

## Per-oral endoscopic myotomy white paper summary

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Orifice Surgery Consortium for Assessment and Research<sup>®</sup>  
(NOSCAR<sup>®</sup>) · Natural Orifice Translumenal Endoscopic  
Surgery<sup>®</sup> (NOTES<sup>®</sup>)

Achalasia is an uncommon esophageal motility disorder in which there is selective loss of inhibitory neurons resulting in loss of peristalsis and failure of adequate relaxation of the lower esophageal sphincter (LES) in response to food bolus. There is no current curative treatment that reverses the pathophysiology of achalasia. The treatment options are aimed at improving the passage of solids and liquids through the gastroesophageal junction (GEJ). The traditional treatment options include surgical myotomy and

endoscopic methods that disrupt or weaken the LES, such as endoscopic balloon dilation and botulinum toxin injection (BI).

Per-Oral Endoscopic Myotomy (POEM) represents a Natural Orifice Translumenal Endoscopic Surgery<sup>®</sup> (NOTES<sup>®</sup>) approach to Heller myotomy. Preliminary data suggest that this minimally invasive endoscopic procedure may achieve clinical results similar to those of surgical myotomy. As part of the annual Natural Orifice Surgery Consortium for Assessment and Research<sup>®</sup> (NOSCAR<sup>®</sup>) meeting held in Chicago in July 2012, a conference was organized to collaboratively review POEM and develop a consensus document on the current status of POEM. An International POEM Survey (IPOEMS) was designed and conducted by the session moderators as part of this NOSCAR initiative to attempt to supplement the scant published literature with current data from POEM early adopters. The survey, which has now been published in

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detail [1], included 5 Asian, 7 North American, and 4 European expert centers with a combined experience of 841 POEM procedures, including all high-volume centers (>30 cases per center) at the time of the survey in July 2012. These data span every aspect of POEM and were made available to the NOSCART POEM panel presenters to assist them with preparation of their panel presentations that served as the basis of this white paper.

This white paper is intended to discuss the development of POEM and outline the current state of POEM with regard to technique, indications and/or contraindications, peri-procedural evaluation and care, efficacy, safety, training, approach to starting a POEM program, and future perspectives. The sources of evidence used included: (1) published data up to December 2013 [given the scarcity of series published in full form, we included selected abstracts with significant numbers of POEMs and adequate discussion of outcomes], (2) data from the IPOEMS, and (3) the minutes of the round-table discussion that followed the presentations by panel members of the POEM section at the annual NOSCART meeting in Chicago in July 2012. This discussion included additional POEM operators from the United States and abroad beyond the panelists.

This document represents the shorter print version of a more detailed online white paper document.

### **Per-oral endoscopic myotomy for achalasia: the historical and pre-clinical laboratory experience**

Initial work by the Mayo Clinic Developmental Endoscopy Unit and the Apollo Group on widespread endoscopic mucosal resection, identified that with this endoscopic technique, the mucosa readily separates from the deeper layers of the gut wall, often referred to as delamination [2]. The 2004 Submucosal Inside Out Project began to transform the submucosa into an endoscopic working space [3–6]. Strategies were developed to work beneath the mucosa toward the lumen to enable en bloc excision of mucosal disease. Strategies also were developed to exit the gut wall by using a tunneled offset entry point for safe entry into body cavities, by means of a myotomy, with the overlying mucosa serving as a protective sealant flap (submucosal endoscopy with mucosal flap). Animal studies confirmed the feasibility and safety of exiting the esophagus into the mediastinum through a 2-cm myotomy [5, 6]. It was suggested that the myotomy could be applied as an alternative therapy for achalasia. A subsequent animal study confirmed that submucosal endoscopy with mucosal flap combined with incision of the inner circular muscle layer could reduce the LES pressure in pigs [7]. Shortly thereafter, POEM was performed by using the submucosal endoscopy with mucosal flap principle with a technique

adapted from endoscopic submucosal dissection (ESD) to create the submucosal space [8]. The initial work and subsequent work by other investigators involved blunt balloon dissection to create the submucosal tunnel to protect the overlying mucosa from injury and to expedite esophageal dissection [9]. Animal studies demonstrated that submucosal endoscopy with mucosal flap dissection deep within the gastric cardia (at least 2 cm) and cardiomyotomy are the potential defining components of a successful myotomy to treat achalasia [10]. Further, NOSCART-supported animal studies compared circular muscle layer versus full-thickness myotomy. These studies demonstrated that the effect on LES pressure was similar with either method and that full-thickness myotomy was easier and more expeditious [11].

### **Indications, contraindications, and pre-procedural evaluation and preparation**

POEM appears to be a safe and effective alternative for the treatment of classic achalasia [12–30]. However, its role and efficacy in patients with other hypertensive motor disorders, prior conventional achalasia treatments, end-stage achalasia, age extremes, and significant comorbid diseases is not clear.

### *POEM for other hypertensive motor disorders*

Preliminary data in the literature suggest POEM efficacy in motor disorders other than classic achalasia. Successful application of POEM in a small number of patients with diffuse esophageal spasm [1, 16, 31–33], hypertensive LES [1, 33, 34], type III spastic achalasia [1, 14, 17, 21], nutcracker esophagus [17, 33], and jackhammer esophagus [35] has been reported. It has been suggested that pain, a prominent symptom in many of these disorders, responds less well to POEM than does dysphagia, the predominant symptom in patients with typical achalasia [17]. In the international POEM survey, 11 of the 16 participating centers reported performing POEM for these extended manometric indications (accounting for 28 % of the 841 POEMs reported in the survey) [1]. Possibly somewhat diminished POEM efficacy was reported in patients with diffuse esophageal spasm and type III achalasia but excellent efficacy in hypertensive LES and nutcracker esophagus [1]. Based on the case reports in the literature and IPOEMS responses, longer esophageal myotomy is being performed for spastic disorders such as diffuse esophageal spasm that are characterized by long spastic segments of the distal esophagus [1]. POEM may be superior to laparoscopic Heller myotomy (LHM) in these patients because the myotomy can be extended proximally in the body of the esophagus.

