

Per-Oral Esophageal Myotomy Is It a Safe and Durable Procedure for Achalasia?

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Keywords

- Peroral endoscopic myotomy
- Achalasia
- Interventional endoscopy
- Laparoscopic Heller myotomy

Key points

- Adequate surgical knowledge and endoscopic skill is a necessity, with appropriate preclinical training in a high-volume esophageal center.
- A learning curve of approximately 20 cases exists for straightforward cases.
- Per-oral esophageal myotomy (POEM) has durable relief of dysphagia and regurgitation with appropriate decreases in lower esophageal sphincter pressure and esophageal bolus clearance.
- Rates of gastroesophageal reflux disease after POEM may be slightly higher, but are comparable with that seen after laparoscopic Heller myotomy.
- Long-term clinical and cost-effectiveness studies are needed to fully understand the impact of POEM for the treatment of achalasia.

INTRODUCTION

Idiopathic achalasia is the most common primary esophageal motility disorder, estimated to affect 1 to 2 per 100,000 in the population [1]. Characterized by failure of relaxation of the lower esophageal sphincter in response to a swallow and loss of coordinated peristalsis in the distal esophageal body, achalasia results in dysphagia and regurgitation. Treatment has traditionally been

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accomplished by surgical disruption of the lower esophageal sphincter with a laparoscopic Heller myotomy (LHM).

Based on endoscopic submucosal dissection (ESD) techniques, Inoue performed the first clinical per-oral esophageal myotomy (POEM) in Japan in 2008. Subsequently, an estimated 5000 POEMs worldwide have been performed for patients with achalasia as well as other esophageal motility disorders. Although the reported early to midterm outcomes after POEM have been excellent thus far [2–12], there are limited studies with longer term results that include robust physiologic data. As with other promising, novel techniques, key questions regarding where POEM should be performed as well as safety and durability must be answered. We discuss existing data regarding safety and durability of POEM, specifically addressing the skill set required, aspiration precautions, the standardization of POEM, learning curve, complications, appropriate preoperative workup and postprocedure follow-up.

HIGH-VOLUME ACHALASIA/ESOPHAGEAL CENTER

Preoperative workup and diagnosis

Owing to the rarity of achalasia, POEM should be done in centers with significant achalasia and esophageal volume. Validated, disease-specific questionnaires can help to establish the diagnosis of achalasia, assess disease severity, and establish baseline values to compare against to evaluate treatment success. The most widely used and reported instrument for achalasia is the 4-item Eckardt symptom score (Table 1) [13]. Higher scores represent increasingly severe disease, and postintervention scores of less than or equal to 3 are associated with treatment success [6].

Diagnostic studies to confirm and characterize achalasia include timed barium esophagram, esophagogastroduodenoscopy, and esophageal manometry. Timed barium esophagram is useful for both the evaluation of esophageal body and esophagogastric junction (EGJ) anatomy and to quantify a baseline height of the barium column and degree of esophageal emptying. It also allows detection of sigmoid esophagus, hiatal hernia, and epiphrenic diverticulae. Esophagogastroduodenoscopy is a required part of the achalasia preoperative

Table 1

The Eckardt symptom score

Symptom	Score			
	0	1	2	3
Dysphagia	None	Occasional	Daily	With every meal
Regurgitation	None	Occasional	Daily	With every meal
Chest pain	None	Occasional	Daily	Several times a day
Weight loss (kg)	0	<5	5–10	>10

The scores from the 4 symptom domains are summed to create a total score ranging from 0 to 12, with higher scores indicating worse disease severity.

workup to rule out pseudoachalasia. High-resolution esophageal manometry is the gold standard for confirming the diagnosis of idiopathic achalasia, given its increased sensitivity in the diagnosis of esophageal motility disorders and its ability to subcategorize achalasia patients according to the Chicago Classification system [8,14]. Type III achalasia, associated with premature, spastic contractions of the distal esophagus and impaired EGJ relaxation, has the worst prognosis [15] and may be better treated with POEM owing to the ability to extend the myotomy proximally.

