Overview of the treatment of achalasia

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Literature review current through: **Sep 2023.**
This topic last updated: **Sep 05, 2023.**

INTRODUCTION

Achalasia is thought to result from progressive degeneration of ganglion cells in the myenteric plexus in the esophageal wall leading to failure of relaxation of the lower esophageal sphincter (LES) accompanied by a loss of peristalsis in the distal esophagus.

This topic will review the management of achalasia. Our recommendations are based on society guidelines and data suggesting that achalasia treatment is best rendered in a phenotype-specific manner [1-4]. The pathophysiology, etiology, clinical manifestations, and diagnosis of achalasia, as well as a more detailed discussion of pneumatic dilation, botulinum toxin injection, and surgical management of achalasia, are presented separately. (See "Achalasia: Pathogenesis, clinical manifestations, and diagnosis" and "Pneumatic dilation and botulinum toxin injection for achalasia" and "Surgical myotomy for achalasia" and "Peroral endoscopic myotomy (POEM)".)

TREATMENT APPROACH

Treatment of achalasia is aimed primarily at decreasing the resting pressure in the lower esophageal sphincter (LES) to a level at which the sphincter no longer impedes the passage of ingested material (image 1) [5,6]. This can be accomplished by mechanical disruption of the muscle fibers of the LES (eg, pneumatic dilation, surgical myotomy, or peroral endoscopic myotomy [POEM]) or by pharmacologic reduction in LES pressure (eg, injection of botulinum toxin or use of oral nitrates). For any of the invasive therapies, results are best for patients with type II achalasia. Unfortunately, no treatment can reverse the degeneration of ganglion cells, restore the lost esophageal neurons, and hence, normalize esophageal function. Consequently, available treatments do not normalize swallowing; they merely improve it. Moreover, the efficacy of all these treatments tends to decrease with time. Consequently, patients will require long-term follow-up and will frequently need repeated or alternative treatments [7].

Choice of treatment — For patients who have average surgical risk, preferred options for treatment include pneumatic dilation, laparoscopic Heller myotomy with a partial fundoplication, and POEM (algorithm 1). Preoperative evaluation and risk assessment are discussed separately. (See "Evaluation of cardiac risk prior to noncardiac surgery" and "Evaluation of perioperative pulmonary risk".)

POEM has been proposed as the procedure of choice for type III achalasia because POEM can deliver a longer myotomy that is generally not possible with pneumatic dilation or the Heller procedure, and a longer myotomy might be more effective at controlling symptoms caused by the esophageal spasm of type III achalasia [2,8]. Short-term results of POEM for types I and II achalasia are at least as effective (and perhaps even better) compared with pneumatic dilation and surgical myotomy, while data on long-term outcomes of POEM are accumulating [8-10]. The efficacy of POEM for achalasia is presented in more detail separately. (See "Peroral endoscopic myotomy (POEM)", section on 'Outcomes of POEM for achalasia'.)

Pneumatic dilation, laparoscopic Heller myotomy, and POEM all are considered comparable effective therapies for patients with type I or type II achalasia. All of these invasive procedures ideally should be performed in high-volume centers of excellence, and the choice of initial therapy should be guided by the results of high-resolution manometry, patients' age and sex, patients' preference, and local institutional expertise. Patients with the best outcomes after pneumatic dilation are those older than 40 years, female patients, those with narrow esophageal diameter, and those with a type II pattern by high-resolution manometry [11-16] (see "Pneumatic dilation and botulinum toxin injection for achalasia", section on 'Predictors of outcome' and "Achalasia: Pathogenesis, clinical manifestations, and diagnosis", section on 'High-resolution manometry'). For patients treated initially with myotomy (POEM or laparoscopic Heller myotomy) that fails to control symptoms, reasonable treatment options include pneumatic dilation or redo myotomy using either the same or an alternative myotomy technique (POEM or laparoscopic Heller myotomy) [8].

For patients who elect to undergo pneumatic dilation, surgical myotomy or POEM can be performed subsequently if symptoms persist despite several attempts at pneumatic dilation.

(See 'Pneumatic dilation' below and "Pneumatic dilation and botulinum toxin injection for achalasia", section on 'Predictors of outcome' and 'Surgical myotomy' below.)

