Achalasia

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Achalasia is an uncommon but important disease that is the best understood and most readily treatable esophageal motility disorder. It serves as a prototype for disorders of the enteric nervous system and is characterized by degeneration of the myenteric neurons that innervate the lower esophageal sphincter (LES) and esophageal body. Over the past decade, investigations into the pathogenesis have highlighted the importance of nitric oxide and the possible role of an autoimmune response to a viral insult in genetically susceptible individuals. Advances in diagnostic testing have delineated manometric variants of achalasia that have implications for management. Treatment studies have demonstrated the limited efficacy of botulinum toxin as well as less than ideal, long-term effectiveness of pneumatic dilation and Heller myotomy. This article incorporates these recent developments into the current understanding of achalasia.

CLINICAL FEATURES

Achalasia can be diagnosed at any age but most commonly presents in patients between the ages of 25 and 60 years. An increasing incidence with age has been observed with an equal male-to-female gender distribution. It has an estimated prevalence in the United States of 10 cases per 100,000 with an incidence of 0.6 cases per 100,000 per year. Dysphagia to solids and liquids is the most common presenting symptom, experienced by greater than 90% of patients. A small subgroup of patients deny the presence of dysphagia despite having radiographic and manometric features consistent with achalasia. This situation may be due to several factors, including impaired visceral sensation, the absence of primary and secondary peristalsis in response to retained esophageal contents, and the adaptation to chronic esophageal obstruction and dilation. Regurgitation is the second most common symptom, occurring in approximately 60% of patients and usually in the postprandial period. Nocturnal regurgitation of esophageal contents can lead to nighttime cough and aspiration. Difficulty belching is reported in a large proportion of patients, most likely reflecting the inability of the upper and lower esophageal sphincters to relax in response to esophageal and gastric distension, respectively. The absent belch reflex is an important...
factor responsible for rare cases of upper airway obstruction secondary to a massively dilated esophagus that extrinsically compresses the posterior aspect of the trachea. Weight loss occurs in end-stage disease and usually does not exceed 5 to 10 kg before patients seek medical attention.

Chest pain is reported in 20% to 60% of patients. It is more common in younger patients and often diminishes over the course of the disease. Proposed etiologies include secondary or tertiary esophageal contractions, esophageal distension by retained food, gastroesophageal reflux, neuropathic pain related to the enteric neuropathy, and esophageal irritation by retained food and bacteria. The presence of pain cannot be predicted from radiographic or manometric findings. Improvement in pain does not necessarily accompany improvement in dysphagia after either pneumatic dilation or Heller myotomy. This discrepancy likely reflects the varied mechanisms responsible for chest pain. Pain due to esophageal distension, stasis esophagitis, or secondary peristalsis should improve following reduction of LES pressure, whereas neuropathic pain or pain associated with spastic contractions will persist.

Heartburn is reported in a large number of patients with achalasia, which is surprising given that achalasia is mechanistically the antithesis of gastroesophageal reflux disease. One study reported this symptom in 30% of achalasia patients. Although heartburn disappeared at the onset of dysphagia in one third of the patients, the remaining two thirds reported persistent heartburn at the time of their presentation with achalasia. The etiology of heartburn in patients with impaired LES relaxation may be related to direct irritation of the esophageal lining by retained food, pills, or acidic byproducts of bacterial metabolism of retained food. Poor esophageal clearance of even small amounts of refluxed gastric acid may also be an important factor. Abnormal amounts of acid reflux have been detected in as many as 20% of untreated achalasia patients by 24-hour ambulatory pH monitoring. Gastroesophageal reflux is, of course, a recognized sequela of successful treatment of achalasia.

**DIAGNOSIS**

Upper endoscopy is often the first diagnostic test in a patient with dysphagia or suspected achalasia (Fig. 1). Findings can include a dilated esophagus with retained food or secretions; however, endoscopy appears normal in as many as 44% of patients with achalasia. Difficulty traversing the esophagogastric junction should raise suspicion for pseudoachalasia due to neoplastic infiltration of the distal esophagus or gastric cardia. A barium esophagram can be highly suggestive of the diagnosis of achalasia, particularly when there is the combination of esophageal dilatation with

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**Fig. 1.** Endoscopic findings in idiopathic achalasia. The esophageal lumen is markedly distended with retained food and saliva. Following evacuation, the underlying esophageal mucosa shows changes of stasis esophagitis that include nodularity and patchy erosions.
retained food and barium and a smooth tapered constriction of the gastroesophageal junction. Nevertheless, in the series mentioned previously, the diagnosis of achalasia was suggested in only 64% of barium examinations.  

