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Treatments for achalasia in 2017: how to choose among them

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Abstract

Purpose—To review recent advances in achalasia diagnostics and therapeutics.

Recent findings—The cardinal feature of achalasia, impaired lower esophageal sphincter relaxation, can occur in association with varied patterns of esophageal contractility. The Chicago Classification distinguishes among these as follows: without contractility (type I), with pan-esophageal pressurization (type II), with premature (spastic) distal esophageal contractions (type III), or even with preserved peristalsis (esophagogastric junction outlet obstruction). Physiological testing also reveals achalasia-like syndromes that also benefit from achalasia therapies. Coincident with this has been the development of per-oral endoscopic myotomy (POEM), an endoscopic technique for performing an esophageal myotomy. Hence, the option now exists to either selectively ablate the lower esophageal sphincter (pneumatic dilation, laparoscopic Heller myotomy, or POEM) or to ablate the sphincter and create a myotomy along some or the entire adjacent smooth muscle esophagus (POEM). Each achalasia syndrome has unique treatment considerations; type II achalasia responds well to all therapies while type III responds best to POEM.

Summary—Emerging data support the concept that optimal management of achalasia is phenotype-specific, guided by HRM and, in some instance, functional luminal imaging probe studies. This opinion paper reviews the varied characteristic and treatment considerations of achalasia syndromes as currently understood.

Keywords

achalasia; esophageal motility disorders; high-resolution manometry; per-oral endoscopic myotomy; functional luminal imaging probe

Introduction

High-resolution manometry (HRM) [1,2] and the development of the Chicago Classification [3] have substantially revised the classification of esophageal motility disorders (EMD). Nowhere is this more evident than in our concept of achalasia, now differentiated into three subtypes and a fourth entity, esophagogastric junction (EGJ) outflow obstruction. These four entities are distinguished not by differences in EGJ function, but by the associated

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contractility pattern of the distal esophagus, which ranges from absent contractility to intact peristalsis. Hence, to keep pace with this evolution, achalasia treatment options need to be evaluated in the context of this disease spectrum.

Coincident with the widespread adoption of the Chicago Classification into clinical practice came a major therapeutic advance in the management of EMD, per-oral endoscopic myotomy (POEM) [4]. The POEM procedure allows for performing a myotomy of the lower esophageal sphincter (LES) through a mucosotomy in the proximal esophagus rather than through laparoscopy, thereby reducing the morbidity of the procedure. Furthermore, the POEM procedure allows for creation of an extended myotomy, potentially encompassing the entire smooth muscle esophagus. Together, the developments of HRM and POEM have fostered an increasing emphasis on targeting therapy to specific regions of esophageal dysfunction as assessed by physiologic testing. This opinion paper examines the relative merits of achalasia treatments in this new landscape.

Achalasia Syndromes Within and Beyond the Chicago Classification

The Chicago Classification is an analysis scheme for HRM studies comprised of ten 5-ml swallows performed in a supine or reclined position. The three fundamental metrics utilized in the Chicago Classification are the integrated relaxation pressure (IRP), the distal contractile integral (DCI), and the distal latency (DL). Using an algorithmic approach, these measurements are applied to identify esophageal motility disorders.

The adequacy of deglutitive LES relaxation, key to the recognition of achalasia, is measured by the IRP, defined as the mean pressure during the 4 seconds of maximal deglutitive relaxation in the 10-second window beginning at UES relaxation. The IRP is expressed as a median value of the ten test swallows with 15 mmHg being the upper limit of normal. However, as with any metric, an IRP >15 mmHg is neither 100% sensitive nor 100% specific for clinically relevant EGJ outflow obstruction. When initially applied to a series of 400 patients and 73 controls, including 62 patients with achalasia, an IRP value >15 mmHg was found to be 98% sensitive and 96% specific for detecting achalasia [5,6].

The metrics employed to characterize the deglutitive contraction in the distal esophagus are the DCI and the DL. The DCI integrates the length, vigor, and persistence of the distal esophageal contraction spanning from the transition zone to the EGJ, expressed as mmHg•s•cm [7]. The DCI is used to define hypercontractile swallows (DCI> 8,000 mmHg•s•cm), weak swallows (DCI<450 mmHg•s•cm) and failed peristalsis (DCI<100 mmHg•s•cm). The other major abnormality of peristalsis is of premature contractions, defined by the DL. Premature contractions imply inhibitory neuronal dysfunction in the distal esophagus and are the defining characteristic of distal esophageal spasm (DES) and type III achalasia [8]. The DL is measured from upper sphincter relaxation to the contractile deceleration point, the inflection point in the wave front velocity just proximal to the EGJ [9, 10]. A DL value of <4.5 seconds defines a premature contraction.

