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Personalized Approach to the Management of Achalasia: How We Do It.

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dysphagia; manometry; endoscopy; reflux

Introduction:

Achalasia lends itself to a personalized management approach as clinical sub-classification facilitates direction of targeted management.^{1–3} We utilize comprehensive esophageal evaluation with endoscopy, high-resolution manometry (HRM), functional luminal imaging probe (FLIP), and timed-barium esophagram (TBE) to ensure accurate identification of achalasia, clinical phenotyping based on physiology and anatomy, and direction of targeted, multidisciplinary treatment options. Here, we describe our approach to offer personalized management of achalasia.

Diagnosis and phenotyping achalasia

Our approach to effective management of achalasia begins with accurate identification of achalasia. While achalasia typically presents with dysphagia, regurgitation, and possibly chest pain or weight loss, there is substantial overlap with the subjective presentations of other esophageal conditions; thus diagnosis requires objective testing (Table 1).

Endoscopy with thorough inspection may identify an objective alternative diagnosis to achalasia (and thus exclude secondary causes potentially related to pseudoachalasia), but can also be suggestive of achalasia. Other important endoscopic features related to management direction include presence of hiatal hernia and epiphrenic diverticula. However, unless an

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Conflicts of interest:

Dustin A. Carlson and John E. Pandolfino hold shared intellectual property rights and ownership surrounding FLIP panometry systems, methods, and apparatus with Medtronic Inc.

Dustin A. Carlson: Medtronic (Speaking, Consulting)

John E. Pandolfino: Crospon, Inc (stock options), Given Imaging (Consultant, Grant, Speaking), Sandhill Scientific (Consulting, Speaking), Takeda (Speaking), Astra Zeneca (Speaking), Medtronic (Speaking, Consulting), Torax (Speaking, Consulting), Ironwood (Consulting), Impleo (Grant)

alternative diagnosis is identified on endoscopy, motility testing remains essential to confidently diagnose and phenotype the patient (Table 1).

Achalasia has traditionally been defined by esophageal manometry with sub-classification facilitated by HRM (Figure 1).^{1, 3-5} Type II achalasia is the most likely to have a positive treatment outcome, followed by type I and then type III.^{1, 5} Results from the randomized, prospective European achalasia trial comparing pneumatic dilation (PD) and laparoscopic Heller's myotomy (LHM) demonstrated similar outcomes between PD and LHM among patients with type I and type II achalasia, but that patients with type III achalasia yielded greater benefit from LHM than PD.^{5, 6} Thus, an essential component of phenotyping the achalasia patients is sub-classification of non-spastic (types I and II) versus spastic (type III) achalasia.^{1, 5} Further, the anatomic location and/or extent of spastic esophageal contractions can be identified with EPT which facilitates *tailoring* myotomy length to the extent of spastic contraction of the esophageal body.⁷

The functional luminal imaging probe (FLIP) objectively measures opening parameters at the EGJ and the esophageal contractile response to volume-controlled distension (likely related to secondary peristalsis) in the sedated patient at the time of endoscopy.⁸ We utilize FLIP at the time of our initial endoscopy when the endoscopy is normal or achalasia is suspected. FLIP panometry is consistently abnormal in patients with achalasia and includes findings of reduced EGJ opening and an abnormal contractile response to distension (Figure 2).^{8,9} Thus, if FLIP panometry demonstrates normal EGJ opening and a normal contractile response (repetitive antegrade contractions; RACs), our management is directed toward reflux or functional causes.¹⁰ If FLIP panometry demonstrates reduced EGJ opening or an abnormal contractile response, then we proceed with HRM +/- TBE to make sure we can adjudicate cases where one of the tests does not fit.

We also attempt to obtain a TBE in all patients with confirmed or suspected achalasia prior to therapy. TBE facilitates confirmation of the diagnosis, provides a baseline to objectively monitor treatment response, and provides anatomic characterization that supplements the clinical phenotypes and helps direct treatment decisions. While we generally interpret a column height >5cm at 5 minutes as significant retention, we interpret TBE on a case-by-case basis, incorporating other factors (e.g. esophageal anatomy, retention at 1 or 2 minutes, passage of barium tablet), instead of applying rigid thresholds for clinical application.