### *POEM after failed conventional treatments of achalasia*

Prior BI causes submucosal fibrosis which, to varying degrees, obliterates the surgical planes that adversely affect surgical myotomy and possibly POEM [36]. In IPOEMS, 43 % of the 841 reported POEMs were performed in patients with prior failed treatments [1]. The general consensus among POEM operators is that the submucosal fibrosis caused by prior BI does result in a slower and more challenging dissection, but the effect is moderate and may be overcome by operator experience [1]. Although most POEM series have included a substantial proportion of patients, ranging from 18 to 69 % [14, 15, 17, 18], with prior standard achalasia treatments, outcomes specific to these patients have not been presented until recently, when two groups attempted to examine the effect of before-POEM endoscopic treatment on POEM outcomes. During subgroup analysis of patients with or without histories of endoscopic intervention, one group found no difference in procedure duration, intraoperative adverse events, or efficacy [37], whereas the other group found prior endoscopic treatment to be a predictor of increased procedure time [38]. The discordant findings may be related to methodologic issues such as the very small numbers of previously treated patients included in these studies (4 and 12, respectively). POEM after failed surgical Heller myotomy is reported to be more challenging, but recent reports demonstrate excellent efficacy when POEM is performed by experienced operators [1, 13, 18, 22, 27, 39, 40].

### *POEM for end-stage achalasia*

POEM in severe sigmoid achalasia and megaesophagus was reported in only 3 and 4 %, respectively, of all POEMs in IPOEMS [1]. Patients with severe sigmoidization and megaesophagus (end-stage achalasia) respond poorly to LHM, based on the LHM literature, and may ultimately come to esophagectomy [36]. Unlike LHM, POEM appears to cause minimal adhesions [19], and, therefore, it should not significantly affect subsequent esophagectomy. Therefore, it could be considered as an initial treatment in these patients, with esophagectomy reserved for those with inadequate clinical response. Most published series have excluded patients with severe sigmoidization and/or megaesophagus (stage IV achalasia). One center has performed POEM in 20 stage IV patients [27]. POEM in such patients is more challenging than in stage I–III patients, with significantly longer procedure times (mean procedure time in 20 stage IV patients = 129 min compared with 100 min in 80 patients at other stages ( $p < .02$ , unpublished data)). No significant difference in efficacy or adverse events was noted.

### *POEM in children and the elderly*

Another concern regarding POEM revolves around age extremes. There are reports of successful POEM in patients as young as 3 years and as old as 97 years, which suggests that POEM may be a feasible treatment option for appropriately selected patients, even at extremes of age [1, 20, 27, 41–43].

### *POEM in patients with comorbid conditions*

The majority of IPOEMS respondents considered POEM contraindicated in patients with a history of severe pulmonary disease, cirrhosis with portal hypertension, severe coagulopathy, and prior interventions resulting in significant submucosal fibrosis such as esophageal irradiation, ablation therapy, and extensive EMR (Table 1) [1].

### *Pre-procedural evaluation and preparation*

Pre-procedural evaluation and preparation do not differ significantly from those of LHM. IPOEMS collected detailed data on evaluation and preparation and revealed mostly minor variations among respondents [1]. A more detailed discussion is presented on the online full-length version of this white paper.

### *POEM technique*

Many, but not all, centers perform an EGD 1–3 days before the POEM procedure in order to remove any solid or liquid material from the esophagus as well as to evaluate for *Candida* esophagitis or any other esophageal or gastric lesions.

The POEM procedure is generally performed with the patient in the supine position under general anesthesia and with airway intubation [13]. Intravenous antibiotics are given before the procedure. A high-definition, forward-viewing gastroscope with a plastic cap is used with CO<sub>2</sub> insufflation [13]. The GEJ distance from the incisors is determined. A location 10–15 cm proximal to the GEJ is chosen as the site of initial submucosal entry. A submucosal injection consisting of saline solution stained with blue dye (e.g., indigo carmine) is used to create a mucosal bleb prior to performance of a mucosal incision (mucotomy) [13]. A 2-cm, longitudinal incision is made with cutting current to expose the submucosa. In most centers, a right-anterior orientation (2 o'clock position) is used for the submucosal tunnel and myotomy, as initially described by Inoue [12]. However, in some POEM centers, a posterolateral orientation (5 o'clock position) is favored [1].

There are variations in dissection technique. The technique described by Inoue involves pure electro-surgical dissection of the tunnel by using an ESD technique with the

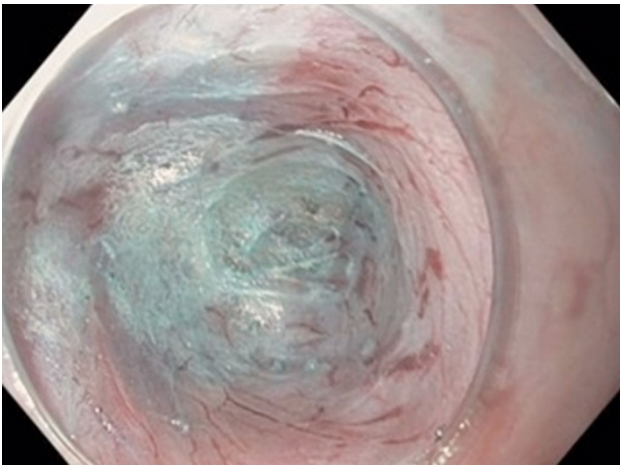
**Table 1** POEM in patients with comorbidities

Comorbidities not deemed contraindications for POEM by most IPOEMS respondents	Comorbidities deemed contraindications for POEM by most IPOEMS respondents
Immunosuppression (examples)	Prior irradiation to mediastinum or esophagus
Patient with IBD on maintenance anti-TNF	Severe pulmonary disease (example)
Patient with rheumatoid arthritis on methotrexate	Extensive bullous disease
Patient with HIV on HAART with CD4 count of 200–500/mm <sup>3</sup>	Prior lung resection
Moderate pulmonary disease (examples)	Home oxygen dependent
COPD	ASA class III
Pulmonary fibrosis	Forced expiratory volume/1 s
ASA class II	Forced vital capacity <70 %
Medically managed cardiovascular disease (examples)	pCO <sub>2</sub> ≥ 45
Ejection fraction <20 % with automatic internal cardiac defibrillator	pO <sub>2</sub> < 75
Medically managed coronary artery disease	Coagulopathy
Coagulopathy (examples)	Baseline platelet count <30,000–50,000/mm <sup>3</sup> (examples)
Metallic cardiac valve or high risk for venous thromboembolism	Immune thrombocytopenic purpura
Need for anticoagulation within 36–48 h after POEM	Myelodysplastic syndrome
High-risk cardiac stent requiring anti-platelet agent resumption within 3–5 days after POEM	Hypersplenism
Baseline platelet counts at >50,000 and <100,000/mm <sup>3</sup>	Prior esophageal EMR or other mucosal ablative treatment (examples)
Obesity, body mass index ≥35	Photodynamic therapy
Prior mediastinoscopy	Radio frequency ablation
Prior surgery in posterior mediastinum in POEM field	Compensated cirrhosis with portal hypertension even if no or trace esophageal varices on EGD
Patient with end-stage renal disease on hemodialysis	
Compensated cirrhosis without portal hypertension	

