

ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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The European Experience of Achalasia Treatment

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G&H What is achalasia?

GB Achalasia is a debilitating disease of the esophagus, in which neurons disappear, leading to severely disturbed motility of the esophagus. Peristalsis in the esophagus is lost, and relaxation of the lower esophageal sphincter is reduced. As a consequence, passage of food from the mouth to the stomach is hampered, causing dysphagia and leading to weight loss, retrosternal pain, and regurgitation of undigested food. Other symptoms include bad breath, nocturnal coughing, and increased risk of aspiration pneumonia. Achalasia is quite rare, with an incidence of approximately 1 in 100,000 individuals each year.

G&H What are the causes of achalasia?

GB We do not definitively know what causes this disease. It is currently believed, but has not yet been proven, that neurons are destroyed by the immune system (T cells) as part of an aberrant immune response to a viral infection.

G&H What are the most common treatment options for achalasia in Europe?

GB The current treatment for achalasia is to dilate or disrupt the sphincter, the physical barrier between the esophagus and the stomach that is causing the problem; this intervention reduces resistance at the transition between the 2 organs. The 2 main treatment modalities currently used in Europe (as well as in the United States) are pneumodilation (in which an endoscopist ruptures

the sphincter by dilating it via a balloon) and Heller myotomy (in which the sphincter is cleaved by a surgeon). The treatment approach is usually determined by the experience of the treating physician, although enthusiasm for the surgical approach has grown enormously since the introduction of laparoscopic surgery.

G&H What are the advantages and disadvantages of these 2 procedures?

GB The main advantage of the surgical approach is that the patient requires only 1 treatment session. Occasionally, the patient can go home the same day the procedure is performed or the following day. The disadvantage of surgery is that the entire sphincter muscle is cleaved and, thus, damaged, causing an increased risk of gastric contents and acid being refluxed into the esophagus. Thus, a Dor antireflux procedure is performed with every Heller myotomy, although the risk of reflux is still high.

The main advantage of pneumodilation is that it can be performed on an ambulatory basis, and the patient can go home as soon as the effects of the anesthetic agent wear off (usually within a few hours). The disadvantage of this procedure is its risk of esophageal perforation (1–3%). In a large European study that my colleagues and I conducted, perforation occurred in 4% of patients. Another disadvantage is that patients usually have to be re-treated several times.

G&H What did you and your colleagues find in your study?

GB We conducted a trial examining the 2 treatment modalities for achalasia in order to confirm or reject the current understanding that laparoscopic Heller myotomy was superior to the endoscopic approach. To our surprise, we found no significant difference between the 2 treatment arms. We examined 217 patients with achalasia in multiple centers in Europe and randomized patients to either surgical or endoscopic treatment. After following patients for at least 2 years, we found

that the percentage of patients who were successfully treated was similar in both treatment arms. (Success was defined as having an Eckardt score lower than 4; this score evaluated patients' severity of dysphagia, weight loss, retrosternal pain, and regurgitation.)

The study also found that the risk of a perforation during pneumodilation was higher when the first dilatation was performed with a 35-mm balloon. If the series of dilatations was started with a 30-mm balloon, a much smaller percentage of perforation (4%) was observed. In addition, predictors of treatment failure were found to include daily chest pain before treatment, impaired emptying of radiologic contrast from the esophagus (measured via a timed barium esophagram), and having an esophagus less than 4 cm wide before treatment. Finally, risk factors for the need to be redilated more often included younger age (<40 years), impaired emptying after treatment, and daily chest pain before treatment.

G&H What have other comparative studies reported regarding these procedures?

GB There have been only 1 or 2 randomized studies comparing Heller myotomy with pneumodilation for the treatment of achalasia. This lack of research is mainly because achalasia is a rare disease, and conducting a well-powered study comparing 2 different treatment modalities requires a large number of subjects. Before initiating our study, my colleagues and I calculated that it would be necessary to enroll at least 200 patients in order to produce results of sufficient statistical power; these conditions would be nearly impossible to meet without conducting a multinational, multicenter study. The very few studies that have been conducted in the past involved much fewer patients than our study. Thus, although the findings of these studies were interesting, the studies did not have sufficient power to produce valuable and statistically sound conclusions. What makes our study unique is its size, randomized and prospective nature, objective criteria, and use of both surgeons and gastroenterologists.

G&H How effective are pneumodilation and Heller myotomy over the long term?

GB Currently available data have shown excellent long-term efficacy for both pneumodilation and surgery. However, success rates for both treatment modalities have been shown to steadily drop over the long term, likely because achalasia is a progressive disease in which the function of the esophagus continuously decreases over time. It should also be emphasized that most outcome studies do not have very long follow-up periods (1–3 years at most). Very few studies have followed patients for longer periods of time, such as 10 years or more. Success rates vary between 40–60% in studies with longer (>10 years) follow-up periods. Although

my colleagues and I reported success rates around 90% for both treatment arms at the end of the study, it is likely that these rates will decrease over prolonged follow-up periods as well; however, it is unclear how far they will fall.

G&H How does a physician usually decide which of these procedures to perform in a patient?

GB Usually, the decision is based mainly on the experience of the treating physician. If a patient visits a gastroenterologist who has experience performing endoscopic dilation, the patient will probably be encouraged to undergo pneumodilation. On the other hand, if the patient visits a surgeon who is experienced at performing Heller myotomy, the patient will probably be encouraged to undergo the surgical approach.