Achalasia can also be clinically present but not fit neatly into the Chicago Classification (CCv3.0) subtype criteria.⁴ The comprehensive esophageal evaluations is especially important in these patients and often includes adjunctive maneuvers on HRM, FLIP, and TBE to clarify the clinical impression. Additionally, treatment of these patients is generally pursued in a conservative, step-wise manner.

Management of achalasia: A personalized approach

Management strategy in achalasia targets relieving the esophageal obstruction created by impaired relaxation of the LES and if present, spastic contraction of the esophagus. Effective treatments with durable effects (*definitive therapies*) include PD, LHM, and per-oral

esophageal myotomy (POEM); Table 1. Botulinum toxin injection is less durable than the definitive treatment options and we generally reserved it for patients with comorbidities associated with unacceptable operative risks.

Because of the multiple effective treatment modalities available, we utilize the baseline evaluation and phenotyping to offer targeted therapies (Table 1). Patients with non-spastic (i.e. type I or type II) achalasia on HRM appear to have relatively similar response rates (with caveat) to PD, LHM, or POEM.^{5, 6, 11} In patients with spastic achalasia, we preferentially offer POEM with an extended, tailored myotomy.⁷ If patients with type I or type II achalasia based on CCv3.0 have spastic features evident during provocative HRM maneuvers or FLIP panometry, we may recommend treatment in a similar manner to spastic achalasia.

Our protocol for PD is to perform the initial dilation of 30mm and then based on clinical response, perform the 35mm dilation if needed; we do not perform 40mm pneumatic dilation. We always use fluoroscopy as the balloon and sphincter can move and we always perform a second look with endoscopy to assess for perforation as early recognition can facilitate non-surgical treatments with stents. This second look endoscopy has essentially removed our need for routine post dilation gastrograffin esophagram, unless the patient is having symptoms consistent with perforation in recovery.

Laparoscopic Heller myotomy is performed with a partial fundoplasty, either a Dor or Toupet. In patients with types I or type II achalasia, we offer POEM with a standard length myotomy and in type III achalasia, with a tailored (extended) myotomy.⁷

When multiple treatment options are deemed reasonable, we employ a multidisciplinary discussion with our patients regarding pros and cons associated with each modality and then allow the patient to choose based on their preferences (Table 2). To facilitate these multidisciplinary discussions, our esophageal center utilizes shared clinic visits with both an esophagologist (experienced with PD) and foregut surgeon (experienced with LHM and POEM). Additionally, we hold every-other-week multidisciplinary conferences to discuss cases and generate collaborative management decisions.

Evaluation and management after achalasia therapies

Although therapies in achalasia are effective at improving symptoms, the therapies are not curative of this chronic disorder and thus we routinely follow all achalasia patients in a standard manner (Figure 2). Additionally, there is a recognized disconnect between esophageal symptoms and function, thus we obtain objective follow-up testing in even asymptomatic patients (Figure 3).¹²

Symptom persistence or recurrence after definitive achalasia treatment may be the result of various methods of treatment failure: Beyond incomplete myotomy, other mechanisms to be considered include GERD +/- obstructive sequelae (esophagitis, stricture), failure of the fundoplasty (slips, twists, herniation) after LHM, persistent spasm of the esophageal body, and additionally a unique and problematic mechanism of treatment failure that occurs after myotomy with either LHM or POEM, a blown-out-myotomy (BOM); Figures 3 and 4.

Mechanisms related to functional esophageal disorders (e.g. hypersensitivity, hypervigilance, and anxiety) are also considered if physiologic testing is otherwise normal. Finally, a lack of response to treatment may generate consideration of an inaccurate initial diagnosis and thus we often revisit baseline tests with an added sense of scrutiny. Thus, we typically pursue a comprehensive step-wise evaluation involving TBE, endoscopy with FLIP, HRM, and sometimes ambulatory esophageal pH testing in attempt to identify a specific etiology for symptoms. Ultimately, when the specific mechanism for symptoms after achalasia therapy is identified, targeted therapy can be pursued (Figure 2).

Conclusions

Our approach to achalasia involves a comprehensive evaluation of physiology and anatomy at both the baseline evaluation and during follow-up after therapies for achalasia to aid direction of specific, targeted therapy. Further, multiple treatment options (including endoscopic and surgical) are often available, thus we utilize a multidisciplinary approach to offer the array of treatment options and further involve patient perspectives and preferences into management decisions. Ultimately, our practice approaches management of achalasia in a personalized manner in an attempt to improve the likelihood of favorable outcomes.