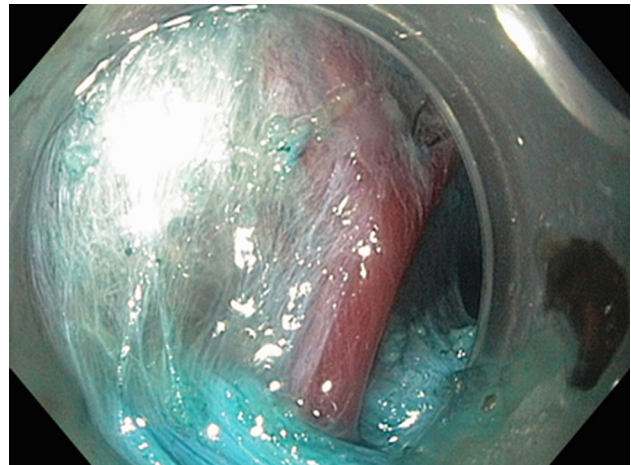
*POEM* per-oral endoscopic myotomy, *IPOEMS*, international POEM survey, *IBD* inflammatory bowel disease, *TNF* tumor necrosis factor, *HAART* highly active anti-retroviral therapy, *COPD* chronic obstructive pulmonary disease, *ASA* American Society of Anesthesiologists Physical Status Classification System

Olympus triangular-tip knife (Olympus, Center Valley, PA, USA) [22]. Another technique uses electrosurgical dissection with the T-type hybrid knife (ERBE, Tübingen, Germany), an ESD knife that allows injection of saline solution through the tip of the knife, obviating the need for repeated accessory exchanges between needle injector and knife that are needed with the triangular-tip knife [44]. An alternative technique, possibly more accessible to those with modest ESD experience, uses a through-the-scope dilation balloon such as a short-nosed biliary extraction balloon or a longer esophageal dilation balloon (CRE; Boston Scientific, Natick, Mass) to dissect the submucosal tunnel without electrosurgery [9, 23]. The group at Zhongshan Hospital, Shanghai, compared the T-type hybrid knife and triangular tip knife in a head-to-head, prospective, randomized study of 100 patients, which revealed shorter procedure time, lower bleeding rate, and less frequent use of coagulation forceps to control bleeding with the T-type hybrid knife [44]. No other comparative data exist regarding tunnel dissection techniques.

Irrespective of dissection technique, the dissection plane for the submucosal tunnel dissection is maintained in proximity to the muscularis propria to avoid accidental injury of the mucosal flap. The submucosal tunnel is extended until the endoscope is 2–3 cm beyond the GEJ in the submucosa of the gastric cardia as confirmed by (1) endoscopic measurements; (2) initial narrowing of the submucosal space at the level of the GEJ, with increased resistance followed by prompt expansion of the submucosal space at the gastric cardia, along with increased vascularity including “spindle” shaped veins (Fig. 1); (3) visualization of palisading vessels on the mucosal flap, which mark the distal extent of the esophagus (Fig. 2); (4) large-caliber, perforating vessels in the cardia representing branches of the left gastric artery (Fig. 3); (5) visualization of aberrant longitudinal muscle bundles at the GEJ (Fig. 4); or (6) visualization of a blue hue on intraluminal inspection of the mucosa of the gastric cardia (caused by the blue dye used in the injectate) (Fig. 5) [22]. The most useful of these GEJ indicators appear to be numbers 2 and 6, based on the IPOEMS [1].



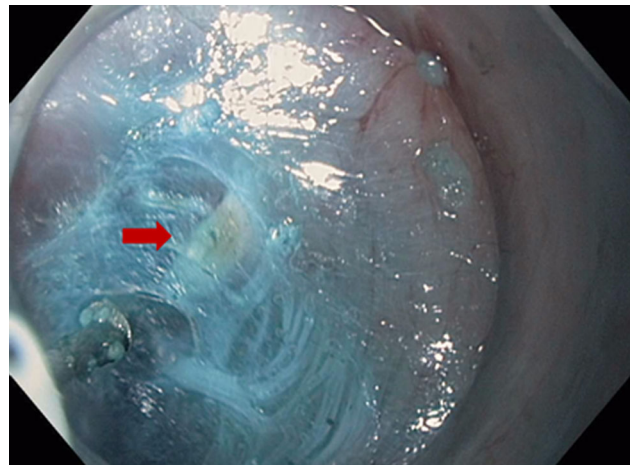
**Fig. 1** Expansion of the submucosal space at the gastric cardia with increased vascularity; note the spindle shaped veins best seen on the side of the muscularis. (Courtesy Winthrop University Hospital.)



**Fig. 3** Increased submucosal vascularity in the gastric cardia. There is a wider submucosal space with large submucosal vessels that are seen in the gastric cardia. Large, penetrating branches of the left gastric artery can be seen as shown in this image. (Courtesy Winthrop University Hospital.)



**Fig. 2** Palisading vessels. Long, thin palisading vessels are seen on the under side of the mucosa at the level of the gastroesophageal junction at 7 o'clock to 11 o'clock. (With permission Elsevier, Gastrointestinal Endoscopy Clinics of North America, 2013.)

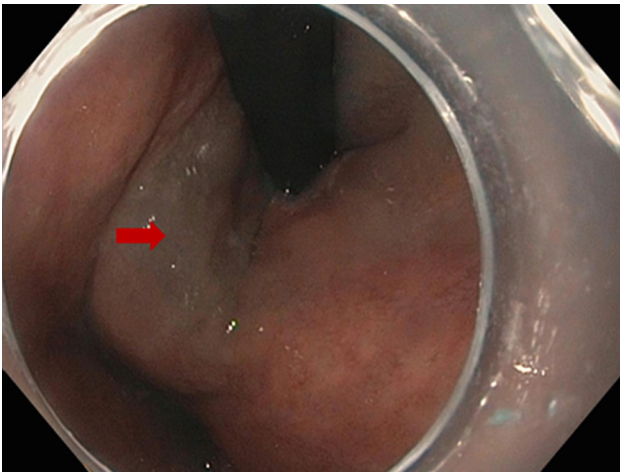


**Fig. 4** Bundles of aberrant inner longitudinal muscle fibers. Short bundles of aberrant inner longitudinal muscle fibers running in the submucosa and inserting into the circular layer of the muscularis propria are a marker that the level of the gastroesophageal junction has been reached. (With permission Elsevier, Gastrointestinal Endoscopy Clinics of North America, 2013.)