Patients typically are restricted to a clear liquid diet for 48 hours and kept nil per os (NPO) overnight before the procedure. A 7-day preoperative course of oral fluconazole is prescribed preoperatively as prophylaxis against esophageal candidiasis. Prophylactic aspirin and clopidogrel are typically held for 7 and 5 days preoperatively, respectively.

Postoperative and long-term follow-up

Immediate postoperative care includes the administration of standing intravenous antiemetics and analgesia as needed, and NPO status pending further evaluation. In the absence of concerning symptoms or signs that suggest leak, patients are given a tray of clear liquids the next morning and discharged after tolerating a full liquid lunch. A full liquid diet is maintained until the first clinic visit at 1 to 2 weeks, at which point soft foods and then solids are gradually introduced.

Patients are discharged on daily proton pump inhibitors (PPI) that are continued until physiologic, off-PPI 24-hour pH testing can be performed at 6 months to assess for the presence or degree of gastroesophageal reflux (GER). If this study is normal the PPI is stopped, but if abnormal esophageal acid exposure is seen, PPI therapy is continued indefinitely. In addition to the 24-hour pH study, we perform routine follow-up high-resolution manometry, upper endoscopy, and timed contrast esophagram at 6 to 12 months after POEM. Physiologic follow-up every 3 years after treatment is performed, with completion of validated questionnaires and intermittent physiologic testing to track long-term outcomes.

SAFETY

Although POEM is seemingly less invasive than LHM, it should still be considered a major operation, and serious complications can occur; esophageal perforation, pneumothorax, and subcutaneous emphysema have been reported [4–6,16,17]. Risk of adverse events ranging from capnoperitoneum and post-procedural esophagitis to inadvertent mucosotomy is around 14%, with the vast majority being self-limited and requiring little additional intervention. The chance of requiring an additional surgery after POEM for complications is approximately 0.2% [17]. The safety of POEM depends on skill set, learning curve, the risk of aspiration, standardization of the POEM procedure, CO₂ consideration, and bleeding.

Adequate skill set

Technically, POEM most closely resembles ESD, although clinical experience with ESD should not be seen as a prerequisite for POEM. A surgeon who has substantial experience with interventional flexible endoscopy as well as LHM is well suited to learn the techniques required for POEM. However, some form of laboratory training, ideally including an instructed course, should be undertaken before transitioning to performing POEM clinically. Physicians new to POEM should consider proctoring by an operator with significant experience for at least their first clinical case.

Learning curve

The POEM learning curve has been evaluated by several centers including ours [10,18,19]. Various metrics of proficiency include number of inadvertent mucosotomies, number of cases to achieve submucosal access and perform myotomy, and length of time of the procedure. A learning curve “plateau” of around 20 cases has been proposed by some [19], although other series have determined efficiency to be achieved after 40 cases and mastery after 60 cases [10].

Aspiration precautions

Because of chronic esophageal dilatation secondary to outflow obstruction, food clearance is poor in patients with achalasia and leads to a very high aspiration risk. Preoperative dietary restriction to clear liquids for 2 days in preparation for the procedure as well as the use of a “rapid sequence” intubation technique by anesthesia (limited preoxygenation/bag masking) can help to minimize the risk of aspiration during induction. If needed, awake fiberoptic intubation in the upright position can be used in the patients at greatest risk.

Standardized procedure (critical steps and error avoidance)

As with any surgery, establishing a standardized procedure and identifying critical steps is crucial to error avoidance and outcome optimization. We attempt to highlight key elements of the procedure in the context of promoting a safe operation.

POEM often is performed in an operating room, although it can be done in an advanced endoscopy suite. The equipment and ability to decompress the abdomen and/or bilateral pleural spaces must be available immediately. Once the endotracheal tube is positioned and secured to the right, the abdomen is prepped and draped to provide access in the event that Veress needle decompression of a capnoperitoneum is required.