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References

1. 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(5):1526–33. [PubMed: 18722376]
2. Rohof WO, Hirsch DP, Kessing BF, Boeckstaens GE. Efficacy of treatment for patients with achalasia depends on the distensibility of the esophagogastric junction. *Gastroenterology*. 2012;143(2):328–35. [PubMed: 22562023]
3. Pandolfino JE, Gawron AJ. Achalasia: a systematic review. *JAMA*. 2015;313(18):1841–52. [PubMed: 25965233]
4. Kahrilas PJ, Bredenoord AJ, Fox M, et al. The Chicago Classification of esophageal motility disorders, v3.0. *Neurogastroenterol Motil*. 2015;27(2):160–74. [PubMed: 25469569]
5. Rohof WO, Salvador R, Annese V, et al. Outcomes of treatment for achalasia depend on manometric subtype. *Gastroenterology*. 2013;144(4):718–25; quiz e13–4. [PubMed: 23277105]
6. Moonen A, Annese V, Belmans A, et al. Long-term results of the European achalasia trial: a multicentre randomised controlled trial comparing pneumatic dilation versus laparoscopic Heller myotomy. *Gut*. 2016;65(5):732–9. [PubMed: 26614104]
7. Hungness ES, Sternbach JM, Teitelbaum EN, Kahrilas PJ, Pandolfino JE, Soper NJ. Per-oral Endoscopic Myotomy (POEM) After the Learning Curve: Durable Long-term Results With a Low Complication Rate. *Annals of surgery*. 2016;264(3):508–17. [PubMed: 27513156]
8. Carlson DA, Kahrilas PJ, Lin Z, et al. Evaluation of Esophageal Motility Utilizing the Functional Lumen Imaging Probe. *Am J Gastroenterol*. 2016;111(12):1726–35. [PubMed: 27725650]
9. Carlson DA, Kou W, Pandolfino JE. The rhythm and rate of distension-induced esophageal contractility: A physiologic marker of esophageal function. *Neurogastroenterology and motility : the official journal of the European Gastrointestinal Motility Society*. 2020:e13794.

10. Baumann AJ, Donnan EN, Triggs JR, et al. Normal Functional Luminal Imaging Probe Panometry Findings Associate With Lack of Major Esophageal Motility Disorder on High-Resolution Manometry. *Clin Gastroenterol Hepatol*. 2020.
11. Ponds FA, Fockens P, Lei A, et al. Effect of Peroral Endoscopic Myotomy vs Pneumatic Dilation on Symptom Severity and Treatment Outcomes Among Treatment-Naive Patients With Achalasia: A Randomized Clinical Trial. *JAMA*. 2019;322(2):134–44. [PubMed: 31287522]
12. Vaezi MF, Baker ME, Achkar E, Richter JE. Timed barium oesophagram: better predictor of long term success after pneumatic dilation in achalasia than symptom assessment. *Gut*. 2002;50(6):765–70. [PubMed: 12010876]
13. 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. *The American journal of gastroenterology*. 2012;107(12):1817–25. [PubMed: 23032978]
14. Jain AS, Carlson DA, Triggs J, et al. Esophagogastric Junction Distensibility on Functional Lumen Imaging Probe Topography Predicts Treatment Response in Achalasia-Anatomy Matters! *The American journal of gastroenterology*. 2019;114(9):1455–63. [PubMed: 30741739]
15. Kraichely RE, Arora AS, Murray JA. Opiate-induced oesophageal dysmotility. *Aliment Pharmacol Ther* 2010;31(5):601–6. [PubMed: 20003176]

Figure 1. Clinical phenotypes of achalasia.

A) Type I achalasia characterized on HRM (*top*) by elevated integrated relaxation pressure (IRP) and absent contractility without pressurization. Single liquid swallows are indicated by pink arrows. Associated functional luminal imaging probe (FLIP) panometry (*bottom, left*) demonstrated reduced esophagogastric junction (EGJ) opening, EGJ-distensibility index (DI) $0.7 \text{ mm}^2/\text{mmHg}$ and absent contractile response and timed-barium esophagram (TBE; *bottom, right*) demonstrated a narrowed EGJ, esophageal dilatation, and barium retention.