Esophageal manometry has the highest sensitivity for the diagnosis of achalasia, with the defining characteristics of aperistalsis of the distal esophageal body and incomplete or absent LES relaxation. Supportive features include a hypertensive LES and low amplitude esophageal body contractions. Because variations of typical manometric findings exist, additional features and methodology have been used to reinforce the diagnosis. An increase in the intraesophageal basal pressure that exceeds the intra-abdominal or intragastric pressure is a significant finding in achalasia, as are “common cavity” phenomena that represent bolus entrapment within the tubular esophagus.

High resolution esophageal manometry (HRM) combined with contour plots topographic analysis is a recent enhancement to conventional manometry that improves the accuracy of esophageal manometry. HRM allows for automated analysis of more detailed quantitative data. An example of the utility of this methodology is the interpretation of impaired LES deglutitive relaxation in the setting of exaggerated respiratory contractions of the crural diaphragm. Intrabolus pressure elevations are more readily apparent and quantified using HRM. A recent retrospective study subclassified 99 achalasia patients into those with classic achalasia with minimal esophageal pressurization, those with achalasia with esophageal compression pan esophageal pressurization in excess of 30 mm Hg, and those with achalasia with spasm. Examples of these three patterns are illustrated in Fig. 2. Pan esophageal pressurization was a positive predictor of treatment response, whereas esophageal spasm was a negative predictor.

Characteristics of achalasia using multichannel intraluminal impedance have also been described. The main feature identified as characteristic of achalasia was a low baseline impedance thought to be secondary to chronic fluid retention. Although this finding has been confirmed in subsequent studies, the low baseline impedance and air trapping in the proximal esophagus may prevent this modality from being able to accurately assess esophageal emptying. Further investigation is required before multichannel intraluminal impedance is integrated into the routine diagnostic evaluation for achalasia.

Manometric variants of achalasia exist. The best known is vigorous achalasia, defined by the presence of normal to high amplitude esophageal body contractions in the presence of a nonrelaxing LES. The distinction between esophageal pressurization, also referred to as common cavity phenomena, and esophageal spastic contractions may be an important one as suggested in a recent HRM study (Fig. 2B, C). In some cases, vigorous achalasia may represent an early stage of achalasia in which myenteric ganglion cells remain intact. Vigorous achalasia is indistinguishable from classic achalasia with respect to the age of onset, gender, and the duration of dysphagia before presentation. Botulinum toxin has been reported to be more effective in patients with vigorous achalasia. Additional manometric variants of achalasia include patients with intact peristalsis through the majority of the esophageal body and others with preservation of either deglutitive or transient LES relaxation. These manometric variants, although appearing to challenge the typical manometric criteria for achalasia, can still be consistent with the diagnosis. Esophageal functional testing with HRM or impedance should improve the recognition of achalasia that presents with atypical manometric features.

Secondary forms of achalasia are important considerations during the diagnostic evaluation (Box 1).
These entities are all less common than the diagnosis of idiopathic achalasia, with the exception of Chagas' disease in endemic areas of Central and South America. Chagas' disease is a parasitic infection caused by *Trypanosoma cruzi*. The esophagus is the most common area of the gastrointestinal tract involved, and the disease manifests as secondary achalasia in 7% to 10% of chronically infected individuals.15 Chagas' disease should be a consideration in the evaluation of achalasia patients in the United States given that the gastrointestinal sequelae can manifest years or decades following the acute infection and in view of the large number of immigrants from Central and South America.