The myotomy is generally performed starting 2 cm distal to the mucosal entry point in a proximal-to-distal direction, although, anecdotally, a few centers perform the myotomy in distal-to-proximal direction, especially in the area of the LES [1]. Circular muscle dissection alone is carried out in most centers, although some centers dissect both circular and longitudinal muscle layers, especially in the area of the LES [1]. The group at Zhongshan Hospital, Shanghai, retrospectively compared patients who had full-thickness myotomy versus circular muscle myotomy. This study revealed shorter procedure time in the full-thickness myotomy group but no difference in efficacy, adverse events, or GERD between the groups [45]. Following the tenets of LHM, POEM length is at least 6 cm long (2 cm in the esophagus, 2–3 cm LES, 2 cm cardia) and averages

8–10 cm [1]. After the myotomy is performed, the endoscope can be withdrawn from the submucosal tunnel and inserted into the lumen for inspection of the mucosa and to ensure mucosal integrity and confirm easy passage of the endoscope through the LES, consistent with an adequate myotomy. The mucosal entry site is usually 2–3 cm long and typically is closed with 5–10 endoscopic clips [13]. Mucosal closure with clips avoids the potential leakage of esophageal contents into the track and the mediastinum.

Patients are hospitalized after POEM procedures for observation and are maintained with nothing by mouth until postoperative day 1, when a Gastrografin (Bracco



**Fig. 5** Blue discoloration of gastric cardia mucosa. Blue discoloration of the cardia mucosa is seen on retroflexion (from the blue dye used in the submucosal injectate) once the submucosal tunnel is successfully extended to the cardia. (With permission Elsevier, *Gastrointestinal Endoscopy Clinics of North America*, 2013.)

Diagnostics Inc, Princeton, NJ) esophagram is obtained (and/or a second endoscopy in some centers) [1]. If no loss of mucosal integrity or leak is noted, a liquid or pureed diet is started, which is continued for several days to a week and then gradually advanced to a regular diet.

#### Efficacy of POEM

The efficacy of achalasia treatments is assessed with several metrics including the widely used after-treatment Eckardt score of  $\leq 3$ , LES pressure decrease (usually  $>50\%$  decrease), and improvement of esophageal emptying as assessed by timed barium esophagram. Current POEM efficacy data from the literature are summarized in Table 2. There are no randomized, controlled trials comparing POEM with other treatments or to no treatment. All data are from uncontrolled series. Data were extracted from the 14 reports currently available in the English literature, 10 published as full articles and 4 in abstract form, with outcomes data based on a total of 804 patients [12–21, 24–30]. In all series, therapeutic success was seen in  $>80\%$  of patients, with dramatic reductions noted in the Eckardt score as well as the LES pressure. Only a small number of studies have reported efficacy based on objective assessment of esophageal emptying by timed barium esophagram (Table 3). EndoFLIP (Endolumenal Functional Lumen Imaging Probe; Crospon, Inc, Carlsbad, Calif) represents a promising new modality that provides a rapid quantitative assessment of luminal patency and sphincter distensibility. It uses a balloon catheter equipped with a series of electrodes that is inserted across the LES and via impedance planimetry permits determination of minimal luminal diameter and cross-sectional area at the level of the LES. An index of sphincter

distensibility also can be calculated by dividing the cross-sectional area by the balloon pressure that is also recorded by the device. EndoFLIP may allow intraoperative assessment of myotomy adequacy during POEM and may predict degree of dysphagia relief [26, 46–49].

#### Adverse events in POEM: recognition, prevention, and management

In the published series, POEM has been successfully performed with a low rate of serious adverse events. Nonetheless, efforts should be taken to avoid adverse events, recognize them when they do occur, and manage them appropriately once identified. The following review describes the data that have been published, uses information from the IPOEMS survey [1], and recounts experience to estimate the incidence of adverse events. The approximate incidence of POEM adverse events is summarized in Table 4.

#### *Intraoperative adverse events*

Standard surgical precautions and guidelines should be followed for this procedure. (See online full white paper document for details). One important consideration is the risk of aspiration during induction and intubation, and communication with the anesthesiologist is important. Standard airway protection methods should be used, such as rapid induction sequence, aggressive aspiration of mouth contents during intubation, and even endotracheal intubation with the patient in a semierect position in cases of severe esophageal stasis. It is also important to use  $\text{CO}_2$  as the insufflation gas because gas escape into the mediastinum and abdomen—and sometimes the thorax—is common. For  $\text{CO}_2$  insufflator setups that allow adjustments to  $\text{CO}_2$  flow, this should be set to the lower flow setting once the submucosal tunnel, and particularly the muscularis propria, is breached. Irrespective of whether an adjustable  $\text{CO}_2$  insufflator is used, the endoscopist should take care to use insufflation sparingly while in the submucosal tunnel. Adverse events related to the use of air insufflation have been reported for some NOTES procedures and more recently during POEM [18].

During dissection, inadvertent perforations of either the longitudinal muscle layer or the mucosa can occur. As mentioned, several centers routinely perform full-thickness myotomies during POEM. However, if a full-thickness muscle breach occurs directly under the initial mucosal incision, consideration should be given to a more robust closure (e.g., endoscopic suturing or an over-the-scope clip) [50]. If the mucosa is breached during tunnel creation, usually by inadvertent energy application, the resulting mucosotomy should be closed with clips to prevent leakage of luminal contents into the submucosal tunnel.