For patients who are not candidates for surgery, pneumatic dilation or POEM, or who are unwilling to undergo these procedures, we suggest a trial of botulinum toxin injection as this may improve swallowing. (See 'Botulinum toxin injection' below and "Pneumatic dilation and botulinum toxin injection for achalasia", section on 'Botulinum toxin injection'.)

For patients who are unwilling or unable to tolerate surgery, pneumatic dilation, or POEM, and have failed botulinum toxin injections, we suggest pharmacologic therapy with nitrates. (See 'Pharmacologic therapy' below.)

Options

Pneumatic dilation — Forceful dilation with pneumatic balloon dilation of the LES weakens the LES by circumferential stretching or tearing of its muscle fibers [17]. Pneumatic dilation should be performed by an experienced endoscopist. Multiple endoscopies are frequently required for graded pneumatic dilation. Patients undergoing pneumatic dilation must be good surgical candidates because perforations related to pneumatic dilation may require surgical repair. The technique, efficacy, and complications of pneumatic dilation are discussed in detail separately. (See "Pneumatic dilation and botulinum toxin injection for achalasia", section on 'Pneumatic dilation'.)

Pneumatic dilation appears to be the most cost-effective treatment for type II achalasia and has the advantage of being less invasive as compared with surgical myotomy or POEM [18]. Initial success rates are high (85 percent at one month) and sustained in the short term (12 to 24 months), but efficacy wanes over time [11]. Over four to six years, nearly one-third of patients have symptom relapse and require retreatment [12,19-21]. Post-procedure complications include symptomatic esophageal perforation (approximately 2 percent) and heartburn (15 to 35 percent) [11,22]. Subsequent pneumatic dilations are progressively less likely to result in a sustained remission [22,23]. Other forms of therapy should, therefore, be considered for patients who have recurrent or persistent dysphagia after several pneumatic dilations. Patients who have undergone pneumatic dilation also may be at an increased risk of intraoperative complications if they subsequently require surgical myotomy, although this remains controversial [24]. (See "Pneumatic dilation and botulinum toxin injection for achalasia", section on 'Efficacy of PD'.)

Esophageal dilation with a tapered dilator (bougienage) or through-the-scope balloons is highly effective in the treatment of peptic esophageal strictures, but usually provides only temporary and incomplete relief, if any, for patients with achalasia [25]. Definitive dilation therapy requires more forceful stretching of the LES than can be achieved with bougienage or through-the-scope balloons.

Surgical myotomy — Surgical myotomy, in which the LES is weakened by cutting its muscle fibers, has been the primary alternative to pneumatic dilation for achalasia. Heller myotomy is usually performed laparoscopically [22,23,26-30]. Since LES disruption can cause reflux esophagitis, it is frequently combined with an antireflux procedure such as a partial fundoplication (Dor or Toupet fundoplication). Operative management of achalasia is discussed in detail separately. (See "Surgical myotomy for achalasia", section on 'Fundoplication' and "Surgical myotomy for achalasia", section on 'Addition of a fundoplication'.)

- **Overall efficacy and safety –** Initial symptom relief is achieved in 90 percent of patients after surgical myotomy, which is similar to the rate reported in studies looking at medium-term outcomes (12 to more than 36 months) [22]. As with endoscopic procedures, symptom relief wanes with time and patients often require retreatment. In one study that included 62 patients who had undergone surgical myotomy and partial fundoplication at a mean follow-up of 19 months, 38 percent of patients reported some dysphagia [31]. Another large retrospective study included 1461 patients with achalasia, of which 81 percent had pneumatic dilatation and 19 percent had surgical myotomy as their first procedure [32]. The cumulative risk of any subsequent treatment (dilatation, myotomy, or esophagectomy) after 1, 5, and 10 years was 37, 56, and 63 percent after initial pneumatic dilatation and 16, 30, and 37 percent after initial treatment with myotomy.

  The major disadvantages of surgery are the protracted recovery period and associated complications. Complications of laparoscopic myotomy include gastroesophageal reflux disease (GERD), perforation, pneumothorax, bleeding, vagal injury, and infection [33]. However, the risk of GERD is significantly lower if an antireflux procedure is performed (9 versus 32 percent) [22]. Pneumatic dilation has been performed in patients who fail to improve following surgical myotomy [34,35]. (See "Surgical myotomy for achalasia", section on 'Postoperative complications' and "Pneumatic dilation and botulinum toxin injection for achalasia", section on 'Patients who failed myotomy'.)