Achalasia subtypes

A diagnosis of achalasia stipulates both impaired deglutitive EGJ relaxation and absent peristalsis [11]. However, absent peristalsis is not synonymous with absent pressurization or contractility. In fact, both esophageal pressurization and non-peristaltic contractility are quite common in achalasia. A seminal observation with HRM was that absent peristalsis accompanying impaired EGJ relaxation (achalasia) can occur with three different patterns of esophageal contractility: 1) type I, with negligible pressurization within the esophagus; 2) type II, with panesophageal pressurization wherein non lumen-occluding contractions cause uniform pressurization spanning from the upper sphincter to the LES; or 3) type III, with premature (spastic) contractions [12]. In multiple reported HRM series from major centers around the world, type II achalasia is the most common subtype.

Achalasia syndromes other than type I, II, and III achalasia

There is no biomarker of achalasia and, although we recognize that the underlying pathology is of a myenteric plexopathy [13], the diagnosis is not established by neuropathology. Rather, achalasia is usually diagnosed using HRM to demonstrate that dysphagia, regurgitation, and/or chest pain is occurring as a result absent peristalsis and esophageal outflow obstruction that cannot be attributed to a stricture, tumor, vascular structure, implanted device, or infiltrating process [11]. Consequently, there are two fundamental limitations of the Chicago classification with respect to diagnosing achalasia: 1) the IRP can be less than 15 mmHg in achalasia; and 2) there can be instances with preserved peristalsis. Furthermore, the disease evolves over a variable timespan and when there is a gradual transition from normal function to absent peristalsis and EGJ outflow obstruction there will be intermediate time points in the natural history of achalasia when these abnormalities may not achieve the requisite diagnostic thresholds.

The stipulation that the IRP must be >15 mmHg in order to have achalasia is not always true, particularly in type I disease. This is partly because, in the absence of esophageal pressurization, especially with advanced disease, some achalasics have a very low LES pressure. In fact, Lin et al proposed reducing the IRP cutoff for defining type I achalasia to 10 mmHg based on a classification and regression tree (CART) model showing that value to better discriminate between type I achalasia and the diagnosis of absent contractility [14]. However, not even that suffices as evident in a recent publication reporting achalasics with extremely low IRP values (3 mmHg, 5 mmHg) in who impaired sphincter function was demonstrable using functional luminal imaging probe (FLIP) technology and stasis on the barium esophagram [15]. In the end, the fact is that no metric or technology has perfect sensitivity and specificity for defining relevant sphincter dysfunction and one has to weigh the entire dataset. There are instances in which measurement of the distensibility index with FLIP using a threshold of 2.8 mm^2/mmHg is diagnostic [16], instances in which minimal bolus flow time on a high-resolution impedance manometry study is diagnostic [17, 18], instances when a timed barium esophagram is most demonstrative, instances in which a rapid drink challenge will elicit esophageal pressurization [19, 20], and, of course, many instances in which an IRP >15 mmHg on HRM will suffice.

Fragments of peristalsis are often seen in follow-up HRM studies after achalasia is treated by relieving the EGJ outflow obstruction with myotomy. Roman et al reported that more than half of 30 achalasia patients studied before and after myotomy exhibited instances or either intact peristaltic contractions or remnants of distal peristalsis in their post-treatment HRM study [21]. This likely occurs both because of variability in the pattern and intensity of distal esophageal myenteric plexus degeneration among patients and because weak peristalsis is undetectable by HRM in the setting of esophageal outflow obstruction. Hence, it is more accurate to think of post-treatment peristalsis as being ‘unmasked’ as opposed to ‘recovered’. Reappearance of peristalsis after myotomy supports the concept of progressive stages in achalasia pathogenesis. Such progression was also suggested in a recent study showing greater ganglion cell loss in type I achalasia compared to type II achalasia, supporting the notion that type II is an earlier stage of the disease [22]. Within this construct, recovery of peristalsis after myotomy might indicate an inflamed, but surviving, distal esophageal myenteric plexus, whereas lack of recovery might indicate progression to aganglionosis. Along the same line, FLIP detected non-occluding or occluding contractions in all of 10 type III achalasia patients, in two-thirds of the 26 type II achalasia patients tested, and in one-third of the 15 type I achalasia patients tested [23].

