

ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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Antireflux Surgery: Efficacy, Side Effects, and Other Issues

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G&H In which patients is surgery an option for treatment of reflux?

LL Antireflux surgery is performed mainly in 2 groups of reflux patients. The first group consists of patients with well-established chronic reflux disease who request antireflux surgery, if it is available, as an alternative to lifelong medical therapy. This group of patients represents the largest proportion of those who will undergo the operation. A variety of factors may be involved in the patient's wish to undergo surgery; for example, a patient may not want to remain on chronic medication indefinitely, or a patient may want to follow in the footsteps of a friend or relative who underwent successful antireflux surgery.

The second group of patients who undergo antireflux surgery are those with well-established chronic reflux disease who are not doing well on proton pump inhibitor (PPI) therapy (ie, patients who are partial or complete failures on medical therapy) or other antireflux therapies. This group of patients is small, but it is larger than initially thought. Included in this group are patients who have volume reflux with significant regurgitation or who aspirate during the night. In addition, this group may include very complex cases of so-called "extraesophageal syndrome," which may be represented by respiratory complications of reflux disease. However, extraesophageal syndrome is a very uncommon indication, and these patients are very difficult to assess and evaluate.

Barrett esophagus is not included in the above symptoms, as I consider it to be represented in chronic reflux disease; thus, in these patients, it does not matter whether a patient has Barrett esophagus.

G&H How effective is antireflux surgery in the short term?

LL In the short term (ie, 1–2 years), antireflux surgery is extremely effective if it meets specific, high-quality criteria (eg, it is performed by an experienced surgeon in a high-volume, expert center). More than 90% of these patients will be satisfied with their symptom control over a period of 1–2 years. However, because surgery is not always performed in expert centers, it may be less effective in some patients.

G&H How effective is antireflux surgery in the long term?

LL By far the longest follow-up period is 20 years, an experience conducted under very well-controlled conditions that will soon be reported in *Annals of Surgery*. There have also been a reasonably large number of well-controlled, prospective, randomized studies with follow-up periods of approximately 1 decade. As all of these trials have been conducted in expert centers, we are rather confident regarding the 10-year outcome of antireflux surgery performed in this setting. However, we are much more uncertain regarding the long-term outcome of antireflux surgery performed in smaller or general hospitals throughout the country; some data have shown that this outcome is not as good as the outcome associated with expert centers.

G&H What are the various types of surgical procedures for treatment of reflux?

LL Two types of surgical procedures have been compared in various randomized, controlled clinical trials: total fundoplication (Nissen type) and partial fundoplication

(anterior or posterior). These funduplications have been examined for both short- and long-term treatment efficacy in patients with reflux.

G&H How do the 2 types of funduplications vary in terms of efficacy?

LL This issue is still a matter of debate. However, by applying principles of evidence-based medicine and looking at the data, we find that no data show a difference in the level of long-term reflux control between a partial and a total fundoplication, provided that the fundoplication is 180 degrees. An incomplete partial fundoplication (ie, a fundoplication that encircles only, say, 90 degrees of the esophageal circumference) is not as effective at reflux control as a total or partial fundoplication of 180 degrees.

G&H How does a surgeon determine which fundoplication to perform?

LL In our institution, surgical training is based on evidence, so residents are taught to perform partial fundoplication whenever possible. In contrast, the only type of fundoplication traditionally taught to surgeons in most institutions in the United States is total fundoplication.

G&H What side effects are associated with these surgeries?

LL Total fundoplication is mainly associated with obstructive mechanical side effects; a proportion of patients will experience difficulty swallowing and slightly compromised passage of food through the esophagus into the stomach. Another side effect associated with total fundoplication is the inability to vent air from the stomach, which makes it more difficult to burp and causes more gas to pass through the intestine, resulting in bloating and flatulence. These are the 2 main types of side effects. According to randomized, controlled clinical trials, these side effects occur less frequently with partial fundoplication.

G&H Are there any methods for reducing the number or severity of side effects associated with total fundoplication?

LL Unfortunately, no. Data have shown that additional division of the short gastric vessels (eg, making the fundoplication more floppy) does not decrease the number of mechanical side effects associated with total fundoplication. The most effective method for reducing the number and severity of side effects is to perform a partial fundoplication instead of a total fundoplication. However, a recent study with a 5-year follow-up period in expert centers

showed that the number of side effects, even for a total fundoplication, is very small if a very strict, standardized surgical protocol is followed.

G&H Is antireflux surgery still performed as frequently as in the past?

LL The number of antireflux surgeries performed annually peaked approximately 10 years ago; since then, there has been a declining number of operations. This number is currently so low that some patients who would benefit from surgery are not being offered this option. This is a major problem that needs to be addressed by surgeons, in conjunction with gastroenterologists, because there is ample information in the literature and from clinical practice to guide doctors in selecting the right patients and institutions.

G&H Why has the number of antireflux surgeries declined?

LL Many gastroenterologists have negative associations with antireflux surgery. Unfortunately, there are good reasons for this negative opinion, as gastroenterologists have seen many failed antireflux operations. The greatest mistake with antireflux surgery was its dissemination to nearly every hospital. As previously discussed, these procedures should be reserved for expert centers. Essentially, the product originally delivered by surgeons was not good enough; the decline in referrals to surgery is likely due to patients who returned to their gastroenterologists after surgery complaining of side effects and/or suboptimal efficacy. Gastroenterologists thus began to stop referring patients to surgeons, thinking that it was better to stick with medical therapy, which was not perfect but at least did not result in side effects such as bloating or dysphagia. Ultimately, surgeons have only themselves to blame, not gastroenterologists. Communication between expert centers and gastroenterologists needs to be revitalized in order to inform the latter group of the positive data associated with antireflux surgery. If we accomplish this goal, the number of operations should rise, although probably not to the peak rates seen 10 years ago.