**Table 2** Overview of POEM efficacy data

Location of primary investigator	Year	No. of patients	Age, mean (range) y	Myotomy length, mean (range) cm	Eckardt score <sup>a</sup> (before/after)	LES pressure, mmHg (before/after)	Follow-up, mo	Recurrent dysphagia (no. of patients)	Efficacy, %
Yokohama, Japan [12] (Inoue)	2010	17	41 (18–62)	8.1 (3–15)	10/1.3	52.4/19.8	5 <sup>c</sup>	0	100
Shanghai, China [28] (Zhou) <sup>b</sup>	2012	205	44 (6–75)	10.2 (7–13)	Relief in 199 patients	–	8.5 <sup>c</sup>	3	97
Hamburg, Frankfurt [14] (von Renteln)	2012	16	45 (26–76)	12 (8–17)	7.8/0.7	27.2/11.8	3	1	94
Rome, Italy [15] (Costamagna)	2012	11	41 (23–68)	10	7.1/1.1	45.1/16.9	3	0	100
Portland, Oregon [17] (Swanstrom)	2012	18	59 (22–88)	9 (7–12)	6/0	45/16.8	6	1	94
Hong Kong, China [21] (Chiu)	2013	16	47 (22–87)	10.8 (7–15)	5.5/0	43.6/29.8	3	0	100
Chicago, Illinois [19] (Hungness)	2012	18	38 (22–69)	9 (6–14)	7/1	19/9	6 <sup>d</sup>	2	89
Nagasaki, Japan [25] (Minami)	2013	28	52 (19–84)	14.4 (10–18)	6.7/0.7	71.2/21	16 <sup>d</sup>	0	100
Seoul, Korea [24] (Lee)	2013	13	40 (12–60)	8.5 (6–13)	6.4/0.4	30.3/15.3	6.9 <sup>c</sup>	0	100
European MCT [29] (von Renteln)	2013	70	45	13 (5–23)	6.9/1	27.6/8.9	12	9	82
Mineola, New York [27] (Stavropoulos) <sup>b</sup>	2013	66	52 (18–93)	9 (3–17)	7.9/0.2	42.5/15.4	13 <sup>c</sup>	2	96
Yokohama, Japan [20] (Inoue) <sup>b</sup>	2013	300	45 (3–87)	14.1	6.13/1.33	27.3/13.4	12	5	98
Düsseldorf, Germany [30] (Neuhaus) <sup>b</sup>	2013	21	19–76	12	6.62/1.39	46/22	9 <sup>c</sup>	1	95
Amsterdam, The Netherlands [26] (Fockens)	2013	10	43	–	8/1	20.5/6.8	3	0	100

POEM per-oral endoscopic myotomy, LES lower esophageal sphincter, – data not available, MCT multicenter trial

<sup>a</sup> Eckardt Scale score

<sup>b</sup> Abstracts

<sup>c</sup> Mean follow-up

<sup>d</sup> Median follow-up; remainder are minimum follow-up

**Table 3** Objective measurements of POEM efficacy

Location of primary investigator	No. of patients with TBE data after POEM	Before-POEM TBE	After-POEM TBE
Mineola, New York [27] (Stavropoulos)	26	–	Mean emptying at 5 min 22/26: 100 % emptying 25/26: >50 % emptying
Chicago, Illinois [19] (Hungness)	13	Median height: 1 min 17 cm (9–31) 2 min 16 cm (9–31) 5 min 14 cm (0–31)	Median height: 1 min 7 cm (0–15) 2 min 5 cm (0–13) 5 min 0 cm (0–9) ( <i>p</i> < .001)
Portland, Oregon [17] (Swanstrom)	16	–	Median emptying at 5 min 15/16: 80–100 % emptying 1/16: <80 % emptying
Amsterdam, The Netherlands [26] (Fockens)	10	Median height: 1 min 11.7 cm (IQR 10.4–13.1) 2 min 10.9 cm (IQR 8.8–12.1) 5 min 10.1 cm (IQR 5.7–10.8)	Median height: 1 min 3.2 cm (IQR 0.5–6.5) ( <i>P</i> = .005) 2 min 2.7 cm (IQR 0.4–5.2) ( <i>P</i> = .005) 5 min 2.3 cm (IQR 0–3.2) ( <i>P</i> = .005)

POEM per-oral endoscopic myotomy, TBE timed barium esophagram, – data not available, IQR interquartile range

**Table 4** Approximate incidence of POEM adverse events

Type of risk	Very rare <0.1 %	Rare <1 %	Occasional <10 %	Common >10 %
Anesthesia				
Aspiration	✓			
CO2 retention				✓
Cardiopulmonary compromise			✓	
Operative				
Capnothorax		✓		
Capnoperitoneum				✓ <sup>a</sup>
Mucosal perforation			✓ <sup>a</sup>	
Full-thickness incision into mediastinum at tunnel orifice		✓		
Mediastinal exposure				✓ <sup>b</sup>
Bleeding			✓ <sup>a</sup>	
Postoperative				
Bleeding		✓		
Mediastinitis/abscess/leak	✓			
Other (mucosal slough, pain, food impaction)	✓			

<sup>a</sup> Best considered as technical errors; usually correctable during the procedure without clinical sequelae

<sup>b</sup> Inconsequential, unclear whether it represents a true adverse event; frequently seen, especially with full-thickness myotomy

Bleeding can occur at any point but is most common at or distal to the GEJ. Usually it is immediately controllable via coagulation with the tip of the knife, but availability of an electrosurgical hemostatic forceps (e.g., Coagrasper; Olympus, Center Valley, Pa) for coagulation of larger

vessels is essential. When the bleeding overwhelms endoscopic visualization, some investigators have anecdotally reported success in achieving temporary hemostasis by removing the endoscope from the tunnel, advancing it into the true lumen, and using the tip of the endoscope to