In addition to the three subtypes of achalasia, the Chicago Classification recognizes EGJ outflow obstruction as another potential achalasia phenotype. With this entity, the IRP is >15 mmHg, but there is sufficient evidence of peristalsis such that the ‘absent peristalsis’ criterion for achalasia is not met. Even with its initial description, EGJ outflow obstruction was recognized to be a heterogeneous group, with only some such patients benefitting from achalasia treatments [24]. Consequently, EGJ outflow obstruction always requires more intense clinical evaluation (e.g. endoscopic ultrasound, FLIP, computerized tomography, etc) to clarify its etiology. The spectrum of potential etiologies include incompletely expressed or early achalasia, esophageal wall stiffness from an infiltrative disease or cancer, eosinophilic esophagitis, vascular obstruction, sliding or paraesophageal hiatal hernia, abdominal obesity, or the effects of opiates [25]. Similar manometric findings can also be observed in patients with dysphagia after anti-reflux or bariatric surgery [26, 27, 28], sometimes making it very difficult to establish cause and effect. The natural history and heterogeneity of EGJ outflow obstruction was studied in two recent series reporting that many of these patients were minimally symptomatic or asymptomatic, that in 20–40% of cases the ‘disorder’ resolved spontaneously, and that only 12–40% of them end up being treated as achalasia [29, 30]. Table 1 summarizes the spectrum and characteristics of potential achalasia syndromes.

Phenotype-Directed Treatment

No current treatment halts or reverses the immunologically driven plexopathy ultimately driving the progression of idiopathic achalasia [13]. Rather, treatments aim to alleviate the hallmark abnormality of the disease, esophageal outflow obstruction. Relieving outflow obstruction reduces strain on the distal esophagus and halts the progressive esophageal dilatation that drives the long-term morbidity of the disease. However, while all achalasia phenotypes share the common element of EGJ outflow obstruction, the associated pattern of esophageal contractility varies from absent contractility at one extreme to spastic contractions at the other and one of the original observations with the description of

achalasia phenotypes was that treatment success varied with phenotype [12]. Treatment outcomes were best in type II achalasia and likely worst in type III achalasia. Subsequent reports of patients treated either by myotomy, pneumatic dilation, or in a randomized controlled trial comparing pneumatic dilation to myotomy have confirmed these observations, especially with respect to excellent treatment outcomes in type II achalasia patients which ranged from 90 to 100% [31–33]. Going forward, it is time to compare therapies within disease subtypes, be that type I–III achalasia or the achalasia syndromes detailed in Table 1. Each entity has unique treatment considerations and each likely has a unique optimal management strategy [34]. Beyond deglutitive sphincter dysfunction, relevant features to consider are the location and extent of obstructive contractility of the distal esophagus, the severity of esophageal dilatation and sigmoid deformation, the presence of hiatus hernia, presence of a significant epiphrenic diverticulum, and for some of the achalasia syndromes, mechanical esophageal outflow obstruction.

Pharmacological treatments for achalasia

Although conceptually appealing, there are minimal supportive data for the use of current drugs to treat achalasia by reducing LES pressure. The most studied drugs are nitrates [35], calcium channel blockers [35], botulinum toxin [36–39], and, more recently, 5′-phosphodiesterase inhibitors [40]. However, these series are of brief duration, uncontrolled, small, and predate the concept of achalasia subtyping. Although smooth muscle relaxants may provide some symptomatic benefit, they are not durable therapies, they are often associated with intolerable side effects, and they do not halt the progression of esophageal dilatation and food retention. In the case of botulinum toxin injection into the LES, about two thirds of achalasia patients report an improvement in dysphagia, but most relapse within a year and repeat treatments have diminished effectiveness. Nonetheless, these treatments can be useful in patients who are not fit for more durable therapies because of severe comorbidity. They can also be useful in situations of uncertainty regarding the diagnosis.

Durable achalasia treatments

Until recently, the only durable treatment options for achalasia were pneumatic dilation (PD) or laparoscopic Heller myotomy (LHM). Pneumatic dilation is done with a 30-, 35-, or 40-mm cylindrical balloon positioned across the LES fluoroscopically and inflated using a handheld manometer. Currently, the most widely used dilator in the USA is the Rigiflex non-compliant polyethylene balloon with radio-opaque markers on the shaft within the balloon (Boston Scientific, Boston). A recent variation on this was the introduction of a 30-mm hydraulic dilator used in conjunction with FLIP technology and not requiring concomitant fluoroscopy (Crospon Galway, Ireland) [41]. The standard surgical alternative to PD is LHM, in which the circular muscle layer of the LES is surgically divided. Most surgeons advocate that the myotomy be anterior and about 7 cm in overall length; 2 cm onto the gastric cardia and 5 cm onto the tubular esophagus. Because of the propensity for that to cause reflux, LHM is usually combined with a partial fundoplication. An extensive literature has compared LHM with PD [42], culminating in a multicenter European randomized controlled trial comparing the two, concluding that both were about 90% effective without a significant difference between them [43, 44]. However, that trial and for that matter, all preceding trials, did not consider achalasia subtypes in their design or in their assessment of