A mucosotomy is made 12 cm above the EGJ (can be increased when a longer myotomy is planned) by first using an endoscopic needle to create a submucosal wheal at the planned starting location. We use a saline solution containing dilute indigo carmine (or methylene blue) and epinephrine (only added for the initial injection and at the GEJ). The electrocautery knife is used to create a 1- to 2-cm longitudinal mucosotomy overlying the bleb (Fig. 1). The submucosal tissue underlying the mucosotomy is cleared with

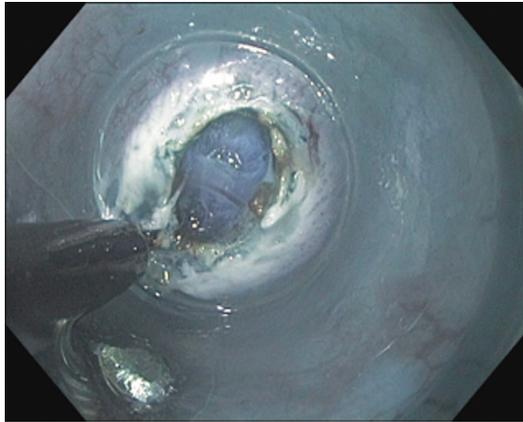


Fig. 1. A longitudinal mucosotomy is created in the anterior esophagus approximately 12 cm proximal to the esophagogastric junction. The transparent dissecting cap can be seen circumferentially toward the outside of the endoscopic image.

cautery, so that the circular muscle layer is exposed, and the scope bluntly maneuvered through the mucosotomy and into the submucosal space.

Once the scope is in the submucosal space, a longitudinal tunnel is created down the length of the anterior esophageal body, across the EGJ, and onto the stomach wall using a combination of blunt and electrocautery dissection. Distal progression of the submucosal tunnel is facilitated by alternating hydrodissection (with additional saline solution) and cautery to divide the thin fibers connecting the mucosa to the inner, circular muscle layer (Fig. 2). The

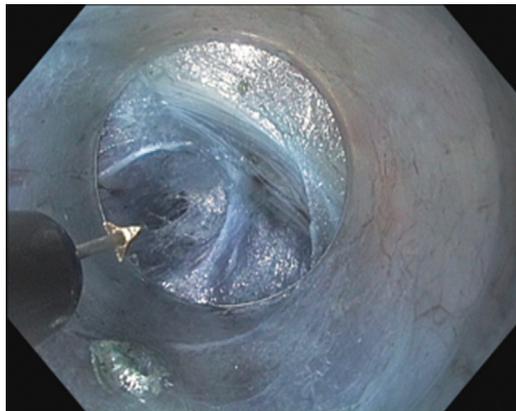


Fig. 2. A view from inside the submucosal tunnel, which is dissected clear from the mucosotomy to at least 3 cm distal to the esophagogastric junction.

dissecting cap is used to push the muscle layer anteriorly and the mucosa posteriorly, creating a wide “zone of safety” and allowing for safe cauterization of the submucosal tissue (Fig. 3). Dissection should trend toward the muscle side (ie, anteriorly) to help avoid mucosal injury and perforation. Because failure to achieve symptomatic relief after LHM has been linked to inadequate distal myotomy length [20], it is essential during POEM that the tunnel and myotomy extend at least 2 cm beyond the EGJ. Using scope markings alone to gauge tunnel length is often inaccurate owing to scope bowing. Anatomic evidence of the EGJ is provided when the muscle and mucosa become much more closely adhered, narrowing the zone of areolar tissue between them. Dissection at this level is more difficult, especially in the context of prior episodes of inflammation or previous treatment modalities such as pneumatic dilatation. Beyond the EGJ, the area between the muscle and mucosa widens again and blood vessel architecture changes. Switching back to an injection solution containing both dye and dilute epinephrine can aid in demarcating the distal extent of the submucosal tunnel (the endoscope can be withdrawn from the submucosal tunnel and passed into the stomach lumen to obtain a retroflex view of the EGJ; Fig. 4).