**Fig. 2.** Contour plot topographic analysis of esophageal motility in achalasia. Topographic analysis is a method of axial data interpolation derived from computerized plotting of data from multiple, closely spaced, solid state recording transducers. The interpolated pressure information is plotted as a two-dimensional contour plot in which pressure amplitude is coded by color. (A) Plot depicts achalasia with complete esophageal aperistalsis and absent pressure activity within the esophageal body. The LES is hypertensive and demonstrates incomplete deglutitive relaxation. (B) Plot illustrates achalasia with pan esophageal pressurization or common cavity phenomena in response to a water swallow. Failed deglutitive relaxation of the LES is evident. An esophagogastric pressure gradient is seen in the esophagus before the swallow. (C) Plot depicts achalasia with spastic contractile activity in the distal esophageal body with long duration contractions that exceed 300 mm Hg.
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<th>Box 1 Secondary forms of achalasia</th>
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Mexico and South America. The most concerning secondary etiology is cancer, which can present as achalasia through mechanical obstruction of the gastroesophageal junction, infiltration of the submucosa and muscularis of the LES, or paraneoplastic syndrome associated with small cell lung carcinoma with production of type I antineuronal nuclear autoantibodies, also known as anti-Hu antibodies. Progressive symptoms for less than 6 months in patients older than 60 years with associated weight loss and difficult passage of the endoscope across the esophagogastric junction increase the likelihood of a patient having cancer-associated achalasia.

Additional secondary forms of achalasia exist. Esophageal manometry cannot reliably distinguish primary from secondary forms of achalasia. Additional evaluation, such as a CT scan, esophageal biopsy, and endoscopic ultrasonography, may be necessary to confirm the diagnosis. An increasingly recognized etiology is post fundoplication achalasia caused by mechanical obstruction of the gastroesophageal junction by the fundoplication or diaphragmatic crural closure. Similar cases have been described following bariatric surgery using a gastric band device which constricts the proximal stomach a few centimeters below the LES. It is important to distinguish this complication from the inadvertent surgery in a patient with achalasia whose symptoms were mistaken for “refractory gastroesophageal reflux disease.” A preceding history of dysphagia and preoperative manometry can generally differentiate postoperative achalasia from primary achalasia. Eosinophilic esophagitis can produce secondary achalasia that may respond to medical or dietary therapy, thereby obviating the need for invasive therapeutic procedures.

**PATHOPHYSIOLOGY**

In addition to pathologic demonstration of the diminution of neurons within the myenteric plexus in achalasia (Fig. 3), physiologic studies have shown an imbalance between excitatory and inhibitory elements of the enteric nervous system. Intact cholinergic, excitatory neural function was demonstrated in a controlled study of achalasia patients by administering cholinergic and anticholinergic agents.16 This paradigm provides the rationale for the use of botulinum toxin, a potent anticholinergic agent. Many studies have also confirmed the finding of abnormal or absent inhibitory myenteric innervation.17,18 These data support the concept that the loss of inhibitory neurons is the primary insult responsible for the failed LES relaxation and loss of deglutitive inhibition that characterizes achalasia.

Although the etiology of primary achalasia remains unknown, several hypotheses have been proposed. Several studies have implicated viral agents. A study using DNA hybridization techniques found evidence of varicella-zoster virus in three of nine myotomy specimens from patients with achalasia.19 The herpesvirus family was specifically targeted in this study given its neurotropic nature. The predilection of the herpesvirus for squamous epithelium as opposed to columnar epithelium makes this an attractive hypothesis. Such tissue selectivity could explain why achalasia involves only the esophagus while sparing the remainder of the gastrointestinal tract. More recent studies using polymerase chain reaction techniques failed to detect the presence of measles, herpes, or human papilloma viruses in myotomy specimens of 13 patients with achalasia. This negative study does not exclude the possibility of either an alternate viral species or past viral infection with clearance of the inciting pathogen from the host tissue. Supporting the viral hypothesis is a recent study demonstrating immunoreactivity of lymphocytes from the LES of patients with achalasia in response to HSV-1 antigens.20 In this study, analysis of oligoclonal expansion
of T cells provided evidence for immune activation by a viral pathogen that could result in autoimmune destruction of enteric neurons.

An autoimmune etiology of achalasia is supported by the presence of circulating autoantibodies against the myenteric plexus. Circulating antibodies against the myenteric plexus have been shown in a few studies to be more prevalent in achalasia patients than in controls; however, the most recent study detected significantly higher immunostaining of esophageal myenteric plexus neurons using serum from patients with achalasia and those with gastroesophageal reflux disease in a comparison with controls, suggesting that the antineuronal antibodies represent an epiphenomenon rather than causative factor.21 The presence of a lymphocytic inflammatory infiltrate in the myenteric plexus not found in controls is also supportive of an autoimmune etiology.22 Two studies have characterized the infiltrative cells as CD3 and CD8+ T cells.20,23

An association between achalasia and class II MHC genes has been described. A significant association was demonstrated in a prospective case-control study with more than 80% of the case population having class II HLA DQw1,24 attributing a 3.6