treatment efficacy. Indeed, retrospectively analyzed, the European achalasia trial found the efficacy of PD for treating type II achalasia to be 100% [45]. Considering that the cost of PD is substantially less than LHM and that the risk of perforation between techniques is comparable (about 1% in expert hands) [46], this argues for PD as the preferred initial treatment for type II achalasia.

The widespread adoption of the POEM procedure has been a major advance in achalasia therapeutics. The POEM procedure involves making a mucosal incision in the mid-esophagus and creating a submucosal tunnel to the gastric cardia using a standard endoscope and electrocautery [4]. A circular muscle layer myotomy is then achieved from within the submucosal tunnel, beginning at the gastric cardia and progressing proximally across the LES. Therein lies a unique attribute of POEM; the myotomy can be made longer if desired, potentially involving the entire length of smooth muscle esophagus. This is especially relevant with type III achalasia, noted to have less robust outcomes with therapies limited to the LES. Supportive of that hypothesis, a recent meta-analysis of uncontrolled POEM series reported a weighted pooled response rate of 92% [CI 84–96%] in type III achalasia with the length of myotomy averaging 17.2 cm [47].

If it is advantageous to extend the length of myotomy in some cases, might it not also be advantageous to limit its extent in others? To date, this is an unexplored avenue. However, two problems associated with long-term outcomes of Heller myotomy are post-procedure reflux and the formation of a pseudodiverticulum with associated bolus stasis in the esophageal segment included in the myotomy. Conceptually, both of these problems would be minimized by limiting the extent of the myotomy to the LES in type I and II achalasia, diseases in which there is no associated obstructive physiology in the distal esophagus. Intraoperatively, this could be gauged by HRM, or better, FLIP. Table 2 details the preferred therapeutic interventions for the achalasia syndromes based on physiological considerations, or, in a few cases, supportive data. The suggestions assume that all options are available and affordable, which in reality is rarely the case.

Conclusions

It is now recognized that the cardinal feature of achalasia, impaired LES relaxation, can occur in several disease phenotypes: without peristalsis, with premature (spastic) distal esophageal contractions, with panesophageal pressurization, or with peristalsis. Furthermore, physiological testing with HRM, and sometimes FLIP, reveals a number of syndromes not meeting Chicago Classification criteria for achalasia that also benefit from therapies formerly reserved for achalasia. With HRM and the Chicago Classification we have come to conceptualize achalasia syndromes as involving the LES with or without obstructive physiology of the distal smooth muscle esophagus. This is now particularly relevant with the development of a minimally invasive technique for performing a calibrated myotomy of the esophageal circular muscle, the POEM procedure. Hence, a major implication of this is a shift in management strategy toward rendering treatment in a phenotype-specific manner: e.g. POEM calibrated to patient-specific physiology as defined by HRM for spastic achalasia, PD for disorders limited to abnormal LES function, especially

type II achalasia, and a surgical myotomy limited to the LES for more advanced disease with esophageal dilatation, sigmoid deformation, or significant epiphrenic diverticulum.

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Abbreviations

CDP	contractile deceleration point
DCI	distal contractile integral
DL	distal latency
DES	distal esophageal spasm
EMD	esophageal motility disorders
EGJ	esophagogastric junction
FLIP	functional luminal imaging probe
HRM	high-resolution manometry
IRP	integrated relaxation pressure
LHM	laparoscopic Heller myotomy
LES	lower esophageal sphincter
POEM	per oral endoscopic myotomy
PD	pneumatic dilation
UES	upper esophageal sphincter