Based on the findings from our study as well as various retrospective studies, including one conducted by Richter, it is important that we work on identifying subclasses of patients in whom each procedure is more effective. For example, surgery should be performed in younger patients, particularly males, as pneumodilation is not as effective in these patients as it is in older patients and females. The decision of which treatment a particular patient should undergo should ideally be based on these types of data, rather than solely on the physician's experience. (Nevertheless, it should be noted that the experience of the treating physician has been shown to be one of the most important criteria of success.)

G&H Are there any safety issues associated with these procedures?

GB The major criteria used to determine whether a patient can undergo surgery is the general condition of the patient, which determines whether he or she can withstand anesthesia. For example, if an elderly patient with a weak heart or pulmonary function is unable to undergo surgery, the patient should be considered for pneumodilation. However, endoscopists should be particularly careful when treating elderly patients with pneumodilation because their risk of developing a perforation during the procedure is higher. In addition, endoscopists should be careful when treating patients with a diverticulum in the lower part of the esophagus (and should consider excluding them). Although there are no studies directly supporting this guideline, it is one of the exclusion criteria for pneumodilation.

G&H Is there a significant learning curve for these procedures?

GB Yes, as with every laparoscopic procedure, there is a significant learning curve. The learning curve for the laparoscopic Heller myotomy is approximately 30 procedures. An exact learning curve has not yet been established for pneumo-

dilation, but this procedure requires practice, particularly for positioning the balloon. As mentioned earlier, the experience of the treating physician is an important factor for determining success, as well as for developing complications.

G&H Do treatment approaches for achalasia differ between Europe and the United States?

GB From discussions that I have had with Richter, there appears to be a tendency to perform myotomy more frequently in the United States than in Europe; in Europe, we are still performing many more pneumodilations than in the United States. Also according to these discussions, the techniques used by surgeons and endoscopists are similar in Europe and in the United States; the only exception may be that endoscopists in the United States tend to start pneumodilation with a 35-mm balloon more frequently than endoscopists in Europe. This is probably based on habit and experience.

Interestingly, one of the findings from our study was that the risk of perforation was significantly higher when we started with a 35-mm balloon dilation; therefore, we decided to amend our study protocol to start the series of pneumodilations using a 30-mm balloon and gradually increase the diameter of the balloon, rather than start with a larger balloon, as is currently done in the United States.

G&H Are any medical therapies used in Europe for treating achalasia?

GB Botox (Allergan) injections are sometimes used, but enthusiasm for this approach is declining; Botox is now usually reserved for elderly patients who cannot undergo surgery or who want to avoid the risk of perforation. The disadvantage of injecting Botox into the esophagus, particularly the lower esophageal sphincter, is its short-lasting effect; the mean duration of success is only approximately 6 months. Moreover, Botox makes dissection of the muscle layer more difficult for the surgeon.

Other medical treatments used for achalasia are smooth muscle relaxant agents (such as calcium antagonists) or nitro derivatives. However, these agents are not very effective, and they have significant side effects, such as headaches and decreases in blood pressure.

G&H In Europe, what is standard follow-up care for achalasia?

GB There is no consensus on follow-up care; however, based on the chronic and progressive nature of achalasia, I think that it is very important that patients be monitored on a

yearly basis. One reason for yearly monitoring is that patients often underreport their symptoms. If patients are advised to return to a physician only if their symptoms return, not on a yearly basis, it is likely that patients will not return until they have almost end-stage disease. End-stage disease should be prevented because undigested food remains in the esophagus for a prolonged period of time in longstanding disease, leading to an increased risk of developing dysplasia and carcinoma. It is important to monitor these patients on a yearly basis to check whether the esophagus is emptying properly; if this is not the case, re-treatment is necessary.

G&H Are any new treatment modalities currently being developed for achalasia?

GB A promising new treatment modality for achalasia is peroral endoscopic myotomy. This technique, which is performed via an endoscope and a submucosal tunnel, is in the early stages of development in Japan, but it is slowly moving to Europe and the United States. Longer follow-up data are needed to confirm whether this approach is a new alternative to Heller myotomy and pneumodilation.

G&H What are the next steps for research?

GB It is very important to identify better criteria for re-treatment, so that patients can avoid developing carcinoma. Also, we should better define when treatment is successful and how to identify patients at risk for developing dysplasia and/or carcinoma.

Another area of important research is to obtain more insight into the causes of achalasia. Our current treatment approaches reduce the discomfort of patients, but they do not actually solve the problem; instead of cleaving or disrupting the muscle, we should aim for restoring its function. We need more insight into how the neurons lost in achalasia can be replaced. Some investigators are currently working on this issue; stem-cell transplantation may play a role.

Suggested Reading

Boeckxstaens GE, Annesse V, des Varannes SB, et al. European Achalasia Trial Investigators. Pneumatic dilation versus laparoscopic Heller's myotomy for idiopathic achalasia. *N Engl J Med*. 2011;364:1807-1816.

Richter JE, Boeckxstaens GE. Management of achalasia: surgery or pneumatic dilation. *Gut*. 2011;60:869-876.

Inoue H, Minami H, Kobayashi Y, et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia. *Endoscopy*. 2010;42:265-271.

Kostic S, Kjellin A, Ruth M, et al. Pneumatic dilatation or laparoscopic cardiomyotomy in the management of newly diagnosed idiopathic achalasia. Results of a randomized controlled trial. *World J Surg*. 2007;31:470-478.

Suárez J, Mearin F, Boque R, et al. Laparoscopic myotomy vs endoscopic dilation in the treatment of achalasia. *Surg Endosc*. 2002;16:75-77.