Fig. 3. Histopathology of achalasia. (A) Normal myenteric plexus demonstrating multiple ganglion cells and minimal lymphocytic infiltration. (B) Mild myenteric inflammation. There is mild lymphocytic inflammation, and ganglion cells can be identified. (C) Moderate myenteric inflammation with lymphocytic infiltrate is present. Ganglion cells are absent. (D) Severe myenteric inflammation with lymphocytes densely clustered within this myenteric plexus. Ganglion cells are absent.75 (From Hirano I, Kahrilas PJ. Esophageal disorders. In: Spiller T, Grundy D, editors. Pathophysiology of the enteric nervous system. Blackwell Publishing; 2004. p. 107; with permission.)
and 4.2 relative risk of developing achalasia in the Caucasian and black population, respectively. These results have been confirmed in subsequent studies. Furthermore, achalasia patients with the HLA allele were found to have circulating antimyenteric antibodies.25

TREATMENT

The primary therapeutic goal in achalasia is to reduce the LES basal pressure. Treatment options include medical therapy, botulinum toxin injection, pneumatic dilation, and surgical myotomy. Symptom relief, particularly relief of dysphagia, is accepted as the primary desired outcome because an ideal physiologic marker of disease severity is lacking; however, symptom scores are not well validated, and symptomatic improvement has limited correlation with improvement in objective measures of esophageal emptying.26 This observation is clinically relevant because persistent inadequate esophageal emptying after treatment despite improvement in symptoms may predict future symptom relapse and an increased risk for complications such as progressive esophageal dilation and aspiration.

Objective measures of esophageal function include measurements of LES pressure and esophageal emptying by barium radiographs, nuclear scintigraphy, and possibly esophageal impedance. An LES pressure of less than 10 mm Hg has been shown to be a significant predictor of long-term response to pneumatic dilation.27 Additional factors such as the integrity of the residual esophageal body contractile function and the sigmoid deformity of the esophagus may affect esophageal clearance even with adequate reduction of LES pressure. A more recent study used a timed barium esophagram as an objective assessment of esophageal emptying.28 The technique involved the ingestion of a fixed aliquot of barium with serial radiographs obtained at 1, 2, and 5 minutes following ingestion with comparisons made in the height and surface area of the barium column (Fig. 4). The surface area of the barium column at 5 minutes had the most significant correlation with LES pressure before and 1 month after treatment. The symptom score had no correlation with the objective findings 1 month after dilation. Multiple prospective studies using botulinum toxin have made similar observations.29,30 These studies highlight important concerns regarding the use of symptoms as the only measure of success of achalasia treatment.

Medical Therapy

Medical therapy for achalasia is inconvenient, only modestly effective, and frequently associated with side effects; consequently, it is reserved for patients who are awaiting or unable to tolerate more invasive treatment modalities. Pharmacologic therapies attempt to decrease the LES pressure by causing smooth muscle relaxation and should be administered by a sublingual rather than oral route. Nitrates were first recognized as an effective treatment of achalasia as early as 1940; unfortunately, their systemic vasodilatory effects and headaches limit their tolerability by patients.31 Calcium channel antagonists have a better side-effect profile when compared with nitrates, with nifedipine being the most widely studied in the literature. The efficacy of calcium channel antagonists varies from 50% to 90% in clinical trials, but as many as 30% of patients report adverse side effects including peripheral edema, hypotension, and headache. An investigation of sildenafil, a phosphodiesterase type 5 inhibitor, demonstrated a significant decrease in LES pressure when compared with placebo.32 The mechanism of action is similar to nitrates, with cGMP-mediated relaxation of smooth muscle. The desired effect of sildenafil was short-lived, and no long-term outcome studies have been performed to date. Side effects and cost are important limitations to the use of sildenafil in therapy for achalasia.
Botulinum Toxin

Botulinum toxin injected into the LES targets the excitatory, acetylcholine-releasing neurons that generate LES basal muscle tone. Botulinum toxin was introduced as a therapy for achalasia in 1995 in a randomized, placebo-controlled trial demonstrating symptomatic improvement in 82% of patients after botulinum toxin injection compared with 10% of those who received placebo. This trial was followed by a prospective, long-term, follow-up study, with two thirds of patients showing a symptom response at a mean follow-up of 2.4 years.

