Borderline Indications and Selection of Gastroesophageal Reflux Disease Patients: 'Is Surgery Better than Medical Therapy'?

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Key Words

Laparoscopic fundoplication · Gastroesophageal reflux disease · Partial response · Proton pump inhibitors

Abstract

Modern medical therapies for gastroesophageal reflux disease (GERD) are totally dedicated to the control of the acid component of the refluxate. In chronic erosive GERD, antireflux surgery has proven to be very efficacious and superior to traditional medical therapies, such as H₂ blockers. The introduction of proton pump inhibitors (PPIs), however, substantially improved medical therapy. Still, treatment failures are inevitable regardless of which of these two effective therapies is chosen. Some recent reports have presented conflicting results from trials comparing antireflux surgery and PPIs. This may be due to differences in trial designs as well as in the structure and content of the therapeutic strategies that are compared. The study with the longest clinical follow-up by far is the SOPRAN study comparing open antireflux surgery and omeprazole. The protocol provides for a follow-up period of more than a decade and the clinical outcomes have recently been published. There has always been concern about the long-term effectiveness of reflux prevention whether by surgery or PPI therapy. It is likely that a marker for an emerging risk for recurrence of GERD is abnormal acid reflux as assessed by ambulatory 24-hour pH-metry. The LOTUS

trial compared maintenance therapy provided by esomeprazole (dose-adjusted when required) with standardized laparoscopic antireflux surgery in patients with good response to acid suppressive therapy. An operation is suitable when symptoms are poorly controlled despite medication, especially for patients who suffer large-volume regurgitation and those who wake at night coughing and choking and who regurgitate acidic fluid or food into their throat and airways. Regurgitation into the throat upon stooping or exercising can limit a patient's ability to work, play sports or even do simple housework. A few patients cannot tolerate medical treatment. If surgery is to be a good option, it must be ensured that the right surgeon performs a standardized operation for the right indications on the right patient and provides good preoperative counseling and testing along with postoperative support. When a patient is refractory to medical treatment, the diagnosis of GERD should be reconsidered before surgery is advised; extradigestive manifestations should be accounted for with care. **Conclusions:** Laparoscopic fundoplication (LF) substantially improves GERD symptoms, although in some individuals symptoms return and acid-suppressive medication use increases. Limited data suggest that LF is less effective at reducing symptoms in partial responders to medical therapy than in complete responders. This may affect cost arguments for using fundoplication surgery rather than acid-suppressive medications, as data are based largely on complete responders.

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Since the introduction of proton pump inhibitors (PPIs) as the main therapy for gastroesophageal reflux disease (GERD), it has become evident that a significant proportion of patients experience only partial or no relief of reflux symptoms even with optimized PPI treatment. These patients are often referred to as partial responders or nonresponders, depending on the degree of symptom alleviation [1]. It is often claimed that partial responders to PPI treatment are commonly referred for laparoscopic fundoplication (LF), even though evidence for the effectiveness of LF in these patients has not been systematically assessed. Antireflux surgery is suitable for a range of patients and for a variety of reasons. An operation can be considered if a patient is fit to have general anesthesia and has a desire to stop medication or to have relief from symptoms experienced in spite of medication [2]. An operation is suitable when symptoms are poorly controlled despite medication – especially for patients who suffer large-volume regurgitation and those who awaken at night coughing and choking and who regurgitate acidic fluid or food into their throat and airways. Regurgitation into the throat when stooping or exercising can limit a patient's ability to work, play sports or even do simple housework. In addition, a few patients cannot tolerate medical treatment. For some patients who are well controlled on acid suppressants but who do not want to stay on pills for the rest of their lives, an operation eliminates the need for long-term prescription medication. The decision in favor of an operation to control reflux symptoms should come from the patient's desire for symptom control and/or quality of life issues. Persistent symptoms in spite of PPI medication constitute a major reason for considering surgery. No generally accepted definition of PPI refractoriness is currently available [1, 3], and according to the surgical antireflux literature, there seems to be no efforts to find a suitable definition and reach a consensus on what is meant by refractoriness to medical therapy. This is problematic since the only grade A evidence that we have on the efficacy of LF as compared to modern medical therapy comes from studies in which responsiveness to chronic PPI therapy was an inclusion criterion [4–8].

Acid-suppressing drugs are sometimes associated with significant side effects: most commonly diarrhea and headache and more rarely tingling in the head, face and neck. Hypomagnesemia can also be a problem. If these limit the quality of life of someone who suffers heartburn, an operation can end those problems. Some 10% of patients on full-dose PPIs still suffer from persistent heartburn and even more suffer from regurgitation.

This group is sometimes said to have refractory reflux. It does not comprise a uniform group of patients and they fall into a number of clinical patterns. Some patients report refractory symptoms that differ from their initial symptoms. PPIs often resolve severe heartburn, but may fail to reduce volume reflux and regurgitation upon stooping or straining. Occasionally, weakly acidic or nonacidic reflux causes persistent symptoms under PPIs and can be detected with impedance monitoring [1]. Clinical follow-up data have shown that patients with such symptoms can have a successful outcome with Nissen fundoplication [7]. There is a further group of patients whose refractory symptoms are due to unusual sensitivity to a normal amount of acid in the esophagus. This is sometimes called acid hypersensitivity, or even functional heartburn. When this can be confidently assessed through 24-hour pH testing in conjunction with good symptom association, it may predict a successful outcome for antireflux surgery [9, 10]. Extraesophageal respiratory symptoms of cough (and occasionally asthma) may also be effectively treated by antireflux surgery when the association with reflux can be confirmed. The grading of evidence in favor of LF in the management of these patients is, however, weak.

