manometry, and ambulatory pH monitoring (9). A detailed work up is necessary since many studies have shown that the presence of esophageal symptoms such as heartburn and regurgitation are not enough to diagnose GERD, leading to an incorrect diagnosis in 30% to 50% of patients (10,11). This situation is even more difficult in the presence of extraesophageal syndromes that may mimic other diseases and may not coexist with esophageal symptoms in up to 75% of the patients in many series (2,12).

### Upper endoscopy

Endoscopy has a low sensitivity and specificity for the diagnosis of GERD based on the finding of esophagitis (13) especially in patients under antacid medication. Even the presence of hiatal hernia and esophagitis was not different in patients with ear, nose and throat (ENT) symptoms in the absence or presence of GERD confirmed by pH monitoring (14).

The major value of endoscopy; however, is to exclude gastric and duodenal diseases and to detect the presence of Barrett's esophagus which is usually present in 10% to 14% of GERD patients (13).

### pH monitoring

Ambulatory 24-h pH monitoring should be routinely performed in the preoperative workup of patients' suspect of having GERD (13,14). In combination with multichannel intraluminal impedance (MII-pH) or not 24-h pH monitoring provides the best GERD diagnoses and quantification, as well as allows a temporal correlation between symptoms and episodes of reflux (15). However, while ambulatory pH monitoring is still the most reliable diagnostic method for establishing a diagnosis of GERD, with well-established reference values for distal reflux, it is still unclear the threshold for proximal reflux (16).

The absence of a widely accepted reference value for

proximal reflux may be explained by individual tissue resistance and visceral sensitivity. A temporal correlation between symptoms and episodes of reflux may indirectly account for these variables (*Figure 1*). It must also be remembered, though that some symptoms may be incited by the immediate presence of noxious refluxate in the target organ, such as in cough, in others, such as hoarseness due to laryngitis, symptoms reflects a chronic vocal cord injury and there is no direct temporal relation between symptoms and reflux.

### Laryngoscopy

Laryngoscopy may be added to the armamentarium of diagnostic tests of extraesophageal symptoms; however, a low positive predictive value for the diagnosis of GERD is anticipated. Laryngoscopic findings suggestive of GERD are not pathognomonic (*Figure 2*). It is known that healthy subjects can display many of the same signs on laryngoscopy attributed to reflux, with a high degree of interobserver variability in rating laryngoscopic findings. This suggests that laryngoscopy is not a specific test for diagnosing esophagopharyngeal reflux (17).

Studies over time (14,18,19) have shown that the laryngoscopic diagnosis of GERD is confirmed at rates around 40% when compared to the results of ambulatory 24-h pH monitoring alone or in combination with MII-pH.

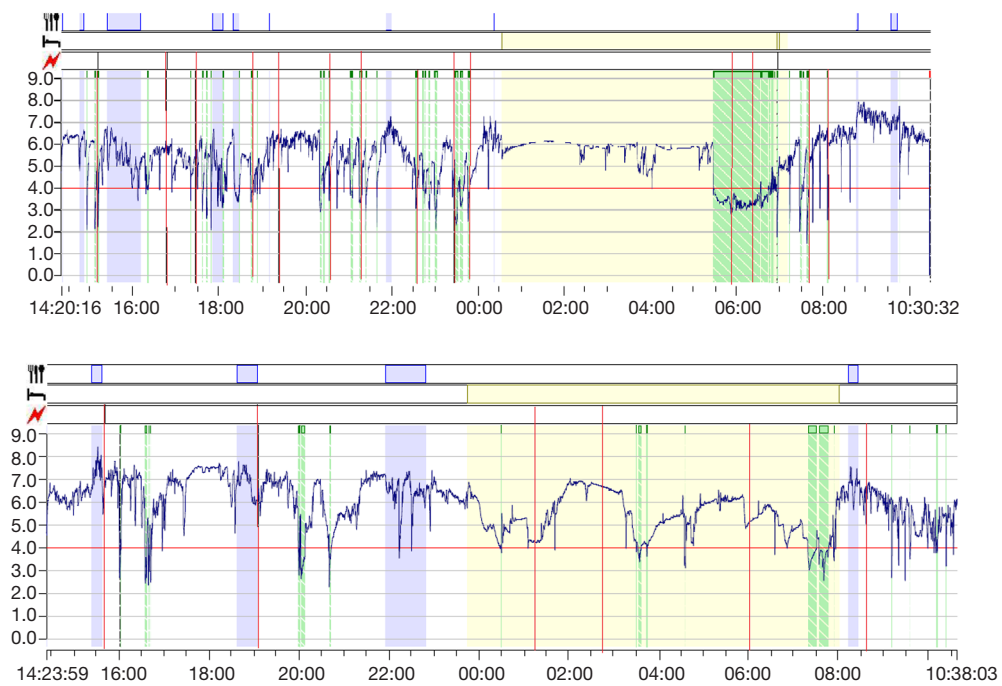
### Empiric trial

Empiric trial may be used to help establish GERD as the real cause for symptoms. The response to antacid therapy may indicate refluxed acid as the causative for presented symptoms.