A myotomy is performed starting 6 cm proximal to the EGJ and advancing to the distal end of the submucosal tunnel, approximately 2 to 3 cm distal to the EGJ. In contrast with a Heller myotomy, during POEM a selective division of only the circular muscle layer is performed. The ESD knife cauterizes the inner circular muscle layer to create a starting point for the myotomy, then takes advantage of the plane between the thick circular and thin, outer longitudinal

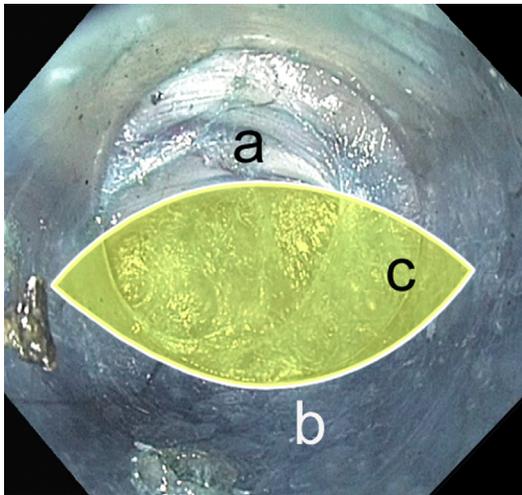


Fig. 3. The dissecting cap pushes the circular muscle layer (a) anteriorly and the mucosa (b) posteriorly, creating a wide zone of areolar tissue (c), which is highlighted in this image.

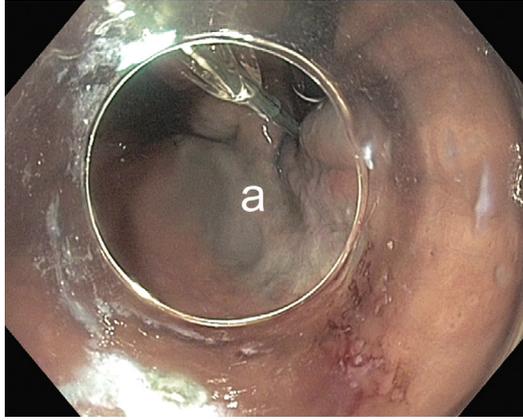


Fig. 4. The distal extent of the submucosal tunnel is assessed by advancing the scope into the stomach. Here on retroflexed view, blue dye from the tunnel can be seen through the gastric mucosa (a), advancing well past the esophagogastric junction.

muscle layers to hook the circular muscle fibers and extend the myotomy distally (Fig. 5). Full-thickness myotomy or splaying of the thin, outer longitudinal muscle fibers is common, especially around the EGJ, potentially exposing the mediastinum. Tracking of CO₂ may cause capnoperitoneum, potentially requiring decompression with a Veress needle or similar device for the remainder of the operation.

Upon myotomy completion, a variety of intraoperative techniques can be used to evaluate for adequacy in relieving esophageal outflow obstruction at

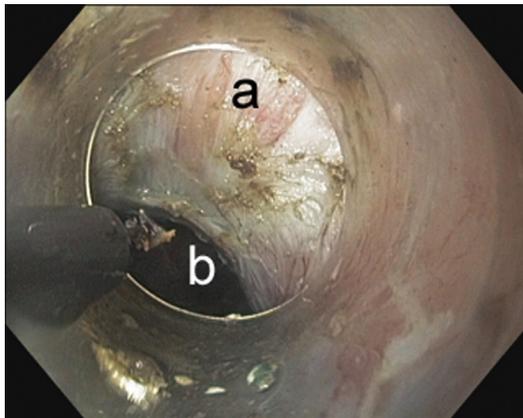


Fig. 5. As the myotomy progresses from proximal to distal, the longitudinal muscle layer (a) is left intact, while the circular fibers (b) are divided selectively.

the level of the EGJ. These can be subjective, based on endoscopic inspection or ease of passage of the endoscope postmyotomy, or quantitative (EGJ distensibility index measurements using the EndoFLIP [21]). The submucosal tunnel is then irrigated with antibiotic solution and the mucosotomy closed with endoscopic clips (Fig. 6).

CO₂ insufflation

Capnoperitoneum occurs in up to 40% to 50% of patients during POEM and should not be considered a complication [9]. Capnothorax progressing to tension physiology or hemodynamic compromise is exceedingly rare, but any sudden hemodynamic instability should be assumed to be a result of tension pneumothorax until proven otherwise. The ability and equipment needed to decompress both pleural cavities should be immediately available during the procedure. Diffuse abdominal distension, especially if accompanied by hemodynamic instability or impaired ventilation, is an indication for decompression with a Veress needle (typically in the right upper quadrant, just inferior to the costal margin), but only after the stomach has been decompressed endoscopically.