Botulinum toxin is easy to administer and associated with relatively few side effects or complications. A total of 80 to 100 U of the toxin is injected in divided doses into the four quadrants of the LES. A large multicenter study from Italy of 118 patients reported...

Fig. 4. Timed barium swallow. Following the ingestion of a fixed volume of barium, sequential radiographs are taken at 1, 2, and 5 minutes. The top three panels demonstrate lack of emptying with a column of barium persisting in a dilated esophagus at 5 minutes. The bottom three panels demonstrate the same patient after Heller myotomy. An improvement in emptying and degree of esophageal dilatation is shown.
that a dose of 100 U followed 1 month later by a second 100 U injection in responders was more efficacious than either 50 or 200 U administered in a single dose.\textsuperscript{33} At a mean follow-up of 12 months, relapse was seen in 19% of patients treated with the double injections of 100 U compared with 47% and 43% of the patients receiving 50 and 200 U doses, respectively. The effect of intermittent versus scheduled dosing of botulinum toxin on clinical efficacy has not been studied.

To date, over 15 prospective studies involving more than 450 patients from around the world have examined the efficacy of botulinum toxin. Response rates at 1 month following administration average 78% (range, 63% to 90%). By 6 months, the clinical response rate drops to 58% (range, 25% to 78%) and by 12 months to 49% (range, 15% to 64%). It is apparent that, with repeated injections, the response rates reported are similar or lower to that achieved with the initial injection. The diminishing effect may be due to the development of protective antibodies against the botulinum toxin molecule that have been demonstrated in approximately 5% of patients treated with botulinum toxin for skeletal muscle disorders. Use of a different serotype of botulinum toxin may be a way of prolonging response rates, although this approach remains to be proven. Predictors of response to botulinum toxin include age greater than 50 years and the presence of vigorous achalasia defined by the finding of esophageal contractile waves with amplitudes in excess of 40 mm Hg.\textsuperscript{13} The duration of illness, baseline radiographic features, initial symptom severity, and gender have not been shown to be predictive of response.

Objective measures of response to botulinum toxin therapy, such as reduction of LES pressure and improvement in esophageal emptying by barium swallow or radionuclide emptying scans, have demonstrated statistically significant but clinically modest results when compared with pneumatic dilation or surgical myotomy. In the literature, the residual LES pressure post botulinum toxin has averaged approximately 20 mm Hg. This finding is clinically relevant, because posttreatment LES pressure less than 10 mm Hg has been shown to be an important predictor of successful response and the need for future therapy. Given the limitations of the efficacy and durability of response, botulinum toxin is generally reserved for use in patients who are not candidates for more invasive treatments with pneumatic dilation or Heller myotomy.

Recent reports have also raised concerns about the technical difficulty of esophagomyotomy when followed by botulinum toxin injection. An increased risk of intraoperative esophageal perforation has been noted, perhaps secondary to obliteration of tissue planes from an inflammatory reaction created by the biologic agent.\textsuperscript{34,35} On the other hand, a recent study that prospectively followed 305 patients with achalasia after laparoscopic Heller myotomy for 25 months demonstrated that preoperative endoscopic therapy did not affect the difficulty of the surgical procedure or the reported symptomatic outcome.\textsuperscript{36}

Botulinum toxin injection for achalasia has an excellent safety profile. Transient chest pain is usually mild and has been reported in approximately 20% of patients. Significant heartburn is reported in approximately 5% to 10% of patients. Isolated case reports of potential adverse events have included heart block, urinary retention, and pneumothorax. Concerns regarding the potential for systemic neuromuscular paralysis have not been realized in gastrointestinal or neurologic applications because the doses used in practice are 20- to 30-fold lower than lethal doses reported in primate studies.

**Pneumatic Dilation**

With a long track record, pneumatic dilation remains one of the most effective first-line therapies for achalasia. Currently, the Rigiflex pneumatic dilator (Boston Scientific,
Boston, Massachusetts) is the most widely used system for achalasia, but similar devices are available from other manufacturers (Cook Medical, Bloomington, Indiana; Hobbs Medical, Stafford Springs, Connecticut). The polyethylene balloon comes in three sizes that inflate to fixed diameters of 3, 3.5, or 4 cm. This system offers a safety advantage over earlier compliant latex balloons that delivered variable diameters depending on inflation pressure.

