

# ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

Section Editor: Joel E. Richter, MD

## The Surgical Perspective of Laparoscopic Antireflux Surgery

Tom R. DeMeester, MD  
Professor and Chair, Department of Surgery  
University of Southern California  
Los Angeles, California

**G&H** Could you outline the historical use of laparoscopic surgery and medical therapy for reflux?

**TD** To evaluate the historical use of laparoscopic anti-reflux surgery, one must have an appreciation that gastroesophageal reflux disease (GERD) is only approximately 150 years old. For the first 50 years, it was debated whether findings in the distal portion of the esophagus observed at autopsy were caused by premorbid or post-morbid changes. Many believed that gastric juice rose into the esophagus, eating away at it after death, and this argument persisted until the 1900s when Tileston, a pathologist, noted in an autopsy that these changes were associated with people who had peptic ulcer disease and stenosis in the duodenum. He thus theorized that what he saw in the esophagus was merely peptic ulcer disease (ie, "peptic esophagitis") and was caused by acid, indicating that reflux was a hypersecretion disease. In the 1950s, surgeons became interested in this condition as well. A surgeon named Allison proposed that these changes were due to "reflux esophagitis," or regurgitation of acid from the stomach up into the esophagus, which occurred separately from ulcer disease. Thus, two schools of thought were formed to explain the cause of reflux: peptic esophagitis versus reflux esophagitis.

Initially, surgical therapy focused on the repair of the hiatal hernia without much improvement. In time, the focus shifted to improving the lower esophageal sphincter with a marked improvement in results. During this period, surgical procedures such as the Belsey, Nissen, and Hill were developed. The first randomized trial of

treatment options, conducted in 1975 by Behar and colleagues, clearly showed that, compared to previously used medications such as anti-acids, surgery was more effective for treating reflux.

In 1988, Sir James W. Black received a Nobel Prize for discovering a novel methodology for drug development. Up until that point, most drugs had been developed by searching through herbs and various natural plants and extracting drugs such as digitalis. By understanding human physiology and the pathophysiology of disease, Sir Black thought it was possible to build a drug, through chemistry, that would block a physiologic or biochemical process in the body that would counter the pathophysiological process. This concept was called rational drug design structure, and on this basis, he developed the drugs propranolol and cimetidine, introducing the world of acid suppression therapy to a different level. These medications were so successful that they virtually abolished peptic ulcer disease; thus, according to physicians, it would make sense that they would be very effective against reflux and esophagitis as well, as both are hyperacidic acid diseases. Medical therapy thus became an effective alternative to surgical therapy, and surgical therapy started to decline in popularity. However, although suppressing acid eliminated symptoms and healed mucosal injury, it did not necessarily prevent reflux and the complications of Barrett esophagus and the progression to cancer. On the other hand, data showed that if antireflux surgery was competent and performed early enough, Barrett esophagus could be prevented. Although a debate remains over whether surgery interferes with cancer, it is rare for a patient who has had an antireflux operation to develop

cancer; for example, I usually operate in at least 70–100 cancers each year and have seen perhaps 1 case over 10 years in which the patient had previously undergone an antireflux operation.

Medical and surgical therapy went head-to-head in a randomized study by Spechler in 1992 and in another randomized study by Lundell in 2000. Spechler's study suggested that results with surgical therapy exceeded those with cimetidine or H2 blockers. In the Lundell study, surgical therapy was better than proton pump inhibitors at 5 years and after 7 years, even allowing dose escalation. Surgery was beginning to make a comeback. Back in 1991, Dallemagne had introduced laparoscopic surgery, which was very patient-friendly, revitalizing surgery and further expanding its use. During this laparoscopic period, the last of the four important randomized trials, the LOTUS trial, was published in *Gut* and showed equivalency between laparoscopic surgery and acid suppression therapy at 3 years.

### **G&H** In recent years, has laparoscopic surgery continued its popularity and effectiveness as an antireflux option?

**TD** Two significant events occurred recently to diminish its popularity. In 2001, Spechler published a paper in the *Journal of the American Medical Association* re-examining data from his 1992 paper and showed that, among other findings, upon subanalysis, patients who had undergone an antireflux operation died earlier than those who had not. This finding exploded onto the press and was publicized in mainstream media outlets such as *The New York Times* and *Wall Street Journal*. Our offices were flooded with phone calls from patients suddenly scared to undergo surgery. We tried to explain that this was a subanalysis finding and that it did not correlate with our own clinical experience, but patients started to lean away from surgery.

The second event was an article published in the *American Journal of Medicine* by Vakil in 2003. In a study of nearly 80 patients treated in Milwaukee, Wisconsin, only 61% were satisfied with their antireflux surgical treatment. Sixty-seven percent of the patients reported new symptoms, of which gas, bloating, and dysphagia were reported in 28% of the patients. Six percent of patients reported complete dissatisfaction with their surgery. This article, published on the first page of the journal, also had an enormous negative effect on the popularity of surgery.