**Table 5** Subjective and objective GERD data on patients with POEM

Location of primary investigator	No. of patients	Follow-up, mo	GERD symptoms	GERD endoscopic evidence (erosions)	Esophageal pH data
Yokohama, Japan [12] (Inoue)	17	5 <sup>a</sup>	6 %	Esophagitis LA class B 1/17 (6 %)	–
Yokohama, Japan [13] (Inoue)	105	11 <sup>a</sup>	5.7 %	Esophagitis 18 (17 %)	–
Yokohama, Japan [20] (Inoue)	300	–	4.9 %	–	–
Portland, Oregon [17] (Swanstrom)	18	6	33 %	Esophagitis Savory-Miller grade 14/14 (28 %)	6/13 (46 %)
Hamburg, Frankfurt [14] (von Renteln)	16	3	0 %	Esophagitis LA class A 1/16 (6.3 %)	–
European MCT [29] (von Renteln)	70	10.1 <sup>a</sup>	1.5 % daily; 31.3 % occasional at 3 mo. 6.6 % daily; 23.4 % occasional at 6 mo. 7.8 % daily; 29.4 % occasional at 12 mo.	Esophagitis (42 %) LA class A (29.2 %) B (12.3 %)	–
Rome, Italy [15] (Costamagna)	11	3	0 %	0	–
Chicago, Illinois [19] (Hungness)	18	6 <sup>b</sup>	22 %	Esophagitis  LA class A 2/15 (13.3 %) B 2/15 (13.3 %) C 1/15 (6.7 %)	–
Hong Kong, China [21] (Chiu)	16	3	6.3 %	–	3/15 (20 %)
Mineola, New York [27] (Stavropoulos)	66	13 <sup>a</sup>	27 % rarely; 4 % few times a week; 11 % daily	10/33 (30 %)	12/33 (36 %)
Nagasaki, Japan [25] (Minami)	28	3	6/28	Esophagitis 11/28 (39.3 %) LA class M 2/28 A 7/28 B 1/28 C 1/28	–
Amsterdam, The Netherlands [26] (Fockens)	10	3	30 %	Esophagitis (60 %)  LA class A 3/10 (30 %) B 3/10 (30 %)	Only 1 patient reported

*POEM* per-oral endoscopic myotomy, *LA class* Los Angeles classification, – data not available, *MCT* multicenter trial

<sup>a</sup> Mean follow-up; remaining follow-up values represent minimum follow-up in months

<sup>b</sup> Median follow-up

compress the tunnel at the bleeding site for 10–20 min; this may be performed by using the cap at the tip of the endoscope, or a CRE balloon may be used to tamponade the bleeding vessel.

Problems related to CO<sub>2</sub> insufflation may occur with potentially detrimental physiologic effects. Significant subcutaneous emphysema may occur 10–15 % of the time, but this usually is well-tolerated. Capnothorax is rare (<5 % of cases) and may be well-tolerated; however, if significant hemodynamic changes occur, a needle or tube thoracostomy should be expeditiously performed to prevent tension pneumothorax and worsening hemodynamic instability or collapse. Capnoperitoneum happens

frequently (>50 %) and usually is clinically insignificant. However, if ventilatory compromise is noted, treatment options include Veress needle insertion or, rarely, laparoscopic port placement and venting. Teams performing POEM should be familiar with these techniques.

#### *Postoperative adverse events*

The most feared potential adverse event of POEM has been mediastinitis from an esophageal leak. In over 1,000 patients described to date, the incidence of leaks has been remarkably low, and no deaths have been reported. Two leaks (0.2 %) were reported in the IPOEMS data (1 each

**Table 6** Training described in published series

Publication	Laboratory training	Observing/proctoring	Comments related to training
von Renteln 2012 [14] Costamagna 2012 [15]		First 2 cases proctored First 3 cases proctored	POEM appears to be a promising but extremely sophisticated and demanding technique, with a very gradual learning curve. This approach should be therefore performed only by a skilled endoscopist, well trained in ESD techniques, in referral centers.
Ren 2012 [18]			POEM surgery is a difficult procedure to perform and the skills required are great. Only those who have mastered ESD surgery and who have some experience in handling ESD adverse events such as a hemorrhage or perforation are suited to perform POEM surgery.
Kurian 2013 [33]	Pre-clinical training in ex vivo and live porcine model and cadavers	Observed first 3 cases performed by experienced POEM practitioner	Laboratory or simulator training before starting this novel procedure on humans would seem to be mandatory. Proctoring for initial cases by an experienced POEM practitioner would likewise seem to be reasonable, but there are no current guidelines or data that would define how many cases of supervision are needed before competence is obtained.
Teitelbaum 2013 [38]	Preclinical training in both live porcine and human cadaver models	Observed cases performed by experienced POEM practitioner	These surgeons reported that adoption of POEM by their facility was partially because they had “performed various interventional endoscopic procedures prior to POEM, including hybrid transvaginal and transgastric NOTES cholecystectomies using a flexible endoscope.”

POEM per-oral endoscopic myotomy, NOTES natural orifice transluminal endoscopic surgery

from 2 US centers) [1]. Two leaks were reported in subsequent publications, one each from 2 US centers. Both were managed by surgical drainage, with modest morbidity [19, 51]. Postoperative bleeding has been identified as a potential concern, but the incidence appears quite low. Eight postoperative bleeding events (1 %) were reported in IPOEMS [1], and a total of 7 such events were reported in 3 prospective series, with rates of 0.7 % [44], 3 % [29], and 7 % [25], respectively. These bleeding episodes were managed conservatively with hospital observation and/or transfusions and, occasionally, in Asian centers, with endoscopic re-exploration of the tunnel and endoscopic hemostasis or tamponade with Blakemore-type balloons [18, 52]. Other very rare and unusual adverse events have been anecdotally presented and may be center dependent and of little general significance, for example, acute mucosal sloughing, food impaction, and intractable nausea.

#### Late adverse events

Treatment failure caused by incomplete myotomy or GERD are the two most relevant potential late adverse events for POEM. Short-term and intermediate-term data on treatment failure have been reviewed in the section on

POEM efficacy (Table 2). Long-term data are anticipated. Recent studies indicate that, based on objective data (erosive esophagitis on EGD and/or abnormal pH study), GERD prevalence may be 20–46 % after POEM, which is higher than early reports that were largely based on symptom scores or questionnaires (Table 5) [12–15, 17, 19–21, 25–27, 29]. Nevertheless, this prevalence is similar to that observed after surgical Heller myotomy with Dor fundoplication in high-quality prospective trials [53, 54]. The group from Portland, Oregon, reported in a small, retrospective study no statistically significant difference in GERD prevalence on pH studies between patients who had POEM or Heller myotomy with fundoplication (39 vs 32 %;  $p = .7$ ) [55].