References

1. Clouse RE, Staiano A, Alrakawi A, Haroian L. Application of topographical methods to clinical esophageal manometry. Am J Gastroenterol. 2000; 95:2720–30. [PubMed: 11051340]
2. Gyawali CP. High resolution manometry: the Ray Clouse legacy. Neurogastroenterol Motil. 2012 Mar; 24(Suppl 1):2–4. Dr Ray Clouse is widely credited with the development and clinical application of high-resolution manometry. This tribute by one of his mentees chronicles his contributions. [PubMed: 22248101]
3*. Kahrilas PJ, Bredenoord AJ, Fox M, Gyawali CP, Roman S, et al. The Chicago Classification of esophageal motility disorders, v3.0. Neurogastroenterol Motil. 2015 Feb; 27(2):160–74. The Chicago Classification was developed by the Northwestern University esophageal group as an algorithmic, numerical approach to the analysis of high-resolution manometry studies. This subsequently evolved into a consensus process deliberated over by an international group of motility experts. This paper details the most current version of the classification. [PubMed: 25469569]

4. Inoue H, Sato H, Ikeda H, Onimaru M, Sato C, et al. Per-oral endoscopic myotomy: a series of 500 patients. J Am Coll Surg. 2015; 221:256–264. [PubMed: 26206634]
5. Ghosh SK, Pandolfino JE, Rice J, Clarke JO, Kwiatek M, Kahrilas PJ. Impaired deglutitive EGJ relaxation in clinical esophageal manometry: a quantitative analysis of 400 patients and 75 controls. Am J Physiol. 2007; 293:G878–885.
6. Pandolfino JE, Ghosh SK, Zhang Q, Jarosz A, Shah N, Kahrilas PJ. Quantifying EGJ Morphology and Relaxation with High-Resolution Manometry: a study of 75 asymptomatic volunteers. Am J Physiol Gastrointest Liver Physiol. 2006
7. Pandolfino JE, Ghosh SK, Rice J, Clarke JO, Kwiatek MA, Kahrilas PJ. Classifying esophageal motility by pressure topography characteristics: a study of 400 patients and 75 controls. Am J Gastroenterol. 2008; 103:27–37. [PubMed: 17900331]
8. Pandolfino JE, Roman S, Carlson D, Luger D, Bidari K, et al. Distal esophageal spasm in high-resolution esophageal pressure topography: defining clinical phenotypes. Gastroenterology. 2011; 141:469–475. [PubMed: 21679709]
9. Pandolfino JE, Leslie E, Luger D, Mitchell B, Kwiatek MA, Kahrilas PJ. The contractile deceleration point: an important physiologic landmark on oesophageal pressure topography. Neurogastroenterol Motil. 2010; 22:395–400. [PubMed: 20047637]
10. Lin Z, Pandolfino JE, Xiao Y, Carlson D, Bidari K, et al. Localizing the contractile deceleration point (CDP) in patients with abnormal esophageal pressure topography. Neurogastroenterol Motil. 2012; 24:972–975. [PubMed: 22726890]
11. Pandolfino JE, Kahrilas PJ. The second American Gastroenterological Association technical review on the clinical use of esophageal manometry. Gastroenterology. 2005; 128:209–229. [PubMed: 15633138]
12. Pandolfino JE, Kwiatek MA, Nealis T, Bulsiewicz W, Post J, Kahrilas PJ. Achalasia: A New Clinically Relevant Classification by High-Resolution Manometry. Gastroenterology. 2008; 135:1526–1533. This was a landmark HRM paper that first described the subtyping of achalasia by HRM. [PubMed: 18722376]
13. Kahrilas PJ, Boeckxstaens G. The spectrum of achalasia: lessons from studies of pathophysiology and high-resolution manometry. Gastroenterology. 2013; 145(5):954–65. [PubMed: 23973923]
14. Lin Z, Kahrilas PJ, Roman S, Boris L, Carlson D, Pandolfino JE. Refining the criterion for an abnormal Integrated Relaxation Pressure in esophageal pressure topography based on the pattern of esophageal contractility using a classification and regression tree model. Neurogastroenterol Motil. 2012; 24:e356–363. [PubMed: 22716041]
15. Ponds FA, Bredenoord AJ, Kessing BF, Smout AJPM. Esophagogastric junction distensibility identifies achalasia subgroup with manometrically normal esophagogastric junction relaxation. Neurogastroenterol Motil. 2017; 29:e12908. doi:10.111nmo.12908.
16. Pandolfino JE, de Ruigh A, Nicodème F, Xiao Y, Boris L, Kahrilas PJ. Distensibility of the esophagogastric junction assessed with the functional lumen imaging probe (FLIP™) in achalasia patients. Neurogastroenterol Motil. 2013 Jun; 25(6):496–501. [PubMed: 23413801]
17. Lin Z, Imam H, Nicodème F, Carlson D, Lin CY, et al. Flow time through esophagogastric junction derived during high-resolution impedance-manometry studies: a novel parameter for assessing esophageal bolus transit. Am J Physiol. 2014; 307(2):G158–63.
18. Lin Z, Carlson D, Dykstra K, Steinbach J, Hungness E, et al. High-resolution impedance manometry measurement of bolus flow time in achalasia and its correlation with dysphagia. Neurogastroenterol Motil. 2015 Sep; 27(9):1232–1238. [PubMed: 26088614]
19. Fornari F, Bravi I, Penagini R, Tack J, Sifrim D. Multiple rapid swallowing: a complementary test during standard oesophageal manometry. Neurogastroenterol Motil. 2009; 21:718–e741. [PubMed: 19222762]
20. Ang D, Holenstein M, Misselwitz B, Knowles K, Wright J, et al. Rapid drink challenge in high-resolution manometry: an adjunctive test for detection of esophageal motility disorders. Neurogastroenterol Motil. 2017; 29:e12902. doi:10.111nmo.12902.
21. Roman S, Kahrilas PJ, Mion F, Nealis TB, Soper NJ, et al. Partial recovery of peristalsis after myotomy for achalasia; more the rule than the exception. JAMA Surg. 2013; 148:157–164. [PubMed: 23426591]