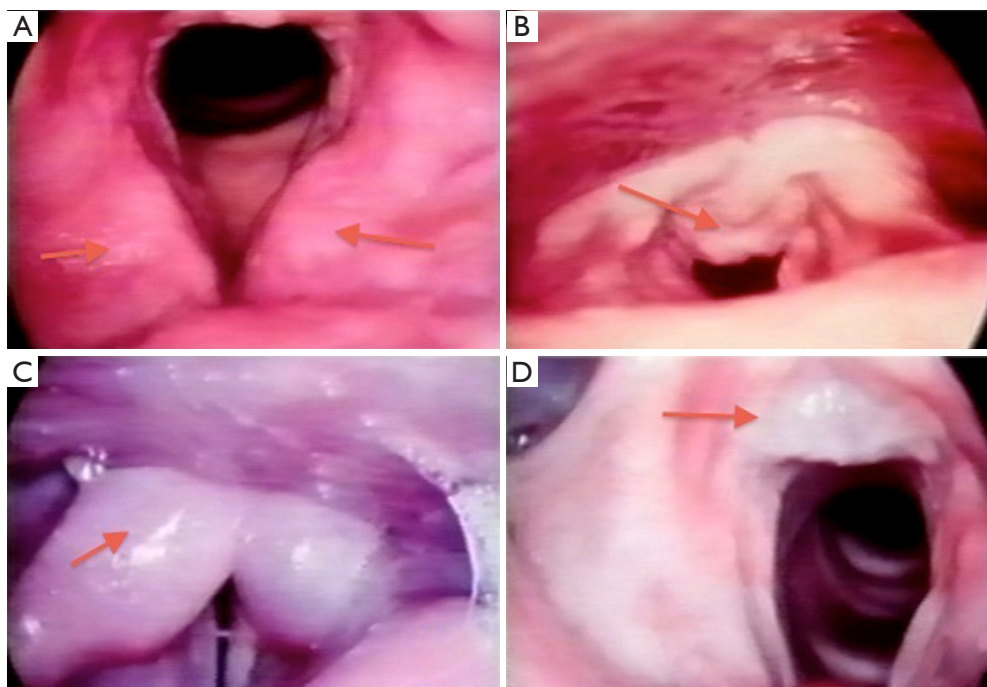
Twice daily proton pump inhibitor (PPI) for 2–3 months is the recommendation (20). Double dose of PPI for a prolonged time is necessary since symptoms may be caused by chronic inflammation that may need extended time for its resolution. Patients unresponsive to this trial should be carefully studied with more specific tests to make a proper diagnosis.

### Other tests

Barium esophagogram, as upper endoscopy, may show gastric reflux to the upper esophagus or even pharynx; however, the sensitivity of this test is poor and no objective parameters can be measured. Besides that, the presence of reflux or hiatal hernia on esophagogram did not correlate with reflux on pH monitoring (13) which also shows its low specificity.



**Figure 1** Temporal correlation between reflux episodes and symptoms at the pH monitoring. A strong correlation may be seen on the patient represented in the upper tracing (simultaneity of episodes of reflux—green vertical bars, and referred symptoms—vertical red bars), different from the patient in the lower tracing.



**Figure 2** Laryngoscopic findings suggestive of GERD. (A) Supraglottic edema; (B) posterior mucosa thickening; (C) interarytenoid edema; (D) posterior thickening. GERD, gastro esophageal reflux disease.

Recently, new diagnosis methods have been developed in order to detect the presence of esophagogastric contents in the oropharynx and bronchus. Further studies are still needed to evaluate the real possibility of its clinical application. Among these should be mentioned the system for measurement of aerosolized droplets of acid in the oropharynx (21) and the detection of pepsin and bile acid in the saliva or bronchiolar lavage (22).

### **Other medical specialists**

Symptoms may be caused by diseases of the target organs other than GERD. The consultation of other medical experts, such as pulmonologists, ENT, allergists, dentists, etc. may be necessary to evaluate these patients.

## **Specific symptoms**

### **Cough**

GERD may lead to cough due to: (I) microaspiration of gastric contents to the upper respiratory system; (II) bronchial reflex due to esophageal chemical stimulation; and (III) as a consequence to upper respiratory system chronic inflammation.

pH monitoring may demonstrate a temporal correlation between reflux and cough in case of microaspiration. A positive correlation predicts a good response to surgical therapy in these cases. Patti *et al.* [2000] (23) showed that cough resolved in 83% of patients in whom a correlation between cough and reflux was found during pH monitoring, but in only 57% of patients when this correlation was absent. Patients that did not present with symptoms during the test had a 0% resolution of cough in the same study.