#### Training for POEM

Training for POEM is unique in several ways. POEM requires specific knowledge, judgment, and technical skills that may be unfamiliar to many individual practitioners. Specific training may be required to become competent in all of the requisite areas. Indeed, POEM requires a skill set that spans both surgery and gastroenterology. It requires

**Table 7** Retrospective comparison of POEM and LHM (Evanston data) [51]

	POEM	LHM	p
No. of patients	18	21	NS
Age, mean $\pm$ SD (y)	64.1 $\pm$ 4.8	60.2 $\pm$ 4.7	NS
Prior achalasia treatment (n)	13	13	NS
BI	4	2	
PD	4	4	
HM	3	3	
BI and PD	2	4	
ASA classification, mean $\pm$ SD	2.3 $\pm$ 0.1	2.5 $\pm$ 0.1	NS
Sex, male/female	13/5	12/19	NS
Operation time, mean $\pm$ SD (min)	155.8 $\pm$ 12.8	154.5 $\pm$ 8.3	NS
Veress needle placed (n)	3	–	NS
Myotomy length, mean $\pm$ SD (cm)	11.2 $\pm$ 2.7	10	NS
Pain medication, mean $\pm$ SD	26 $\pm$ 13.7	90 $\pm$ 48.5	.02
Return to activities of daily living, mean $\pm$ SD (d)	2.2 $\pm$ 0.6	6.4 $\pm$ 1	.03
Length of hospitalization, mean $\pm$ SD (d)	3.4 $\pm$ 1.3	3.4 $\pm$ 0.9	NS
Major adverse event	Leak noted on postoperative day 8 requiring laparoscopic drain placement	Leak noted on postoperative day 7 requiring drainage and repair	
Eckardt Scale score (range 0–12), preoperative/postoperative	6.4/0.7	5.4/1	NS
GERD symptoms, no. patients of total	3/18	4/21	NS

*POEM* per-oral endoscopic myotomy, *LHM* laparoscopic Heller myotomy, *NS* not significant, *PD* pneumatic dilation, *HM* Heller myotomy, *BI* Botox injection, *SD* standard deviation, *BI* botulinum toxin injection, *HM* Heller myotomy, *ASA* American Society of Anesthesiologists Physical Status Classification System, – not available

familiarity and ease with a flexible endoscope as well as the ability to recognize anatomy, maintain orientation, and manage adverse events. A thorough understanding of the pathophysiology and treatment options for achalasia is another essential component. POEM, however, is a

treatment for a rare disease, providing limited opportunity for teaching.

Published POEM series to date either do not mention training strategies at all or briefly mention animal experience and proctoring of the first few cases [12–30]. There is very little published information concerning the extent and goals of preclinical animal or cadaver training and proctoring (Table 6). Kurian et al. [33] analyzed the learning curve for their first 40 POEMs. They used duration of procedure per centimeter of myotomy and incidence of unintended mucosectomies as outcome measures and performed a simple analysis of comparing these two outcomes in five successive blocks of eight procedures each. The learning curve seemed to plateau but not stop at around 20 procedures. A subsequent study that also was based on a small number of procedures (36) found improvement in incidence of accidental mucosectomies and number of clips used and in mucosal entry and myotomy times (both demonstrating a “learning rate” of seven procedures) but not submucosal tunneling times [38]. Submucosal tunneling is arguably the most challenging component of POEM, with possibly the longest learning curve, and this study may have lacked a sufficient number of cases to detect improvement. Based on data from a single-center, single-operator series of 93 POEMs, by using penalized B-spline regression analysis of POEM total procedure times, relative proficiency appears to be attained after 56 procedures. By using cumulative sum analysis, efficiency is achieved after 40 procedures and mastery after 60 procedures [56].

Data accumulated from IPOEMS provided significant information regarding preclinical training and proctoring as well as prior experience of POEM operators with ESD and NOTES, procedures having skill sets that overlap with those of POEM [1]. In this survey, gastroenterologists had more experience in human ESD and endoscopic management of achalasia, whereas surgeons had more experience in human NOTES and Heller myotomy [1]. All gastroenterologists had some experience with endoscopic management of achalasia, whereas many surgeons had none [1]. Ten of the 16 IPOEMS respondents practiced POEM in a model prior to doing human cases, the most popular being a live, porcine model [1]. Greater than 50 % of POEM practitioners considered pre-clinical training mandatory prior to human POEM. All centers surveyed considered proctoring to be either required (56.3 %) or recommended (43.8 %) [1]. Nine of 16 centers (56.3 %) had an outside POEM expert proctor their first cases [1]. The number of proctored cases ranged from 1 to 7 (median 2) [1].

Successful completion of the “fundamentals” programs offered by the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)/American Society for Gastrointestinal Endoscopy didactic and hands-on seminars

**Table 8** Retrospective comparison of POEM and LHM (Chicago data [19])

	POEM	LHM	p value
No. of patients	18	55	
Age, (range), y	38 (22–69)	49 (22–79)	.03
Prior achalasia treatment	None	None	
Anatomic type	Non-sigmoid	Non-sigmoid	
Sex, female/male	5/13	26/29	NS
Duration of symptoms, no. (range) y	1 (.13–30)	1.25 (.25–15)	NS
Operation time, no. (range) min	113 (88–220)	125 (90–195)	< .05
Estimated blood loss, no. (range) mL	≤10 in all cases	50 (10–250)	< .001
Myotomy length, no. (range) cm	9 (6–14)	8.5 (7–10)	NS
Pain score immediately postoperative (0–10), no. (range)	2.5 (0–9)	2 (0–9)	NS
Pain score 2 h postoperative, no. (range)	3.5 (0–8)	2 (0–10)	.03
Pain score on postoperative day 1, no. (range)	1.5 (0–8)	2 (0–10)	NS
Use of narcotics on the day of surgery (mg morphine equivalents)	8.5 (0–36)	6.7 (0–31.4)	NS
Use of narcotics on postoperative day 1	2.5 (0–21)	3.3 (0–18)	NS
Length of hospitalization, no. (range) d	1 (1–13)	1 (1–19)	NS
Minor adverse events, no. (%)	3 (17 %)	7 (13 %)	NS
Major adverse event	A contained leak at the GEJ requiring laparoscopic drain placement	Delayed esophageal leak requiring thoracotomy for drainage and repair	
Preoperative vs 6-week postoperative LES basal and relaxation pressure (mmHg)	Basal: 19 (7–51) vs 9 (0–23) Relaxation: 21 (10–59) vs 12 (6–18)		Both .001
Timed barium esophagram column heights at 1, 2, and 5 min preoperative vs 6-week postoperative, cm	17 vs 716 vs 514 vs 0		All ≤ .001

*POEM* per-oral endoscopic myotomy, *LHM* laparoscopic Heller myotomy, *NS* not significant, *GEJ* gastroesophageal junction, *LES* lower esophageal sphincter