B). Type II achalasia on HRM with elevated IRP and absent contractility with panesophageal pressurization. FLIP panometry demonstrated reduced esophagogastric junction (EGJ) opening, EGJ-distensibility index (DI) $0.9 \text{ mm}^2/\text{mmHg}$ and non-occluding esophageal contractions. TBE demonstrated a narrowed EGJ, mild esophageal dilatation, and barium retention. **C). Type III achalasia** on HRM with elevated IRP and premature contractility. FLIP panometry demonstrated reduced esophagogastric junction (EGJ) opening, EGJ-distensibility index (DI) $1.2 \text{ mm}^2/\text{mmHg}$ and a sustained occluding contractions. TBE demonstrated a narrowed EGJ with cork-screw conformation of the esophagus. Figure used with permission from the Esophageal Center at Northwestern.

Figure 2. Evaluation and follow-up after definitive therapy in achalasia.

Our standard follow-up entails a complete evaluation at 6 to 12 months after therapy (or earlier if symptoms persist or recur) consisting of endoscopy with functional luminal imaging probe (FLIP), timed barium esophagram (TBE), high-resolution manometry (HRM), and reflux testing (off of PPI) if the patient does not have reflux esophagitis. After therapy (especially POEM), PPI therapy is continued for approximately 6 months until endoscopy and reflux testing are performed off medication to determine need for ongoing PPI use. Patients with esophagitis or positive pH tests generally remain on maintenance PPI therapy.

We will have the patient undergo at least TBE and/or endoscopy with FLIP every 3 years. Abnormal objective testing generally results in closer monitoring with earlier follow-up; pursuit of additional definitive therapies are generally not pursued in asymptomatic patients. We do not adhere to any cancer surveillance protocol based on limited data.

Notes: 1) Although the prognosis for a positive response to LES-target therapy is better if an EGJ outflow obstruction (EGJOO) is present than if EGJ opening is normal, we still generally attempt PD or POEM or LHM before pursuing esophagectomy 2) If PD has recently failed, laparoscopic Heller's myotomy (LHM) or POEM may be preferred subsequent option. 2) Smooth muscle relaxants (SMRs) included off label use of nitrates, anticholinergics like hyoscyamine, calcium-channel blockers, or phosphodiesterase type 5 inhibitors. EGD – esophagogastroduodenoscopy; ES – Eckardt score. Figure used with permission from the Esophageal Center at Northwestern.

Figure 3. Evaluation of treatment response in achalasia.

A) An asymptomatic patient with achalasia returned for evaluation 1 year after per-oral endoscopic myotomy (POEM). Endoscopy off of proton pump inhibitor (PPI) therapy demonstrated Los Angeles class B esophagitis (not displayed). FLIP (*left*) demonstrated normal esophagogastric junction (EGJ) opening (EGJ-distensibility index (DI) = 7.0 mm²/mmHg; EGJ-diameter 14mm, pressure 20 mmHg); timed-barium esophagram (TBE) demonstrated only trace barium retention at 1 minute (not shown) and 5 minutes (*middle*). The integrated relaxation pressure (IRP) on high-resolution manometry (HRM; *right*) was 11mmHg. PPI therapy was reinitiated. **B)** A patient with persistent dysphagia after 30 and 35mm pneumatic dilation (PD); ongoing EGJ outflow obstruction was detected by FLIP with reduced EGJ opening (*left*; EGJ-DI = 1.4 mm²/mmHg; EGJ-diameter 8.6mm, pressure 40 mmHg) and TBE (*middle*: 16cm column height at 5 minutes). The IRP on HRM (*right*) was 10mmHg; IRP typically plays only a minor role in our management decisions after initial definitive treatment in achalasia due to its tendency to miss overt obstruction.¹⁴ The patient subsequently chose treatment with laparoscopic Heller's myotomy (LHM) over POEM. Figure used with permission from the Esophageal Center at Northwestern.

Figure 4. Mechanisms of treatment failure in achalasia.