There were also other factors that played into the decline of the use of laparoscopic surgery. The LOTUS trial required that surgeons have experience with at least 40 procedures (20 of which had to be performed at least every year). The trial noted that operations performed by these surgeons were quite effective. However, without this amount of experience, the results were not as good.

It became evident that the operations could not be performed by all doctors, limiting their universal application across the country.

Surgeons also did not appear to follow their patients very carefully, and so they were not learning to hone their skills or adjusting their techniques as much as they should have. Patients were being sent back to their internists, and the internists were discovering a high degree of failure with the operation; as a consequence, enthusiasm for surgery began to fall, at least on a community level.

### **G&H** Has resource overutilization also played a role in the recent decline of laparoscopic antireflux surgery?

**TD** If you examine individual therapies of GERD, it is unlikely that overutilization of surgery, in general, played a role. There are 20 million people in the United States who are on acid suppression therapy for GERD, and this is only a conservative estimate based on a recent American Gastroenterological Association survey. Only fewer than 1% of these patients underwent antireflux surgery, so it is not overutilized at all. In fact, overutilization is more of an issue on the medical side rather than the surgical side.

### **G&H** What about insurance reimbursement?

**TD** This has been a debated issue. The cost of a Nissen fundoplication, in particular, has declined quite a bit. If you consider a Nissen fundoplication by itself and compare it to acid suppression therapy and appropriate follow-up, they are approximately equal in cost. However, as soon as you factor in a Nissen fundoplication failure and the cost to recover that failure, there is a financial benefit to choosing acid suppression therapy. Thus, this is only an issue with incompetent surgery; in other words, if the surgery is not performed correctly, it is not very cost-effective. Over time, the costs of outpatient endoscopy have declined and made the follow-up of medical therapy less costly. In the past, endoscopy cost \$500; now, the cost has fallen to approximately \$150. Surgery has fallen in cost as well, from the perspective of both the professional and the hospital.

### **G&H** Have safety concerns for laparoscopic surgery, particularly compared to proton pump inhibitors, influenced its use?

**TD** The safety of a Nissen fundoplication differs from its outcome. Nissen fundoplication is actually an extremely safe procedure. There are many physicians who have reported performing over 1,000 procedures without a

single death. The mortality rate is less than 0.1%, making it an extremely safe operation.

Several very interesting studies have been reported from Finland on the long-term effects of medical GERD treatment. Most medical treatment mortality occurs from aspiration, though this is often not recorded as a death due to GERD. Surgical therapy is likely safer than medical therapy, which surprises many people. In patients with severe reflux disease, the benefits of surgical therapy become more evident because it is a reflux phenomenon, not acid hypersecretion. Thus, if you treat the heartburn, but not the reflux, damaged antireflux machinery remains in the patients and they are subjected to aspiration. This is a particularly significant issue with older patients with advanced reflux disease. According to Finland's thorough records, it was quite evident that patients who are hard-core refluxers have a significant risk of aspiration.

**G&H** Recently, there has been an increase in the number of gastric bypass procedures performed in patients. Has this affected the use of laparoscopic surgery for the treatment of GERD?

**TD** GERD and obesity are known to be associated with each other. However, we certainly do not operate mainly on obese people. In fact, most of our patients are not obese but young, healthy, vigilant people. Thus, I would find this an insufficient explanation for the decline in laparoscopic reflux surgery.

**G&H** Is this decline in laparoscopic antireflux surgery occurring in all patient subgroups?

**TD** Surgery has always been recommended for the patient who is young and has a defective sphincter. It is becoming evident that it is very difficult to medically control someone who completely loses their lower esophageal sphincter. In recent years, the number of people on either treatment strategy has stayed fairly the same; we continue to perform approximately 50,000 reflux operations yearly, which is not that many, in fact, less than 1% of all people on therapy for GERD, as alluded to above (ie, people being treated by doctors and not merely taking self-prescribed over-the-counter medication, making them fairly well-screened patients). In my opinion, surgical therapy is underutilized in approximately 25–30% of patients with documented GERD.

**G&H** Do you foresee a further decline in the use of laparoscopic antireflux surgery in the future?

**TD** Actually, I suspect that laparoscopic surgery will start increasing in use soon, largely due to the recent emphasis

in the literature on the side effects of proton pump inhibitors. Patients are becoming exceedingly concerned about side effects, particularly in terms of the potential relationship between clopidogrel bisulfate (Plavix, Sanofi Aventis) and mild cardiac infarctions. We have been receiving calls from patients asking for a surgical option to avoid using proton pump inhibitors in this situation. Many arthritic patients are also beginning to experience joint pain, making bone concerns a significant issue. Finally, there was an article recently published online in which 100 normal people were placed on a proton pump inhibitor. A certain number of them continued to experience symptoms (“the rebound effect”), confusing and bothering many patients about taking a drug for a disease that can actually cause the disease. Furthermore, there is a growing acceptance that it is difficult to manage a patient lifelong with medical therapy when the patient has no measurable lower esophageal sphincter. A growing movement back toward surgery is beginning to develop due to the recent negative news on proton pump inhibitors and this difficulty in managing patients with no sphincter.

