Gastroenterology 2017;■:1–7

Clinical Practice Update: The Use of Per-Oral Endoscopic Myotomy in Achalasia: Expert Review and Best Practice Advice From the American Gastroenterological Association

Peter J. Kahrilas, David Katzka, and Joel E. Richter

Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois

The purpose of this review is to describe a place for per-oral endoscopic myotomy (POEM) among the currently available robust treatments for achalasia. The recommendations outlined in this review are based on expert opinion and on relevant publications from PubMed and EMbase. The Clinical Practice Updates Committee of the American Gastroenterological Association proposes the following recommendations: 1) in determining the need for achalasia therapy, patient-specific parameters (Chicago Classification subtype, comorbidities, early vs late disease, primary or secondary causes) should be considered along with published efficacy data; 2) given the complexity of this procedure, POEM should be performed by experienced physicians in high-volume centers because an estimated 20−40 procedures are needed to achieve competence; 3) if the expertise is available, POEM should be considered as primary therapy for type III achalasia; 4) if the expertise is available, POEM should be considered as treatment option comparable with laparoscopic Heller myotomy for any of the achalasia syndromes; and 5) post-POEM patients should be considered high risk to develop reflux esophagitis and advised of the management considerations (potential indefinite proton pump inhibitor therapy and/or surveillance endoscopy) of this before undergoing the procedure.

Keywords: Achalasia; Esophageal Motility Disorders; High-Resolution Manometry; Per-Oral Endoscopic Myotomy.

Within the past decade, per-oral endoscopic myotomy (POEM) has evolved from an exciting concept[1] to a mainstream treatment option for achalasia. Indeed, the pioneering Japanese center for refining the technique recently summarized technical pearls and pitfalls on performing POEM gleaned from their first 1000 procedures.[2] Uncontrolled outcomes data have been very promising comparing POEM with the standard surgical treatment for achalasia, laparoscopic Heller myotomy (LHM).[3] However, concerns remain regarding post-POEM reflux, the durability of the procedure, and the learning curve for endoscopists adopting the technique. Coupled with a recent randomized controlled study comparing pneumatic dilation (PD) and LHM reporting equivalent (excellent) 5-year outcomes,[4,5] the role of POEM in achalasia treatment remains controversial. The purpose of this commentary is to describe when clinicians should consider POEM among the robust therapies currently available for achalasia.

Expansion of the Indications for Lower Esophageal Sphincter Myotomy

High-resolution manometry (HRM)[6,7] and the development of the Chicago Classification, now in its third iteration,[8] have substantially revised the classification of esophageal motility disorders. Nowhere is this more evident than in our concept of achalasia, now differentiated into 3 subtypes and a fourth entity, esophagogastric junction (EGJ) outflow obstruction, which can mimic achalasia in terms of clinical presentation and management.[9–12] A Chicago Classification diagnosis of achalasia stipulates both impaired deglutitive EGJ relaxation and absent peristalsis. However, absent peristalsis does not preclude esophageal pressurization or non-peristaltic contractility and these are quite common in achalasia. In fact, the achalasia subtypes are defined by different patterns of esophageal contractility that accompany impaired EGJ relaxation: type I, with negligible pressurization within the esophagus, often referred to as classic achalasia; type II, with panesophageal pressurization, wherein uniform simultaneous pressurization bands span from the upper sphincter to the lower sphincter; or type III, with premature (spastic) contractions, wherein the latency between upper sphincter relaxation and arrival of a rapidly propagated contraction at the distal esophagus is <4.5 seconds.[13] In multiple reported series, type II achalasia is the most common presenting subtype.

A fundamental difficulty in diagnosing achalasia is that there is no biomarker for the disease. Although the classical pathology is inflammation of the myenteric plexus leading to aganglionosis,[13,14] the diagnosis is not established by biopsy and atypical cases clearly exist.[15] The diagnosis is usually established using HRM to demonstrate that some combination of dysphagia, regurgitation, and chest pain is occurring as a result of absent peristalsis and nonmechanical esophageal outflow obstruction.[16] Consequently, there are 2

Abbreviations used in this paper: **EGJ, esophagogastric junction; HRM, high-resolution manometry; IRP, integrated relaxation pressure; LHM, laparoscopic Heller myotomy; LES, lower esophageal sphincter; POEM, per-oral endoscopic myotomy; PD, pneumatic dilation.**

0016-5085/$36.00
https://doi.org/10.1053/j.gastro.2017.10.001

fundamental limitations of the Chicago Classification criteria for achalasia: 1) the integrated relaxation pressure (IRP), used to define the adequacy of deglutitive lower esophageal sphincter (LES) relaxation,[17,18] can be less than the upper limit of normal in achalasia (eg, the IRP is <100% sensitive), particularly in type I disease[19,20]; and 2) there can be instances with preserved peristalsis (eg, Chicago Classification criteria are <100% specific). Furthermore, the disease evolves over a variable timespan leaving open the possibility that testing is done somewhere along the continuum from normal function to unequivocal achalasia when the requisite diagnostic thresholds are not met, for example, early or incompletely evolved disease. Early in the disease, maneuvers that unmask impaired inhibitory innervation, such as multiple rapid swallows or a rapid drink challenge, may be useful in supporting a diagnosis of achalasia.[21–23] Conversely, late in the disease, both the LES pressure and IRP might be very low, thereby suggesting a diagnosis of absent contractility, with an achalasia diagnosis established by using functional luminal imaging probe technology and presence of stasis on the barium esophagram.[20]