A) Reflux esophagitis (Los Angeles grade C) and peptic stricture in a symptomatic patient after laparoscopic Heller's myotomy (LHM) with Dor. Proton pump inhibitor therapy resulted in healing of esophagitis and the stricture was dilated on follow-up endoscopy. **B)** Endoscopy from a patient with dysphagia that onset years after a LHM with Dor: The Dor was disrupted and a paraesophageal hernia was present. Hiatal hernia repair and re-do Dor was offered. **C)** TBE from a patient with dysphagia and regurgitation that recurred years after LHM with Dor; TBE demonstrated diverticulization of the myotomized segment: a *blown-out-myotomy*.¹⁴ **D)** Spasm on HRM in a patient with occasional dysphagia two years after LHM with Dor. EGJ opening was normal on FLIP (EGI-DI 7.2 mm²/mmHg), though contractility proximal to the myotomy segment was observed. The patient was treated with hyoscyamine with future consideration for extended POEM. Figure used with permission from the Esophageal Center at Northwestern.

Table 1.
Achalasia diagnostic and treatment algorithm.

Per-oral endoscopic myotomy (POEM). Laparoscopic Heller's myotomy (LHM). EGJOO – esophagogastric junction outflow obstruction.

Patients	<ul style="list-style-type: none"> Symptoms of dysphagia +/- chest pain and bland regurgitation Reflux symptoms not responding to PPI therapy 		
Initial diagnostic approach	Step 1: Endoscopy		
	Step 2: Assess motility if endoscopy is negative or suggestive of motility disorder <ul style="list-style-type: none"> FLIP during endoscopy High-resolution manometry (HRM) Timed-barium esophagram (TBE) 		
HRM findings	Type I / Type II achalasia	Type III achalasia *	EGJ outflow obstruction * or absent contractility
Confirmatory Testing	None required	None required	Necessary to confirm diagnosis with TBE and/or FLIP before offering definitive therapy
Treatment	POEM or pneumatic dilation LHM generally for specific scenarios (see Table 2)	Tailored POEM	Consider botulinum toxin injection in equivocal cases

* Both type III achalasia and EGJ outflow obstruction may be associated with chronic opioid use.¹⁴ While opioid cessation or reduction is ideal, and we may we may consider botulinum toxin injection as bridge in therapy. However, if opioid cessation is impossible, we generally treat per our standard approach, e.g. tailor myotomy for type III achalasia.

Table 2.

Outline of patient discussion points related to definitive treatments in achalasia.

	Pneumatic dilation (PD)	POEM	Laparoscopic Heller's Myotomy (LHM)
Pros	<ul style="list-style-type: none"> • Out-patient procedure • Short recovery • Short duration for dietary reintroduction • Similar outcomes to surgical myotomy, but... 	<ul style="list-style-type: none"> • The durable effectiveness of a single intervention • Typically shorter recovery and duration for diet reintroduction than LHM 	<ul style="list-style-type: none"> • The durable effectiveness of a single intervention • Reflux control with partial fundoplasty
Cons	<ul style="list-style-type: none"> • May require repeat dilation to achieve similar outcomes to myotomy • Low rate of perforation¹ 	<ul style="list-style-type: none"> • Short inpatient stay • Increased rates of reflux² • Lack of insurance coverage remains a limitation with some third party payers 	<ul style="list-style-type: none"> • Short inpatient stay • Typically longer recovery and duration for diet reintroduction than POEM or PD • Fundoplasty may become source of failure
Other considerations	<ul style="list-style-type: none"> • In type I and type II achalasia 	<ul style="list-style-type: none"> • Tailored myotomy with POEM preferred approach in spastic achalasia 	Preferential consideration if: <ul style="list-style-type: none"> • Hiatal hernia³ • Epiphrenic diverticula⁴ • Tight angulation of distal esophagus or severe esophageal tortuosity⁵

Notes: 1) While reported rates of perforation range from 1–4% of dilations, our perforation rate is extremely low (< 0.5%).¹³ We believe this is related to our cautious approach starting with 30 mm in all patients and using meticulous fluoroscopic technique for placement of the balloon. 2) However, reflux can generally be managed effectively with daily dosing of proton pump inhibitor. 3) LHM may facilitate hiatal hernia repair with partial fundoplasty while conceptually the risk of reflux after POEM may be even greater. Small hiatal hernia can be present in achalasia, but presence of large hiatal hernia should raise concern for secondary esophageal motor abnormalities, i.e. pseudoachalasia). 4) LHM may facilitate addressing epiphrenic diverticulum if the diverticula is of significant size and contributing to retention. 5) Tight angulation of the distal esophagus may create difficulty in positioning a pneumatic dilator (with possible increased associated risk of perforation) or severe esophageal tortuosity may make submucosal tunnel creation in POEM challenging.