- **Surgical myotomy versus pneumatic dilation –** Laparoscopic Heller myotomy is superior to a single pneumatic dilation in terms of efficacy and durability. However, the superiority of surgical myotomy over pneumatic dilation is less evident when compared with graded pneumatic dilation, which involves repeated dilations as mandated by the clinical response.

In a retrospective study of 179 patients that compared pneumatic dilation with Heller myotomy, the success of Heller myotomy was comparable with pneumatic dilation after six years of follow-up (57 versus 44 percent) [12]. Success was defined as dysphagia or regurgitation less than three times per week or freedom from alternative treatment.

A meta-analysis that compared graded pneumatic dilation with laparoscopic surgical myotomy included three randomized trials with 346 patients published between 2007 and 2011 [36]. After up to one year of follow-up, surgical myotomy was more effective than pneumatic dilation (86 versus 77 percent) and was associated with fewer adverse events (0.6 versus 5 percent). However, there were no differences in post-procedure LES pressure, rate of gastroesophageal reflux, and quality of life.

The largest trial in the meta-analysis included 201 patients who were assigned to either pneumatic dilation or laparoscopic Heller myotomy [11]. Patients were followed for a mean of 43 months. In an intention-to-treat analysis, there was no significant difference between the groups with regard to therapeutic success. At one-year follow-up, the success rate for pneumatic dilation was 90 percent, and for laparoscopic myotomy it was 93 percent. After two years, the success rates were 86 and 90 percent, respectively. In addition, after two years of follow-up there was no significant difference between the groups with regard to LES pressure, esophageal emptying, quality of life, or esophageal acid exposure. Subgroup analyses found that patients younger than 40 years were at increased risk of requiring redilation after pneumatic dilation. However, a number of factors should be considered when interpreting the results of this trial [37]. First, the protocol for pneumatic dilation used in this trial was rigorous, involving up to three sets of balloon dilations over a period of >2 years, with individual sets including as many as three separate dilation sessions. Each dilation session generally means a day lost from work. By contrast, the inconvenience of Heller myotomy is primarily "up front," involving the operation itself and the postoperative recovery. Furthermore, esophageal perforations occurred in approximately 4 percent of patients treated with this rigorous pneumatic dilation protocol, requiring hospitalization and, in some cases, emergency surgical repair with an open (rather than laparoscopic) procedure. In addition, the balloon dilations and operations in this trial were performed by very experienced gastroenterologists and surgeons. It is not clear that their excellent results can be reproduced in community practices. After five years of follow-up, there was no significant difference in success rates between the two groups [38].

Surgery may be less cost-effective than initial pneumatic dilation [18].

Peroral endoscopic myotomy (POEM) — Peroral endoscopic myotomy (POEM), a form of natural orifice transluminal endoscopic surgery (NOTES), is an endoscopic method for performing myotomy of the LES [39-46]. During POEM, the endoscopist makes an incision in the esophageal mucosa, and the endoscope is passed through that incision into the esophageal submucosa, creating a submucosal tunnel that is extended distally into the gastric cardia. A diathermic scalpel then is passed through the endoscope to sever the muscle of the muscularis propria in and around the LES. In addition, the myotomy can extend well above the LES, which may be an advantage in treating type III achalasia in which spasm in the esophageal body contributes to symptoms. Unlike surgical myotomy, which often is combined with fundoplication to prevent reflux, POEM includes no antireflux procedure. Consequently, POEM can result in severe GERD. Indeed, it has been suggested that patients undergoing POEM should be counseled regarding the increased risk of postprocedure reflux compared with other treatments (pneumatic dilation, laparoscopic Heller myotomy) [8].