22. Sodikoff JB, Lo AA, Shetuni BB, Kahrilas PJ, Yang G, Pandolfino JE. Histopathologic patterns among achalasia subtypes. Neurogastroenterol Motil. 2016; 28:139–145. [PubMed: 26542087]

23*. Carlson DA, Lin Z, Kahrilas PJ, Sternbach JS, Eschelbach E, Friesen L, et al. The functional lumen imaging probe detects esophageal contractility not observed with manometry in patients with achalasia. Gastroenterology. 2015; 149:1742–1751. This paper introduces the concept of using the FLIP to diagnose esophageal motility disorders in course of sedated endoscopy. [PubMed: 26278501]

24. Scherer JR, Kwiatek MA, Soper NJ, Pandolfino JE, Kahrilas PJ. Functional esophagogastric junction obstruction with intact peristalsis: a heterogeneous syndrome sometimes akin to achalasia. J Gastrointest Surg. 2009; 13:2219–2225. [PubMed: 19672666]

25. Ratuapli SK, Crowell MD, DiBaise JK, Vela MF, Ramirez FC, et al. Opioid-induced esophageal dysfunction (OIED) in patients on chronic opioids. Am J Gastroenterol. 2015; 110:979–84. Opioids are increasingly recognized as having a major impact on esophageal motility, mimicking spastic achalasia or EGJ outflow obstruction in many cases. This is the best case series to date describing opioid effects in terms of HRM. [PubMed: 26032150]

26. Fox MR, Bredenoord AJ. Oesophageal high-resolution manometry: moving from research into clinical practice. Gut. 2008 Mar; 57(3):405–23. [PubMed: 17895358]

27. Wang YT, Tai LF, Yazaki E, Jafari J, Sweis R, et al. Investigation of Dysphagia After Antireflux Surgery by High-resolution Manometry: Impact of Multiple Water Swallows and a Solid Test Meal on Diagnosis, Management, and Clinical Outcome. Clin Gastroenterol Hepatol. 2015 Sep; 13(9): 1575–83. [PubMed: 25956839]

28. Burton PR, Brown W, Laurie C, Richards M, Afkari S, et al. The effect of laparoscopic adjustable gastric bands on esophageal motility and the gastroesophageal junction: analysis using high-resolution video manometry. Obes Surg. 2009 Jul; 19(7):905–14. [PubMed: 19424766]

29. Van Hoeij FB, Smout AJPM, Bredenoord AJ. Characterization of idiopathic esophagogastric junction outflow obstruction. Neurogastroenterol Motil. 2015; 27:1310–1316. [PubMed: 26095469]

30. Pérez-Fernández MT, Santander C, Marinero A, Burgos-Santamaría D, Chavarría-Herbozo C. Characterization and follow-up of esophagogastric junction outflow obstruction detected by high resolution manometry. Neurogastroenterol Motil. 2016; 28:116–126. [PubMed: 26517978]

31. Eckardt VF, Hoischen T, Bernhard G. Life expectancy, complications, and causes of death in patients with achalasia: results of a 33-year follow-up investigation. Eur J Gastroenterol Hepatol. 2008; 20:956–960. [PubMed: 18787460]