**Table 9** Comparison of POEM and LHM (European data [57])

	POEM	LHM	p value
No. of patients	70	110	
Preoperative Eckardt score	6.91	7.23	.325
Postoperative Eckardt score	0.97	1.43	.05
LES pressure before treatment (mmHg)	27.6	28.5	.659
LES pressure after treatment (mmHg)	8.9	11.7	.01
Reflux symptoms	None 67.2 %Occasional 31.3 %Daily 1.5 %	–	–
<i>POEM</i> per-oral endoscopic myotomy, <i>LHM</i> laparoscopic Heller myotomy, <i>LES</i> lower esophageal sphincter, – data not available	Endoscopic evidence for GERD (erosions)	None 72.1 %Grade A 16.3 %Grade B 11.5 %	.213
	Proton pump inhibitor use	None 78.9 %Occasional 15.6 %Daily 5.6 %	.055

may serve as a foundation for learning POEM. If there is no experience with ESD, experience at animal laboratories, preceded by viewing POEM videos, may be a reasonable starting point. Observation of human cases should be the next step, followed by proctoring with feedback. All

outcomes should be reported. More than one proctoring session may be necessary, with return to the animal laboratory, as needed, especially if there are long periods of time between human cases. A dedicated team that remains consistent throughout the learning curve may best support

POEM. It should be emphasized that, apart from technical expertise, institutional experience in treating patients with esophageal motility disorders should be present.

#### Starting a POEM program

There are five steps in starting a POEM program: collaboration, training, institutional support, institutional review board approval, and technical support. Training was covered earlier in this white paper.

#### Collaborators

It is important to identify individuals who wish to pursue the program. Teams comprising interventional endoscopists and foregut surgeons are ideal. Although a surgeon or interventional gastroenterologist could start a POEM program alone, each will benefit from the other's expertise.

#### Institutional support, coding and reimbursement

Because of medicolegal and reimbursement issues, approval at all levels from the institution is required. It is important to obtain the support of the division chief, department chair, and director of the surgical or endoscopy unit. Informing the credentialing committee is advisable. Given the recommendation for animal laboratory training, approval from the institutional animal care and use committee would be required.

Currently, there is no dedicated billing code for POEM in the United States. Based on data from the 6 U.S. centers that participated in IPOEMS, augmented by informally polling additional US centers, most US centers use the *unlisted esophageal surgery* code (43499), and a few use codes for *EGD with injection of any substance* and *tissue ablation*, or *thoracoscopic Heller myotomy* [1].

#### Institutional review board approval

Because POEM is a new procedure without robust, long-term follow-up data, the vast majority of POEM operators agree that POEM should be done under institutional review board oversight [1], such that outcomes data may be collected and published.

#### Technical support

It is prudent to obtain support from the surgical or endoscopy technologists and nurses and from industry representatives, who can help troubleshoot devices and accessories. Team training is critical. The post-anesthesia care unit personnel and ward nurses should know about the procedure and what types of adverse events to expect.

**Table 10** Comparison of POEM and LHM (Portland data [55])

	POEM	LHM	p value
No. of patients	37	64	
Age, mean (y)	56	57	.7
Operative time (min)	120	160	.003
Preoperative Eckardt score	5.4	5.9	.5
Postoperative Eckardt score	.8	1.8	< .0001
Early dysphagia (2 weeks after surgery)	5 %	10 %	.4
Long-term dysphagia (6 months after surgery)	0 %	29 %	.001
LES pressure before treatment, median (mmHg)	41	37	.2
LES pressure after treatment, median (mmHg)	16	7	.006
Adverse events (n)			
Full-thickness injury	4	11	NS
Bleeding	1	1	
Length of stay, mean (d)	1.1	2.5	< .0001
24-h pH study	39 %	32 %	.7

POEM per-oral endoscopic myotomy, LHM laparoscopic Heller myotomy, LES lower esophageal sphincter, NS not significant

Starting a POEM program is labor intensive. Collaboration, proper training and hands-on experience, institutional support, institutional review board approval, and cooperation from surgery or endoscopy unit staff are key aspects to the creation of a successful program.

#### Future perspectives on POEM

Although the initial results of POEM procedures are encouraging, with excellent short-term outcomes, there are many questions still unanswered. Most importantly, longer follow-up data are needed to understand the durability of symptom relief and to better evaluate the intermediate and long-term adverse events and outcomes. Additional information is needed regarding factors that may affect the success of POEM, including prior therapies such as BI, balloon dilation, or LHM.

POEM will need to be compared, prospectively, against other established techniques such as pneumatic dilation and LHM. Small, retrospective series suggest that POEM and LHM have similar short-term efficacy and safety (Tables 7, 8, 9, 10) [19, 51, 55, 57, 58]. High-quality comparative data from prospective, randomized, controlled trials comparing POEM to pneumatic dilation and LHM would be valuable, and such multicenter trials are underway in Europe. In the United States, given the rapid adoption of POEM by both physicians and patients, its minimal invasiveness, the fact that it essentially represents a Heller myotomy by a

per-oral route, and the uniformly excellent outcomes on prospective series now totaling close to 1,000 patients worldwide, it will be increasingly difficult to enroll patients in randomized trials, particularly those that include LHM. Patient enrollment may be somewhat easier for trials comparing POEM to balloon dilation, which is less invasive than POEM and in which POEM can be reasonably offered as a second-line salvage approach for balloon dilation failures.

As more experience is gained with POEM, advances likely will be made in terms of modifying the procedure to further improve outcomes and minimize risks. The indications for POEM likely will expand beyond classic achalasia as data on POEM's efficacy for other esophageal motility disorders accumulate.

## Conclusion

POEM represents a NOTES approach to Heller myotomy that promises the efficacy and durability of LHM with the minimal invasiveness of endoscopy. It is estimated that over 2,000 POEMs have been performed at expert centers worldwide over the past 5 years. Published studies reporting outcomes of approximately 1,000 POEMs at a mean follow-up of 3–12 months are very encouraging, with clinical success of 82–100 %, self-limited adverse events occurring in <10 % of cases, negligible severe morbidity, and no mortality. On objective testing, the rate of GERD after POEM is 20–46 %, which may not be significantly different from that observed after LHM with Dor fundoplication. Starting a POEM program requires a multidisciplinary team with expertise in surgery, advanced endoscopy, and esophageal physiology and methodical preparation that includes training in animal models, proctoring of initial cases, and institutional review board oversight. The initial favorable outcomes suggest a promising future for POEM.

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