The use of POEM is supported by clinical trials and observational data from highly specialized centers [9,10,47,48]. POEM became available after other therapeutic interventions, and long-term data on outcomes are also awaited (see "Peroral endoscopic myotomy (POEM)", section on 'Outcomes of POEM for achalasia'):

- **POEM versus pneumatic dilation –** In an unblinded, randomized trial that was conducted at six centers with expertise in achalasia management and included 133 adults with newly diagnosed achalasia, POEM resulted in higher rates of treatment success (defined as an Eckardt score ≤3 and absence of severe complications at two years) compared with pneumatic dilation with a 30 or 35 mm balloon (92 versus 53 percent) [10]. No serious adverse events were reported in the POEM group, whereas two serious adverse events occurred with pneumatic dilation (one patient with perforation and one patient with chest pain resulting in hospitalization). However, rates of reflux esophagitis were higher in the POEM group (41 versus 7 percent). The study was limited by the following: unblinded design, use of a 30 or 35 mm balloon (rather than a 40 mm balloon that is often used in clinical practice), and lack of significant differences in physiologic markers of treatment success between groups [49]. Nevertheless, it does appear that POEM performs better than pneumatic dilation for symptom improvement but with a greater risk for erosive esophagitis.

- **POEM versus laparoscopic Heller myotomy –** Relief of dysphagia is similar for patients with POEM and laparoscopic Heller myotomy with fundoplication, whereas the risk of erosive esophagitis is greater after POEM. In a randomized trial including 221 adults with achalasia, rates of clinical success (defined as an Eckardt score ≤3 without use of additional treatments at two years) were not significantly different for patients who underwent POEM compared with laparoscopic Heller myotomy with Dor fundoplication (83 versus 82 percent) [9]. Compared with laparoscopic Heller myotomy, POEM was associated with a lower rate of severe adverse events (2.7 versus 7.3 percent) but with a higher rate of reflux esophagitis (44 versus 29 percent) at two years. Limitations of the trial included lack of blinding and low participation rate among eligible patients.

- **Other studies –** An earlier meta-analysis of mostly observational studies concluded that POEM was more likely to be successful than laparoscopic Heller myotomy for both type I and type III achalasia, and that pneumatic dilation had a lower, but still acceptable, treatment success rate than either POEM or laparoscopic Heller myotomy [50].

Favorable outcomes for POEM have been reported in patients with achalasia conditions that often do not respond well to conventional therapies, such as "end stage" achalasia (markedly dilated, sigmoid esophagus), and in patients who have failed prior endoscopic and surgical achalasia treatments [2,51,52].

Botulinum toxin injection — Botulinum toxin therapy can be considered in patients who are not good candidates for more definitive therapy with pneumatic dilation, surgical myotomy, or POEM, and this approach is consistent with guidelines from the American Society for Gastrointestinal Endoscopy (ASGE) [8]. Botulinum toxin injected into the LES poisons the excitatory (acetylcholine-releasing) neurons that increase LES smooth muscle tone. The net effect is a decrease in basal LES pressure in patients with achalasia, which allows emptying of the esophagus when esophageal pressures exceed that of the partially paralyzed LES.

Botulinum toxin injection has the advantage of being less invasive as compared with surgery and can be easily performed during routine endoscopy. Initial success rates with botulinum toxin are comparable to pneumatic dilation and surgical myotomy [22]. However, patients treated with botulinum toxin have more frequent relapses and a shorter time to relapse [53]. Greater than 50 percent of patients with achalasia treated with botulinum toxin require retreatment within 6 to 12 months. Repeated botulinum toxin injections may also make a subsequent Heller myotomy more challenging [54]. The technique of botulinum toxin injection to treat achalasia, efficacy, and complications are discussed in detail separately. (See "Pneumatic dilation and botulinum toxin injection for achalasia", section on 'Comparative studies' and "Pneumatic dilation and botulinum toxin injection for achalasia", section on 'Botulinum toxin injection'.)

Pharmacologic therapy — Medical therapy is the least effective treatment option in patients with achalasia, but should be considered in patients who are unwilling or unable to tolerate invasive therapy for achalasia and for patients who have failed botulinum toxin injections.

Because nitrates are short-acting, sublingual isosorbide dinitrate (5 mg) (where available) is administered 10 to 15 minutes before meals. Sublingual nitroglycerin 0.4 mg is an alternative if sublingual isosorbide dinitrate is unavailable and nitrate therapy is indicated [55].

Nitrates relax the smooth muscle of the LES both in normal individuals and in patients with achalasia. Treatment with sublingual nitroglycerin may result in short-term symptomatic improvement; however, the benefit is not durable [56]. In addition, side effects such as headache and flushing are common, and contraindications to nitrate use are discussed separately [57,58]. (See "Nitrates in the management of chronic coronary syndrome", section on 'Adverse effects'.)