32. Salvador R, Costantini M, Zaninotto G, Morbin T, Rizzetto C, et al. The preoperative manometric pattern predicts the outcome of surgical treatment for esophageal achalasia. J Gastrointest Surg. 2010 Nov; 14(11):1635–45. [PubMed: 20830530]

33. Pratap N, Kalapala R, Darisetty S, Joshi N, Ramchandani M, et al. Achalasia cardia subtyping by high-resolution manometry predicts the therapeutic outcome of pneumatic balloon dilatation. J Neurogastroenterol Motil. 2011 Jan; 17(1):48–53. [PubMed: 21369491]

34. Kahrilas PJ. Treating achalasia; more than just flipping a coin. Gut. 2016; 65(5):726–7. [PubMed: 26743013]

35. Gelfond M, Rozen P, Gilat T. Isosorbide dinitrate and nifedipine treatment of achalasia: a clinical, manometric and radionuclide evaluation. Gastroenterology. 1982; 83(5):963–969. [PubMed: 6288509]

36. Pasricha PJ, Rai R, Ravich WJ, Hendrix TR, Kalloo AN. Botulinum toxin for achalasia: long-term outcome and predictors of response. Gastroenterology. 1996; 110(5):1410–1415. [PubMed: 8613045]

37. Annese V, Bassotti G, Coccia G, Dinelli M, D'Onofrio V, et al. GISMAD Achalasia Study Group. A multicentre randomized study of intrasphincteric botulinum toxin in patients with oesophageal achalasia. Gut. 2000; 46(5):597–600. [PubMed: 10764700]

38. Vaezi MF, Richter JE, Wilcox CM, Schroeder PL, Birgisson S, et al. Botulinum toxin versus pneumatic dilatation in the treatment of achalasia: a randomised trial. Gut. 1999; 44(2):231–239. [PubMed: 9895383]

39. Zaninotto G, Annese V, Costantini M, Del Genio A, Costantino M, et al. Randomized controlled trial of botulinum toxin versus laparoscopic Heller myotomy for esophageal achalasia. Ann Surg. 2004; 239(3):364–370. [PubMed: 15075653]

40. Bortolotti M, Mari C, Lopilato C, Porrazzo G, Miglioli M. Effects of sildenafil on esophageal motility of patients with idiopathic achalasia. Gastroenterology. 2000; 118(2):253–257. [PubMed: 10648452]

41. Kappelle WF, Bogte A, Siersema PD. Hydraulic dilation with a shape-measuring balloon in idiopathic achalasia: a feasibility study. Endoscopy. 2015; 47(11):1028–34. [PubMed: 26349065]

42*. Pandolfino JE, Gawron AJ. Achalasia a systematic review. JAMA. 2015; 313(18):1841–1852. Very current systematic review of the epidemiology, pathogenesis, and management of achalasia. [PubMed: 25965233]

43. Boeckxstaens GE, Annese V, des Varannes SB, Chaussade S, Costantini M, et al. Pneumatic dilation versus laparoscopic Heller's myotomy for idiopathic achalasia. N Engl J Med. 2011; 364:1807–16. [PubMed: 21561346]

44. Moonen A, Annese V, Belmans A, Bredenoord AJ, Bruley des Varannes S, et al. Long-term results of the European achalasia trial: a multicenter randomised controlled trial comparing pneumatic dilation versus laparoscopic Heller myotomy. Gut. 2016; 65:732–9. [PubMed: 26614104]

45. Rohof WO, Salvador R, Annese V, Bruley des Varannes S, Chaussade S, et al. Outcomes of treatment for achalasia depend on manometric subtype. Gastroenterology. 2013; 144(4):718–25. [PubMed: 23277105]

46. Lynch KL, Pandolfino JE, Howden CW, Kahrilas PJ. Major complications of pneumatic dilation and Heller myotomy for achalasia: single center experience and systematic review of the literature. Am J Gastroenterol. 2012; 107:1817–25. [PubMed: 23032978]

47**. Khan AK, Kumbhari V, Ngamruengphong S, Ismail M, Chen YI, et al. Is POEM the answer for management of spastic esophageal disorders? A systematic review and meta-analysis. Dig dis Sci. 2017; 62:35–44. Very interesting paper proposing that POEM is the treatment of choice for all of the spastic motility disorders: type III achalasia, distal esophageal spasm, and jackhammer. [PubMed: 27858325]