Morbid Obesity

Although antireflux surgery may improve symptoms of GERD, the holistic improvement achieved with bariatric surgery with gastrojejunal bypass, excluding the majority of the stomach from the esophagus, provides complete reflux control in the context of the other benefits of marked weight reduction. For patients with moderate obesity (BMI >35 but <40), Anvari and Allen [11] showed good outcomes for Nissen fundoplication with both symptom control and a moderate degree of weight loss. For patients with a BMI >40, gastrojejunal bypass is the preferable route, but requires a cooperative patient. In contrast, some bariatric procedures such as balloons or bands actually can provoke or aggravate reflux and should be avoided in overweight patients for whom reflux is already a problem.

Preoperative Assessment

Preoperative manometry and a 24-hour pH test should be performed as these can confirm reflux and rule out other diseases such as achalasia or eosinophilic esophagi-

tis that could cause similar symptoms. If these tests exclude reflux, the condition causing the symptoms should be sought and treated appropriately.

Ambulatory reflux monitoring with PPIs twice daily can be proposed to patients with documented GERD to establish a correlation between refractory symptoms and reflux events, and/or to exclude GERD as the cause of the persisting symptoms. Due to the low diagnostic yield of pH recordings alone with PPIs twice daily, 24-hour pH impedance monitoring is recommended. The correlation between refractory symptoms and reflux should rely on a symptom index value above 50%. However, whether other parameters (such as symptom association probability, esophageal bolus exposure or the total number of reflux events) should be taken into account remains to be determined. When both symptom index and symptom association probability are positive, the probability that the residual symptoms are related to GERD is high. When both symptom association indices are negative, GERD is probably not the cause of the remaining symptoms; however, whether this can be attributed to functional heartburn will require further validation. In the case of non-concordant symptom-association tests, one should be very cautious when referring the patient for antireflux surgery [1, 2].

Disadvantages of Antireflux Surgery

Early dysphagia is common after the operation, but usually resolves within 3 months. Late dysphagia (5%) may require dilatation or, rarely, revisional surgery. Early satiety, weight loss and discomfort with large meals may be a benefit or a problem. Associated weight loss after a Nissen fundoplication may facilitate improved lifestyle and activity, but is often reversed after 6 months. There can be hiccup, difficulty burping or vomiting, usually transient but occasionally troublesome, along with feelings of trapped wind, bloatedness and increased flatulence, all of which can occur with other patients, especially after surgery. Heartburn and regurgitation occur in 10% of patients 5–10 years after surgery. This relatively high rate may be improved by following a standardized procedure such as that used by the 40 European surgeons who took part in the LOTUS trial [5]. The quality of surgery is very important and this procedure should be restricted to units with proven experience and high case volume. Revisional surgery can be needed in 2–5% and is often effective [12, 13].

Quality Assurance in Surgery for Refractory Reflux Disease

If surgery is to be a good option, the right surgeon should perform a standardized procedure for the right indications on the right patient and provide good preoperative counseling and testing followed by postoperative support. If a patient does not respond to drug treatment, the diagnosis of GERD should be carefully verified before the patient is referred for surgery; special attention should be given to extradigestive manifestations.

Persistent Severe Symptoms and Complications after Reflux Surgery

In this context it is important to take patient characteristics into account when evaluating the outcome. It has been shown that suboptimal improvement in quality of life and accumulation of side effects without any objective evidence of failure is seen more frequently in patients with preoperative psychiatric comorbidities. Pathological behavior can and should be addressed with structured questionnaires that assess general hypochondriasis, index of hypochondriasis, disease conviction, psychological versus somatic illness perception, affective inhibition, affective disturbance, denial irritability, affective state and disease affirmation. So far, studies have shown that there seem to be no apparent differences in illness behavior categories between patients with postoperative problems and those who are scored as successful with regard to surgical control of reflux disease [12–14].

Gastroenterologists may be called upon to manage patients who have had antireflux surgery that has obviously failed. The available literature on this topic mainly contains retrospective reports and studies written by surgeons who often have focused on technical problems that can lead to failure. Such reports are of limited value to the gastroenterologist seeking guidance on postoperative patient management. Furthermore, the conclusions in the various reports are difficult to compare as there is no standardized definition of failure after this kind of surgery. Patients seen by gastroenterologists after antireflux surgery may present with symptoms incompletely relieved or reappearing early or late after surgery, including persistent gastroesophageal reflux, dysphagia, gas bloat syndrome and diarrhea. Many of these complaints can be extremely difficult to treat and there is virtually no scientific evidence for the efficacy of different regimens.

Patients presenting with severe complaints after anti-reflux surgery should be referred to a specialized unit with a multidisciplinary investigational approach followed by therapeutic interventions agreed upon by the gastroenterologists and surgeons involved in the given case.

Disclosure Statement

The author declares that no financial or other conflict of interest exists in relation to the content of the article.

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