Although 5-phosphodiesterase inhibitors (eg, sildenafil), anticholinergics (eg, atropine, dicyclomine, cimetropium bromide), beta adrenergic agonists (eg, terbutaline), and theophylline have been used to treat achalasia, there are very limited data to support their use.

While studies have described variable efficacy rates for treatment with calcium channel blockers for achalasia [57,59], we avoid the use of short-acting nifedipine because of the risk of adverse effects including severe hypotension and ischemic complications that are discussed in more detail separately. (See "Management of severe asymptomatic hypertension (hypertensive urgencies) in adults", section on 'When the pressure should be lowered over a period of hours'.)

SURVEILLANCE

The risk of esophageal cancer is increased in patients with achalasia, but the absolute risk is low. We therefore do not perform endoscopic surveillance in patients with achalasia. Our recommendations are consistent with the American Society for Gastrointestinal Endoscopy (ASGE) and the American College of Gastroenterology (ACG) [3,60]. (See "Achalasia: Pathogenesis, clinical manifestations, and diagnosis", section on 'Cancer risk'.)

Although some experts have suggested endoscopic or radiographic surveillance in patients with achalasia to predict or detect disease progression, studies are needed to determine whether surveillance improves outcomes [61].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Achalasia".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Achalasia (The Basics)")
- Beyond the Basics topics (see "Patient education: Achalasia (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Background –** Achalasia is thought to result from progressive degeneration of ganglion cells in the myenteric plexus in the esophageal wall. The symptoms and signs of achalasia are due primarily to failure of relaxation of the lower esophageal sphincter (LES), although spasm in the body of the esophagus can also contribute to symptoms, especially in type III achalasia. (See 'Introduction' above.)

- **Approach to treatment –** Treatment options include mechanical disruption of the muscle fibers of the LES (eg, pneumatic dilation, laparoscopic Heller myotomy, or peroral endoscopic myotomy [POEM]) or biochemical reduction in LES pressure (eg, injection of botulinum toxin, use of oral nitrates) (algorithm 1). (See 'Treatment approach' above.)

  Pneumatic balloon dilation, POEM, and surgical myotomy have comparable success rates for the treatment of type I and type II achalasia. POEM appears to be preferable for type

III achalasia. However, the efficacy of all achalasia treatments decrease over time, and many patients will require repeat treatment within 10 years.

Although botulinum toxin has high initial success rates that are comparable to pneumatic dilation and surgery, patients treated with botulinum toxin have more frequent relapses and a shorter time to relapse. Botulinum toxin injection is reserved for patients who cannot undergo more durable therapy. Medical therapy with nitrates is often ineffective and is limited by side effects. (See 'Pneumatic dilation' above and 'Surgical myotomy' above and 'Botulinum toxin injection' above and 'Pharmacologic therapy' above.)

- **Patients who are surgical candidates –** For patients with achalasia who are good surgical candidates, we suggest treatment with pneumatic dilation, surgical myotomy, or POEM rather than botulinum toxin injection (**Grade 2C**). (See 'Choice of treatment' above.)

  Since pneumatic dilation, laparoscopic Heller myotomy, and POEM are comparable effective therapies for type I or type II achalasia, the choice among these procedures should be based on local expertise. In settings where there is equal expertise in these procedures, we have a detailed discussion with the patient on the risks and benefits of the procedures and encourage shared decision-making. Surgical myotomy may be preferable in patients younger than 40 years of age due to an increased need for redilation in this age group. However, other experts, including other authors for UpToDate, disagree and would perform surgical myotomy as initial therapy for the majority of healthy patients. If local expertise in both procedures is lacking, we would refer patients to an esophageal center of excellence. (See "Pneumatic dilation and botulinum toxin injection for achalasia", section on 'Predictors of outcome' and "Surgical myotomy for achalasia", section on 'Surgical myotomy'.)

  POEM is an effective submucosal endoscopic technique for performing myotomy of the LES and more proximal esophageal muscle. In addition, good results for POEM have been reported in patients with achalasia conditions that often do not respond well to conventional therapies, such as type III (spastic) achalasia and "end-stage" achalasia (markedly dilated, sigmoid esophagus), and in patients who have failed prior endoscopic and surgical achalasia treatments. The role of POEM in the treatment of achalasia continues to evolve, although there is a consensus that POEM is the procedure of choice for the treatment of type III achalasia. It has been suggested that patients undergoing POEM should be counseled regarding the increased risk of post-procedure reflux compared with other treatments. (See 'Peroral endoscopic myotomy (POEM)' above.)