G&H Are repeat surgeries or supplemental medical therapies necessary?

LL This is an important question. After undergoing antireflux surgery, a proportion of patients will require supplementary, long-term PPI treatment for recurrent reflux symptoms. The magnitude of this proportion varies among different studies, but it usually ranges from 15% to 25%. Unfortunately, the literature is unclear on why

these patients are being prescribed PPIs; doctors may prescribe PPIs for symptoms that have nothing to do with recurrent reflux. When studied carefully, there appears to be a cumulative increase in the number of patients who require PPIs over time. Until proven otherwise, it is thus reasonable to conclude that the longer these patients are followed, the larger the number of patients who will require supplementary PPI therapy.

G&H What are the contraindications to antireflux surgery?

LL There are 2 important contraindications. Patients who are unfit for surgery should not be offered antireflux surgery because of the unacceptably high risk of severe cardiovascular complications. The second contraindication involves patients who have reflux-related symptoms but no clear-cut reflux. These patients may not actually have reflux, but a different disease (eg, functional heartburn), so antireflux surgery will not help them. When patients are not responding well to PPIs and request surgical treatment, it is important to investigate these patients very carefully. These are the patients who should be sent to expert centers in order to obtain the most comprehensive evaluation possible and avoid unnecessary risks.

G&H Is there a significant learning curve associated with these operations?

LL Yes. The tricky question is: Where does this learning curve plateau? It is difficult to determine exactly where the learning curve plateaus, but the plateau likely appears around 50 operations.

G&H Have any studies compared surgery to medical therapy for the treatment of reflux?

LL There have now been 5 or 6 randomized, controlled clinical trials comparing modern medical therapy (ie, PPI-based therapy) with laparoscopic or open antireflux surgery. Except for 1 trial, all of these trials demonstrated the superiority of antireflux surgery. However, there were some methodologic flaws in several of these trials, which makes it difficult to accurately assess the true efficacy of these therapies in comparison to each other. By far the largest of these trials, the LOTUS trial, a multicenter European expert center trial comparing 500 patients randomized to either standardized antireflux surgery or esomeprazole therapy, showed a nearly equivalent outcome between the 2 study groups. Although surgery has a statistically significant advantage for specific reflux symptom control, this advantage is somewhat neutralized by surgery's greater number of side effects, such as

bloating. Thus, there are no major advantages between the 2 groups; it is merely a matter of how the literature is interpreted and, in my view, how critically these trials are examined, particularly in terms of methodology.

G&H Has there been any cost-effectiveness analysis evaluating these procedures?

LL There are 2 types of cost-effectiveness analyses. One type is based on the Markov model, in which certain criteria are established for management of patients on medical therapy versus surgical therapy. Figures such as recurrence and failure rates can then be calculated with respect to therapy, and the cost of the therapies can be estimated based on these computer-based estimates.

The second type of cost-effectiveness analysis, and in my opinion the more comprehensive method, involves the calculation of costs as they occur during the management of patients. This cost-effectiveness model has been evaluated in only 1 randomized controlled trial comparing antireflux surgery and omeprazole and showed a large variability in costs among various groups, such as different countries. These results are crucially important because costs vary among different countries, reimbursement systems, and so on. Thus, an observation from one country should not be extrapolated to another country. The same rule applies to different time periods; cost estimates performed 5 years ago are not relevant today, particularly in regard to generic PPIs, which are extremely inexpensive. In conclusion, although long-term data show the superiority of antireflux surgery over medical therapy in terms of cost-effectiveness, these data should be interpreted with extreme caution.

G&H What are important areas for future research on antireflux surgery?

LL At the moment, robust, stable data based on good clinical research protocols are needed to determine the efficacy of standardized antireflux surgery in patients who are partial responders or nonresponders to PPI therapy and still have reflux. These patients should be investigated very carefully via impedance technology, concomitant 24-hour pH monitoring, and other tools. Then, these patients should undergo upfront, standardized antireflux surgery, and the outcomes should be assessed in relation to preoperative patient characteristics; this analysis would help teach doctors how to select patients for these operations. An alternative would be to randomize these patients to either optimal medical therapy—which could be achieved in various ways, such as with different doses, the addition of histamine blockers, or the inclusion of baclofen—or to standardized antireflux surgery. The

surgical literature claims that a substantial proportion of patients who have been operated on are partial responders or nonresponders; however, this claim is not true. Patients enrolled in most uncontrolled surgical trials are not well characterized; from this perspective, it is unclear whether the patients are nonresponders or partial responders.

Another issue that should be investigated is how the laparoscopic approach of antireflux surgery compares with new endoscopic techniques that are currently emerging. This comparison is the next issue to evaluate because endoscopic technologies are continuously being developed and are becoming more and more complex. In my opinion, these new technologies are exposing patients to essentially the same risks as laparoscopic operations.

The third area of future research should focus on extraesophageal syndrome and its response to antireflux surgery, which is still unclear. It is also still unclear

whether complete reflux control is really needed and can be achieved in patients with Barrett esophagus.

Suggested Reading

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