**G&H** Is there any upcoming or ongoing research evaluating the use of laparoscopic antireflux surgery that you are anticipating?

**TD** I am very excited about upcoming research. (I am very much active in research, so I offer full disclosure to my participation and potential bias.) Knowing that we now understand reflux disease better; that it is a chronic progressive disease; that the lower esophageal sphincter plays a significant role; that it is more difficult to control people with medicine when the sphincter is gone; that there are issues regarding side effects with proton pump inhibitors; that the operations we currently have are too difficult to be universally applied by all surgeons; and that we are limited in what we can do for reflux just by sheer numbers (fewer surgeons and the rapidly growing number of patients), there is a need for an extremely simple procedure that will halt reflux disease from a surgical perspective. This procedure needs to meet specific criteria: it has to be performed through extremely small and minimal incisions; it needs not to alter the anatomy (as opposed to the Nissen fundoplication); it has to be a very short procedure that can be performed in an outpatient facility; it has to be at least 86–90% effective (as acid suppression drugs are usually about 50% effective at normalizing pH, whereas surgery is approximately 86%); the patient should be able to go home the same day and eat a minimally restricted diet the day after surgery; and the procedure should be reversible, without any downside.

Recently, the concept of sphincter augmentation has been considered in the surgical world. This is a mecha-

nism by which a magnetic bracelet is applied around the sphincter and the magnetic beads, which are arranged in the form of a bracelet, can expand as the patient swallows and then come back together when the swallow passes, augmenting the sphincter. It is a simple procedure, and we have now implanted over 100 of them. Some have been in patients for 2 years, and we are very excited about this potential treatment option. It takes only approximately 20 minutes to perform. The procedure is reversible; when it is taken out, it does not alter the anatomy. This would not be a replacement for Nissen fundoplication; it would not be ideal in a hard-core refluxer. The idea is that surgeons, joined with internists, can meet the needs of GERD patients who are not happy with their acid suppression therapy. This gap in therapy needs to be addressed by both surgeons and internists together. This is the type of procedure that I foresee for the future: a device that is well studied and involves the talents of both internists and surgeons. By using acid suppression as well as augmenting the sphincter, we can bring GERD under control and prevent esophageal cancer, currently the fastest growing cancer.

## Suggested Reading

- Spechler SJ. Comparison of medical and surgical therapy for complicated gastroesophageal reflux disease in veterans. The Department of Veterans Affairs Gastroesophageal Reflux Disease Study Group. *N Engl J Med.* 1992;326:786-792.
- Spechler SJ, Lee E, Ahnen D, Goyal RK, Hirano I, et al. Long-term outcome of medical and surgical therapies for gastroesophageal reflux disease: follow-up of a randomized controlled trial. *JAMA.* 2001;285:2331-2338.
- Lundell L, Attwood S, Ell C, Fiocca R, Galmiche JP, et al; LOTUS trial collaborators. Comparing laparoscopic antireflux surgery with esomeprazole in the management of patients with chronic gastro-oesophageal reflux disease: a 3-year interim analysis of the LOTUS trial. *Gut.* 2008;57:1207-1213.
- Vakil N, Shaw M, Kirby R. Clinical effectiveness of laparoscopic fundoplication in a U.S. community. *Am J Med.* 2003;114:1-5.
- Behar J, Sheahan DG, Biancani P, Spiro HM, Storer EH. Medical and surgical management of reflux esophagitis. A 38-month report of a prospective clinical trial. *N Engl J Med.* 1975;293:263-268.
- Lord RV, DeMeester SR, Peters JH, Hagen JA, Elyssnia D, et al. Hiatal hernia, lower esophageal sphincter incompetence, and effectiveness of nissen fundoplication in the spectrum of gastroesophageal reflux disease. *J Gastrointest Surg.* 2009;13:602-610.
- Streets CG, DeMeester SR, DeMeester TR, Peters JH, Hagen JA, et al. Excellent quality of life after Nissen fundoplication depends on successful elimination of reflux symptoms and not the invasiveness of the surgical approach. *Ann Thorac Surg.* 2002;74:1019-1024; discussion 1024-1025.
- Lundell L, Miettinen P, Myrvold HE, Pedersen SA, Liedman B, et al. Continued (5-year) followup of a randomized clinical study comparing antireflux surgery and omeprazole in gastroesophageal reflux disease. *J Am Coll Surg.* 2001;192:172-179; discussion 179-181.