- **Patients who are not surgical candidates –** For patients who are at high risk for complications of invasive procedures (such as older adults with comorbid illnesses), we suggest injection of botulinum toxin into the LES rather than pharmacologic therapy (**Grade 2C**). Pharmacologic therapy (eg, nitrates) can be considered in patients who cannot tolerate upper endoscopy with sedation or who do not respond to treatment with botulinum toxin. (See 'Botulinum toxin injection' above and 'Pharmacologic therapy' above and "Pneumatic dilation and botulinum toxin injection for achalasia".)

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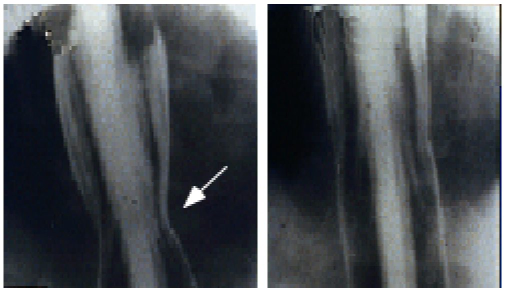
GRAPHICS

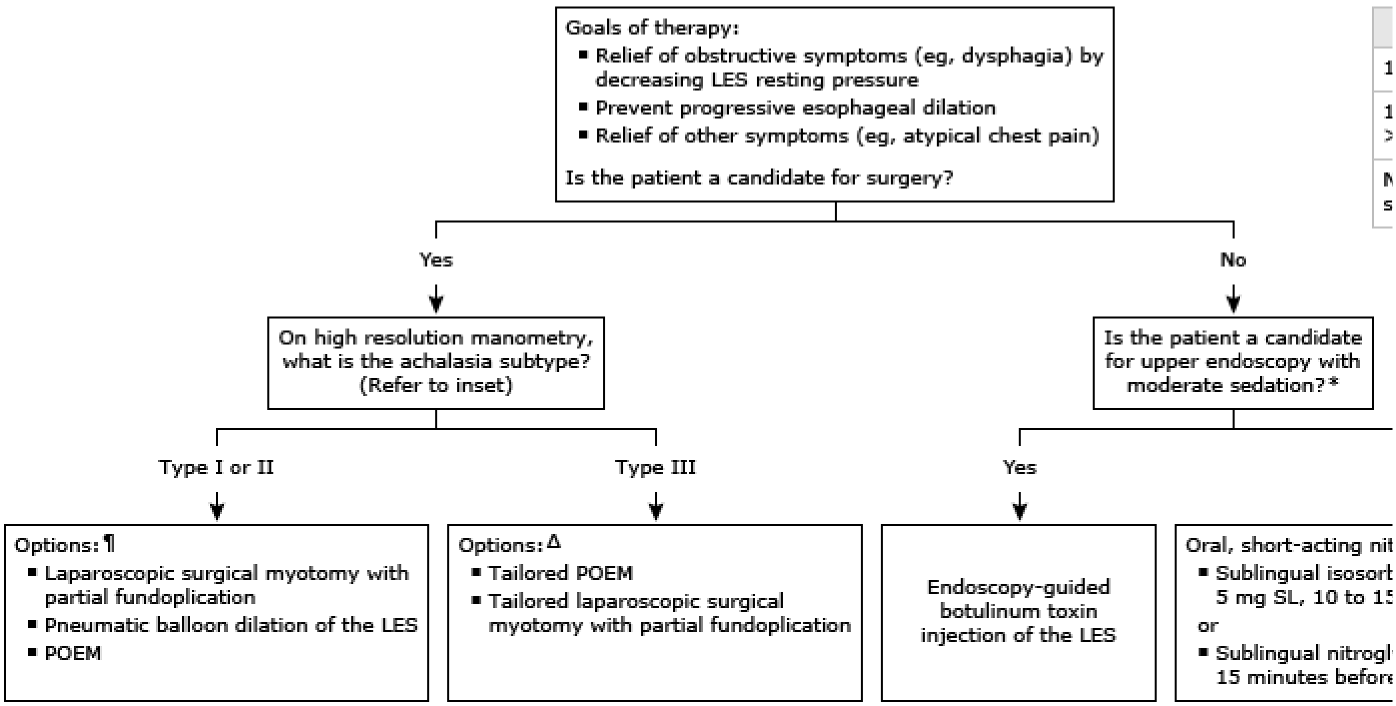
Efficacy of pneumatic dilation for achalasia



Barium radiographs showing the result of pneumatic dilation of the lower esophageal sphincter in a patient with achalasia. Left panel: The balloon is positioned in the lower esophageal sphincter with an hourglass "waist" effect (arrow) caused by the hypertensive sphincter. Right panel: The waist disappears as the dilation progresses.