In addition to the 3 achalasia subtypes, the Chicago Classification recognizes EGJ outflow obstruction as another syndrome in which sphincter dysfunction can cause dysphagia. With EGJ outflow obstruction, the IRP is greater than the ULN, but the "absent peristalsis" criterion for achalasia is not met. Peristalsis may be fragmented or even normal. EGJ outflow obstruction is a heterogeneous group with a spectrum of potential etiologies, including incompletely expressed or early achalasia or an isolated disorder of impaired LES relaxation. Alternatively, EGJ outflow obstruction may also be secondary to 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.[9,24] Consequently, EGJ outflow obstruction always requires more intense clinical evaluation to clarify its etiology (eg, endoscopic ultrasound, computed tomography, timed barium esophagram). Prior surgery should also be considered as similar manometric findings can be found after anti-reflux or bariatric surgery, sometimes making it very difficult to establish cause and effect.[25,26] The natural history and heterogeneity of EGJ outflow obstruction was studied in 4 recent series reporting that many of these patients were minimally symptomatic or asymptomatic, that in 20%–40% of cases the "disorder" resolved spontaneously, but that 12%–40% of them end up being treated as achalasia.[10–12,27] Finally, another disorder often associated with EGJ outflow obstruction is hypercontractile (jackhammer) esophagus. A recent meta-analysis cited a 72% success rate of POEM for this disorder.[28] Although seemingly a disorder of the esophagus proximal to the LES, our opinion is that LES myotomy should be done concomitantly if POEM is applied in these patients.

Evident from the preceding discussion, treating "achalasia" is not limited to treating achalasia, as it would be defined by histopathology. Rather, the clinical evaluation concludes that clinically relevant EGJ outflow obstruction exists as a cause of dysphagia and that the patient is likely to benefit from a therapy targeting that outflow obstruction (eg, an achalasia treatment). This emphasizes a very important limitation of existing data regarding achalasia treatments. Historically, there has been minimal consistency in characterizing the treatment populations and existing treatment data lag substantially behind the current diagnostic considerations detailed here. Consequently, there are several instances in which the published data on treating achalasia need to be interpreted in the context of patient-specific variables.[29] Table 1 summarizes the spectrum and characteristics of achalasia syndromes potentially amenable to achalasia treatments.

Per-Oral Endoscopic Myotomy vs Laparoscopic Heller Myotomy: Strengths and Weaknesses

Coincident with the widespread adoption of the Chicago Classification came the development of POEM,[30] posing the question of why POEM might be considered an advancement over LHM. The POEM procedure allows for performing a myotomy of the LES using endoscopy rather than laparoscopy (as with LHM). The procedure involves making a mucosal incision 10–15 cm proximal to the LES and creating a submucosal tunnel from there, extending distally 2–4 cm onto the gastric cardia using a standard endoscope and electrocautery. A circular muscle myotomy is then achieved from within the submucosal tunnel, beginning at least 2–3 cm distal to the mucosotomy and progressing to the distal point of cardia dissection.[31] Obvious technical advantages of POEM over LHM include lack of abdominal incisions, more rapid recovery, and the option of avoiding general anesthesia with airway intubation. Other, more subtle, advantages include the ease of performing a longer myotomy if desired (because mediastinal dissection is unnecessary), avoidance of vagal nerve injury, and lack of intra-abdominal adhesions that might hinder future surgery. Another ostensible advantage of POEM over LHM is that it is done without gastroesophageal junction dissection. To accurately perform LHM, the EGJ must first be surgically isolated, which entails division of the phrenoesophageal ligament and short gastric vessels, both important anti-reflux mechanisms maintaining the angle of His. Consequently, a posterior (Toupet) or anterior (Dor) fundoplication is typically performed in conjunction with LHM,[32] leaving open the potential for post-LHM fundoplication-related complications, especially obstructive dysphagia, given the aperistaltic esophagus of achalasia.

The widespread adoption of the POEM procedure has been a major shift in achalasia therapeutics. The reported success rate of POEM in multiple uncontrolled studies has been >90% (Table 2).[30,33–44] Inoue et al[30] reported the largest series, a cohort of 500 POEM patients, and found a significant reduction in Eckardt scores and LES pressures at 2 months, 1 year, and 3 years post-procedure. Similar patient outcomes have been reported for POEM in patients with prior PD or LHM.[45–46] Serious adverse events with POEM include perforation, pneumothorax, and bleeding.