A stepwise approach using the Rigiflex system starting with a 3.0 cm balloon and increasing to a 3.5 and then 4.0 cm balloon for patients with no response yielded an overall 93 response rate to dilation over a mean follow-up period of 4 years and has become an accepted methodology of treatment. Over 20 retrospective and prospective studies have reported the effectiveness of pneumatic dilation for achalasia using the Rigiflex balloon dilator. The overall response rates defined by good-to-excellent relief of symptoms average 85% (range, 70% to 92%), with a mean follow-up period of 20 months.

Long-term follow-up studies using older balloon dilators and now the Rigiflex balloon have reported significant symptom relapse of 50% at 10 years; however, a more recent investigation demonstrated that pneumatic dilation may remain an effective treatment if administered in an on-demand fashion. A total of 150 patients were treated with pneumatic dilation until remission was achieved, which occurred in 90% of the patients. Patients were then dilated only if their symptoms returned, and the probability of the patients achieving remission at 5 and 10 years was 97% and 93%, respectively.

Studies examining clinical and technical factors have identified age, balloon diameter, post dilation lower esophageal sphincter pressure, clearance of barium on an esophagram, and prior dilation as predictors of success following pneumatic dilation. Similar to the botulinum toxin experience, several studies have reported that older patients respond better than younger patients. Post dilation LES pressure of less than 10 mm Hg was associated with a 100% 2-year remission rate compared with 71% for pressures between 10 and 20 mm Hg and 23% for pressures over 20 mm Hg. The degree of barium emptying has not been found to be a predictor of symptomatic response; however, patients with no improvement in esophageal emptying of barium had a 90% failure rate at 1 year as defined by the return of symptoms and need for retreatment. Esophageal pressurization, also known as common cavity, was a positive predictor, whereas spastic esophageal body contractions was a negative predictor of treatment response in a recent HRM retrospective analysis.

Complications of pneumatic dilation exist, the most significant of which is esophageal perforation. Published series using the Rigiflex dilator and including more than 10 patients have reported perforation rates of 0% to 8% with a mean rate of 2.6%. The graded approach to pneumatic dilation starting with the smaller diameter dilators has been associated with a lower perforation risk. Although epiphrenic diverticula, hiatal hernias, the presence of esophagitis, prior esophagomyotomy, or vigorous achalasia are often thought to increase the risk for perforation, there are limited data to support or refute these concerns. It also does not appear that patients undergoing emergent esophagomyotomy in the setting of an esophageal perforation after dilation have poorer outcomes than those undergoing elective esophagomyotomy. A laparoscopic Heller myotomy is not an option in patients who have had a perforation from pneumatic dilation. Transmural perforations resulting from pneumatic dilation occur proximal to the LES and necessitate a thoracic approach. Additional reported complications following pneumatic dilation include transient chest pain, gastrointestinal bleeding, esophageal hematoma formation, and symptomatic esophageal mucosal tears. The latter is usually managed conservatively with inpatient observation and
intravenous antibiotics. Gastroesophageal reflux can complicate pneumatic dilation. Prospective studies using pH monitoring have detected significant acid reflux in 25% to 35% of patients following dilation. Most of the patients with significant gastroesophageal reflux did not report heartburn; therefore, empiric proton pump inhibitor therapy should be considered.

**Surgical Therapy**

Surgical treatment of achalasia has undergone substantial changes over the past century since the original myotomy was described by Heller in 1913. Open thoracotomy was later replaced by laparotomy and now the laparoscopic approach used widely today. This technique has success rates in excess of 90% with hospital stays averaging only a few days. Although complications of esophageal perforation and bleeding occur, they are generally recognized and managed at the time of surgery.