Graphic 70627 Version 3.0

Approach to initial management of adults with achalasia



Options for therapy include mechanical disruption of the LES (eg, myotomy or pneumatic dilation) or pharm botulinum toxin injection or oral nitrate). Mechanical disruption of the LES has been associated with more d choice of intervention is informed by patient characteristics, patient preferences, institutional expertise, anc management of achalasia for additional details.

PEP: panesophageal pressurization; LES: lower esophageal sphincter; ASA: American Society of Anesthesiolc disease; POEM: peroral endoscopic myotomy; SL: sublingual.

* The preprocedure evaluation includes a medical history, anesthesia-directed physical examination, and as: UpToDate content on anesthesia for gastrointestinal endoscopy for details.

¶ Higher rates of GERD are reported after POEM than either laparoscopic myotomy or pneumatic dilation. T patients and for those who do not want long-term therapy with a proton pump inhibitor.

Δ The length of the myotomy can be tailored to the length of the spastic esophageal segment as demonstra resolution manometry, functional lumen imaging probe).

Graphic 139061 Version 3.0

Contributor Disclosures

Stuart J Spechler, MD Consultant/Advisory Boards: Castle Biosciences [Barrett's esophagus]; Interpace Diagnostics [Barrett's esophagus]; Ironwood Pharmaceuticals [GERD]; ISOThrive, LLC [GERD]; Phathom Pharmaceuticals [GERD]; Takeda Pharmaceuticals [GERD]. All of the relevant financial relationships listed have been mitigated. **Nicholas J Talley, MD, PhD** Patent Holder: Australian Provisional Patent [Diagnostic marker for functional gastrointestinal disorders]; Biomarkers of irritable bowel syndrome [Irritable bowel syndrome]; Mayo Clinic [Dysphagia questionnaire]; Mayo Clinic [Bowel Disease questionnaire]; Nepean Dyspepsia Index [Dyspepsia]; Nestec [Irritable bowel syndrome]; Singapore Provisional Patent [BDNF Tissue Repair Pathway]. Grant/Research/Clinical Trial Support: Alimetry [Gastric mapping device research collaboration]; Allakos [Gastric eosinophilic disease]; AstraZeneca [Eosinophilic gastritis, eosinophilic gastroenteritis]; Intrinsic Medicine [Bowel syndrome with constipation]; NHMRC Centre for Research Excellence in Digestive Health [NHMRC Investigator grant]. Consultant/Advisory Boards: Adelphi Values [Functional dyspepsia]; Allakos [Gastric eosinophilic disease, AK002]; AstraZeneca [Eosinophilic gastritis, eosinophilic gastroenteritis]; AusEE [Eosinophilic gut diseases]; Bayer [Inflammatory bowel syndrome]; BluMaiden [Microbiome Ad Board]; Comvita Mānuka Honey [Digestive health]; Dr Falk Pharma [Eosinophilia]; GlaxoSmithKline Australia [Educational speaker eosinophilic gut disease]; Glutagen [Celiac disease]; International Foundation for Functional Gastrointestinal Disorders [Advisory board, functional GI disorders]; Intrinsic Medicine [Human milk oligosaccharide]; IsoThrive [Esophageal microbiome]; Planet Innovation [Gas capsule, inflammatory bowel syndrome]; Progenity Inc [Intestinal capsule]; Rose Pharma [IBS]; Viscera Labs [Inflammatory bowel syndrome, diarrhea]. Other Financial Interest: Elsevier textbook royalties [Medical education]. All of the relevant financial relationships listed have been mitigated. **Kristen M Robson, MD, MBA, FACG** No relevant financial relationship(s) with ineligible companies to disclose.

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Conflict of interest policy

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