Cough due to bronchial reflex may be incited by distal esophageal stimulation (24), thus proximal reflux may be absent and a temporal correlation with reflux may be unreliable. In the presence of laryngitis and cough a similar situation may be found. In these patients, a complete work up and the consultation of ENT surgeons are mandatory.

Iqbal *et al.* (25)—in a systematic review of 13 studies—showed a 60–100% improvement in cough after antireflux surgery.

### **Laryngitis**

GERD is a common cause for laryngitis. Different from cough, laryngitis is represented by a chronic inflammation that may persist even after reflux cessation. Thus, the

presence of proximal reflux at the pH monitoring may not be necessary present during the test. Temporal correlation between symptoms of laryngitis (hoarseness, sore throat, etc.) and reflux may not be present for the same reason. Direct evaluation of the larynx (laryngoscopy) may show typical findings to suggest reflux, although with a low accuracy (14).

Few studies focused on the outcomes of laryngeal symptoms after anti-reflux surgery have demonstrated good results in short and middle-term follow-up. Symptomatic improvement ranges from 69% to 97% (26-29). Sala *et al.* (29) showed superior benefits of surgical therapy in patients with laryngeal symptoms responsive to antacid treatment. These studies pointed out better outcomes after operation in patients without some anatomical abnormalities at the laryngoscopy (such as vocal-cord scarring, paresis, granuloma, and carcinoma or subglottic stenosis) and response to PPI treatment.

### **Asthma**

Similarly to cough, asthma symptoms are caused by microaspiration of gastric contents to the upper respiratory system or bronchial reflex due to esophageal chemical stimulation. Adult-onset asthma is more prone to be caused by GERD (30).

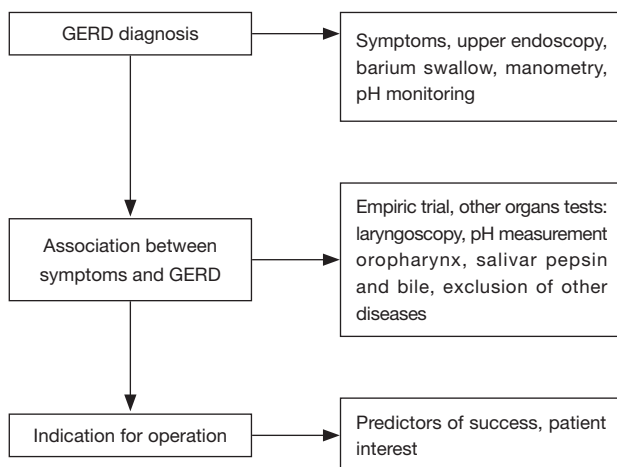
pH monitoring may show reflux but asthma exacerbation will hardly be present during the test to prove GERD as the cause of the disease.

An approach to patients with asthma (with or without concomitant heartburn or regurgitation) is similar to that for patients with chronic cough and laryngitis. A complete workup is necessary and an empiric trial of once- or twice-daily PPIs for 2 to 3 months may be useful (25).

Iqbal *et al.* (25) reviewed studies totalizing 350 asthma patients observed 49–84% improvement of symptoms after surgery. Field *et al.* (31) in another review that included 417 asthma patients showed that antireflux surgery improved GERD symptoms, asthma symptoms, asthma medication use, and pulmonary function in 90%, 79%, 88%, and 27%, respectively. Ekstrom *et al.* (32) in a randomized controlled trial, showed that 12 of 16 patients (75%) had a sustained improvement after antireflux surgery, compared to 9.1% in patients treated medically and 4.2% in the control group.

### **Dental erosion**

Dental erosion due to direct contact of the teeth with



**Figure 3** Road to a successful laparoscopic antireflux surgery in patients with extraesophageal symptoms. GERD, gastro esophageal reflux disease.

refluxed acid leads to characteristic findings of enamel decay.

Although there are no protocols for the investigation of dental erosion due to GERD, we can infer that the same sequence of tests and clinical trial established for other extraesophageal manifestations of GERD should be followed.

There are no data in the literature regarding the outcome of antireflux surgery in the oral repercussions of GERD.

## Conclusions

A successful laparoscopic antireflux surgery in patients with extraesophageal symptoms depends on the answer of three questions (*Figure 3*):

- (I) Does the patient have GERD? An objective test for GERD is mandatory in these patients. The diagnosis of pathological distal reflux is straightforward; however, the diagnosis of proximal reflux and to the target organs may be hard to be established.
- (II) Are the symptoms attributable to GERD? Extraesophageal symptoms may have a different cause than GERD even in the presence of GERD. A rational and complete workup is necessary to answer this question. A single test is not able to correlate symptoms to GERD. Judicious clinical decision based on a sum of different pieces of information is needed.
- (III) Is surgery the appropriate treatment? The correct selection of patients based on predictors for good outcomes shows those who would benefit from surgery. Adequate surgical technical principles should be followed.

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