An area of ongoing controversy in the surgical management of achalasia has been the need for an accompanying antireflux procedure. Reflux is a known sequela of endoscopic and surgical therapies of achalasia. Complications of Barrett’s esophagus and peptic stricture have been documented in several reported series following Heller myotomy. Surgical approaches to the problem have included creation of a loose Nissen, partial posterior Toupet, or partial anterior Dor fundoplication. The use of a Nissen fundoplication is avoided because it adds too much resistance in the setting of esophageal aperistalsis. Controversy exists over the superiority of the Toupet or Dor procedure. The Toupet is a posterior fundoplication attached to either edge myotomy that leaves the cut surface of the LES exposed, whereas the Dor is positioned over the myotomy. Angulation of the gastroesophageal junction is a concern when using the Toupet approach. The Dor approach, on the other hand, may incite fibrosis of the myotomy site that bridges the edges of the myotomy and restores integrity to the LES. A retrospective nonrandomized study suggested that the standard myotomy (1.5 cm over the cardia) with a Dor fundoplication was less effective than an extended myotomy (extending 3 cm onto the cardia) with a Toupet fundoplication. In this series of 115 patients with postoperative follow-up of 45 months, 17% of the patients treated with a standard myotomy and Dor fundoplication required endoscopic or surgical reintervention for recurrent dysphagia, whereas 5% of the patients treated with extended myotomy and Toupet fundoplication required endoscopic intervention. It is unclear from this study whether the benefit that was seen was the result of the extended myotomy, the type of fundoplication, or the time of enrollment because the investigators changed surgical procedures midway through the study period.

Despite the addition of an antireflux procedure, esophageal acid exposure is a known complication of surgical intervention for achalasia. A recent investigation prospectively looked at the incidence of esophageal acid exposure following Heller myotomy and Dor fundoplication in 76 patients for 5 years after operation. Twenty-one percent of patients experienced pathologic acid exposure following surgery. Seventy-three percent of those episodes were characterized by a gradual rather than abrupt drop in esophageal pH, suggesting food stagnation rather than true reflux was responsible.

Dysphagia following Heller myotomy can be subclassified into dysphagia that persists following myotomy and dysphagia that redevelops following surgery. Early postoperative dysphagia can be caused by incomplete myotomy, periesophageal inflammation, underlying esophageal dysmotility, esophageal enlargement with sigmoid deformity, or mechanical obstruction by a fundoplication, paraesophageal herna, or crural diaphragmatic hiatus repair. Despite the use of intraoperative endoscopy and
manometry in an attempt to decrease the rate of incomplete myotomy, this approach has not become the standard of care.\textsuperscript{50,55–57} Even with a successful myotomy, it is expected that patients will have some degree of dysphagia as a consequence of esophageal peristaltic dysfunction. Although return of esophageal peristalsis has been reported following Heller myotomy, it is unclear whether this represents a true recovery of neuromuscular function of the esophageal body or a technical inability of manometric catheters to record esophageal contractile activity preoperatively in the setting of esophageal dilation.\textsuperscript{58}

Delayed recurrence of postoperative dysphagia is most commonly caused by development of a recurrent high pressure zone at the LES or a peptic stricture complicating acid reflux. Less commonly, an obstructed or slipped fundoplication, progressive megaesophagus with sigmoid deformity, or esophageal cancer can manifest. In cases of postoperative dysphagia due to an incomplete myotomy or a recurrent high pressure zone, pneumatic dilation can be employed as an alternative to redo surgery. Concerns over the risks of perforation after a myotomy exist; however, published series have reported success and safety with pneumatic dilation.\textsuperscript{44,59}

Previous studies have suggested that the remission rates for open Heller myotomy deteriorate over time.\textsuperscript{60,61} In one study, 95% success rates at 1 year fell to 77% at 5 years, 68% at 10 years, and 67% at 20 years.\textsuperscript{60} Short-term data with laparoscopic Heller myotomy demonstrated excellent results, with 98% of patients reporting symptomatic improvement at 5.3 years.\textsuperscript{62} Although intermediate-term data for laparoscopic Heller myotomy noted satisfaction with surgery and improvement in dysphagia, 35% of patients reported either moderate or severe dysphagia at 10 years.\textsuperscript{63}

\textbf{Surgery Versus Pneumatic Dilation}

Several retrospective and prospective studies have reported superior success rates for surgery when compared with pneumatic dilation. A recent retrospective longitudinal study using an administrative database in Ontario, Canada, compared the outcomes of 1181 patients treated with pneumatic dilation with that of 280 patients treated with Heller myotomy as initial therapy.\textsuperscript{64} Although the risk of subsequent therapeutic intervention at 10 years was significantly higher with dilation (64%) when compared with surgery (38%), this outcome is expected and was attributed to repeated dilations that did not lead to a significantly higher risk of surgical intervention in the dilation group. On the other hand, the 38% risk of therapeutic intervention after surgery stresses the importance of follow-up after any therapy in achalasia. In a recent prospective study, 51 patients were randomly assigned to undergo repeated endoscopic dilation or laparoscopic Heller myotomy with a posterior fundoplication.\textsuperscript{65} At 1 year follow-up, the pneumatic dilation group demonstrated significantly more treatment failures than the surgical group.