Key Points

- The cardinal finding of achalasia, impaired esophagogastric junction relaxation, can occur with a wide spectrum of contractility in the adjacent distal esophagus ranging from absent contractility (type I achalasia) to spasm (type III achalasia) or even normal peristalsis (esophagogastric junction outflow obstruction).
- The well-established durable treatments for achalasia, pneumatic dilation and laparoscopic Heller myotomy, are both 80–90% effective when done by experienced practitioners.
- Per oral endoscopic myotomy (POEM) is a new endoscopic technique for performing a myotomy of the lower esophageal sphincter and a calibrated length of adjacent esophagus, potentially the entire smooth muscle segment.
- Each achalasia syndrome has unique treatment considerations; type II achalasia responds well to all therapies while type III responds best to POEM.
- Emerging data support the concept that optimal management of achalasia is phenotype-specific, guided by high-resolution manometry and, in some instance, functional luminal imaging probe studies.

Table 1

Clinical achalasia syndromes within and beyond Chicago Classification v3.0. Apart from the achalasia subtypes, these syndromes are not specific for achalasia and may have distinct pathophysiology, but instances occur in which they are optimally managed as if they were achalasia.

Syndrome	Median IRP	Esophageal contractility	Qualifications/notes
Type I achalasia	>15 mmHg	Absent contractility	
Type II achalasia	>15 mmHg	Absent peristalsis Panesophageal pressurization with ≥20% of swallows	
Type III achalasia	>15 mmHg	Absent peristalsis Premature contractions with ≥20% of swallows	
EGJ outflow obstruction	>15 mmHg	Sufficient peristalsis to exclude types I, II or III achalasia	Heterogeneous group • Can be early or incomplete achalasia (12–40%) Can resolve spontaneously • Technical issues
Absent contractility	≤15 mmHg (CART analysis suggested ≤10 mmHg)	Absent contractility	Heterogeneous group • Abnormal FLIP distensibility index or esophageal pressurization with swallows or MRS supports achalasia
Distal esophageal spasm	Normal or increased	≥20% premature contractions (DL<4.5s)	May be evolving type III achalasia
Jackhammer	Normal or increased	≥20% of swallows with DCI>8000 mmHg•s•cm	May be evolving type III achalasia if DL<4.5s with ≥20% swallows
Opioid effect:	>15 mmHg	Normal, hypercontractile, or premature	Can mimic EGJ outflow obstruction, type III achalasia, DES, or jackhammer
Mechanical obstruction:	Normal or increased	Absent, normal, or hypercontractile	EUS or CT imaging of the EGJ may clarify the etiology

CT: computed tomography; DCI: distal contractile integral; DES: distal esophageal spasm; DL: distal latency; EGJ: esophagogastric junction; FLIP: functional luminal imaging probe; IRP: integrated relaxation pressure; MRS: multiple repetitive swallows

Table 2

Preferred treatments for achalasia and achalasia syndromes. See Table 1 for defining criteria. This assumes that all treatments are equally available with an equal degree of expertise. In reality, that is rarely the case and the available local expertise often strongly influences treatment choice.

Syndrome	Preferred treatment (s)	Comments, rationale
Type I achalasia	PD, LHM, POEM	• All are efficacious • Expect more reflux after POEM, especially with hiatal hernia • Extending the myotomy (LHM or POEM) proximal to the LES is probably unnecessary and can lead to diverticulum formation at the myotomy site
Type II achalasia	PD	• PD, LHM, POEM are all highly efficacious; PD has the least morbidity and cost • Anticipate repeat dilations over the years • Extending the myotomy (LHM or POEM) proximal to the LES is probably unnecessary and can lead to diverticulum formation at the myotomy site
Type III achalasia	POEM	• Calibrate the length of myotomy to the spastic segment as imaged on HRM
EGJ outflow obstruction	Calcium channel blockers, nitrates	• Many cases resolve spontaneously • Image the EGJ (EUS, CT) to rule out obstruction • If achalasia therapies are applied, treat as type II achalasia
Absent contractility deemed to be achalasia	PD, LHM, POEM	• Treat as type I achalasia
DES deemed to be achalasia	POEM	• Treat as type III achalasia
Opioid effect	1st choice, discontinue opioid 2nd choice, Botox 3rd choice, POEM	• Time course of reversal with opioid cessation is not known
Obstruction	Conventional dilation Operative reversal if relevant Directed medical therapy if relevant	• Many entities mimic achalasia, sometimes termed ‘pseudoachalasia’: eosinophilic esophagitis, cancer, reflux stricture, post-myotomy stricture, etc

DES: distal esophageal spasm; LHM: laparoscopic Heller myotomy; PD: pneumatic dilation; POEM: per-oral endoscopic myotomy