Studies comparing the cost-effectiveness of pneumatic dilation and Heller myotomy have favored dilation in the past; however, the laparoscopic surgical approach has decreased the length of hospitalization as well as additional surgical costs.\textsuperscript{66} This fact, in combination with long-term pneumatic dilation data suggesting a less than 40% remission rate, will likely shift the cost analysis in favor of laparoscopic Heller myotomy.

The selection of pneumatic dilation or surgery as primary therapy is still debated. Although surgery is more effective at achieving a durable response, recurrent dysphagia occurs in a significant proportion of surgical patients. The laparoscopic surgical technique has reduced the morbidity and hospital stay but exposes patients to risks of gastroesophageal reflux disease as well as concerns related to operative disruption of the normal anatomy of the esophagogastric junction and diaphragmatic hiatus. On
the other hand, pneumatic dilation commonly requires repeated dilations to sustain remission. Response rates in younger patients are substantially lower, whereas even small risks of esophageal perforation may be prohibitive in older patients with comorbidities. The benefits of the minimally invasive surgical approach are not available to patients who have perforations from pneumatic dilation which require a traditional thoracotomy. Currently, the choice of therapy remains an individualized decision that weighs factors including available expertise, the patient’s acceptance of possible risks, and factors such as age and comorbidities.

**Refractory Achalasia**

In patients with achalasia that is refractory to therapy with Heller myotomy, options are limited. Patients with esophageal spasm in addition to LES dysfunction may require medical or surgical therapy directed at the esophageal body as well as LES. Although esophagectomy is considered in patients with marked dilation and sigmoid deformity, such patients may respond to Heller myotomy. Esophagectomy is usually performed with a gastric pull-up via a transthoracic or transhiatal approach. Success rates from larger centers approximate 90%, but significant morbidity includes respiratory complications, anastomotic strictures and leaks, dumping syndrome, regurgitation, and bleeding, and a 2% to 8% mortality rate has been reported. Other treatments for refractory achalasia that have been reported include endoscopic esophageal stent and gastrostomy tube placement. Stenting should generally be avoided owing to a high stent migration rate. Gastrostomy placement is a consideration in patients at unusually high risk for pneumatic dilation or surgery and short survival due to comorbidities. Although providing nutrition and access for medications, gastrostomy tube placement does not address the symptoms and aspiration risks of salivary retention.

**COMPLICATIONS**

The primary complications of achalasia are related to the functional obstruction rendered by the nonrelaxing LES and include progressive malnutrition and aspiration. Aspiration pneumonia can be a substantial cause of morbidity, with patients at risk for postprandial and nocturnal aspiration. Uncommon but important secondary complications of achalasia include the formation of epiphrenic diverticula and esophageal cancer. Epiphrenic diverticula are most commonly detected in the distal esophagus immediately proximal to the LES and pose potential therapeutic technical challenges and perforation risks.

There is an established link between achalasia and esophageal cancer, most commonly squamous cell carcinoma (Fig. 5), with a 16-fold increased risk during years 1 to 24 after initial diagnosis. The overall prevalence of esophageal cancer in achalasia is approximately 3% with an incidence of approximately 197 cases per 100,000 persons per year. A retrospective cohort study evaluated the risk of esophageal adenocarcinoma resulting from the treatment of achalasia. Almost 3000 patients were followed for an average of 10 years, with 22 cases of esophageal cancer identified (6 adenocarcinomas and 14 squamous cell carcinomas). These cases represented a greater than tenfold increased risk of esophageal cancer, equally significant for both squamous cell carcinoma and adenocarcinoma. Furthermore, there was no difference between the patients who underwent esophagomyotomy and those who did not in the development of cancer. Any treatment for achalasia that reduces LES pressure places patients at increased risk for esophageal acid exposure and development of Barrett’s esophagus. Chronic inflammation related to bacterial fermentation of retained food and liquid may be an additive factor. Because the overall risk of
esophageal cancer in patients with achalasia is low, surveillance of patients with achalasia is not generally recommended but is sometimes considered in patients with long-standing disease who would be candidates for esophagectomy.\textsuperscript{72}

REFERENCES

64. Lopushinsky SR, Urbach DR. Pneumatic dilatation and surgical myotomy for achalasia. JAMA 2006;296:2227–33.