Bleeding

Bleeding is most commonly encountered complication during dissection across and distal to the EGJ. Even mild hypertension will compound the bleeding risk inherent to the increased vascularity in the submucosal space of the EGJ and gastric cardia. Mild bleeding can be controlled with application of monopolar electrocautery, whereas brisker bleeding (from larger bridging vessels), should be approached with coagulation forceps. Submucosal tunnel bleeding that obscures visualization can occasionally be temporized by removal of the endoscope from the tunnel and application of direct pressure with the scope or

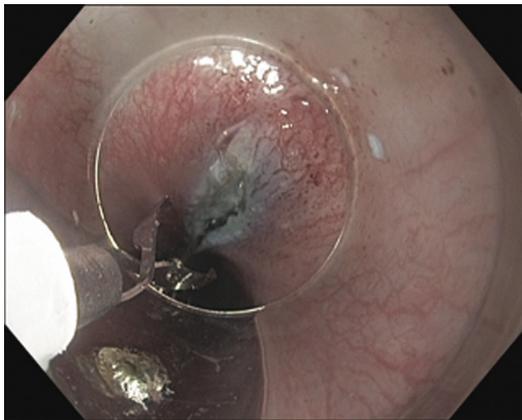


Fig. 6. To complete the procedure, the mucosotomy is closed from distal to proximal with endoscopic clips.

cap from the esophageal lumen for 10 to 20 minutes. Alternative techniques include hemostatic clip application and judicious injection of dilute epinephrine. High-pressure balloons used to control esophageal varices should not be used given the disastrous consequences of esophageal perforation in the setting of a partial or full-thickness myotomy.

DURABILITY

Learning curve

Early published POEM outcomes included data from initial learning cases. A multicenter European POEM trial, in which approximately 1 in 5 patients suffered a recurrence of symptoms or required further intervention [12], raised questions of POEM durability. However, one-half of the treatment failures occurred during the initial 10 cases performed at each participating center, suggesting that a learning curve effect may have biased the estimate of long-term treatment success rate.

Symptomatic relief

Without a cure, current treatment of achalasia is based solely on symptomatic relief. Eckardt score comparison before and after POEM is an objective way to evaluate procedural efficacy. One- to 2-year data confirm that POEM results in significant reduction of Eckardt score with a success rate of 90% to 100% [18,22,23] (Table 2). Two-year and longer outcome data demonstrates some

Table 2
Outcomes from initial published POEM case series

Series	Patients	Follow-up interval (mo)	Clinical success % (ie, Eckardt ≤ 3)	Symptomatic GER (%)	EGJ pressure (mm Hg)	
					Preoperative	Postoperative
Inoue et al [2], 2010	17	—	100 ^a	6	52	20
Costamagna et al [4], 2012	10	3	100	0	45	17
von Renteln et al [3], 2012	16	3	94	0	27	12
Swanstrom et al [5], 2012	18	6	100	33	29	9
Hungness et al [6], 2013	18	6	89	22	21	12
Lee et al [35], 2013	13	6	100	—	26	11

Abbreviations: EGJ, esophagogastric junction; GER, gastroesophageal reflux; POEM, per-oral esophageal myotomy.

^aEckardt symptom score not used.

decrease in those percentages, but success still remains, on average, around 90% (Table 3). This outcome is comparable with LHM [24–26], suggesting durability of the POEM procedure. A metaanalysis comparing LHM and POEM (1-year follow-up average) demonstrates no difference for reduction in Eckardt score [27]. Additionally, operative time, postoperative pain scores, analgesic requirements, and complications are similar, whereas duration of hospital stay is significantly lower for POEM. The high rate of symptomatic relief achieved in patients with type III achalasia, a group that has traditionally been regarded as more difficult to treat, provides additional evidence to support the benefit of performing an extended proximal myotomy in those patients [28].

Improved physiologic outcomes

In addition to a profound resolution of symptoms, POEM seems to result in a normalization of EGJ pressures as measured by manometry (see Table 2). There is also emerging evidence that POEM often results in a return of some degree of peristalsis of the esophageal body, contradicting the long-held dogma that achalasia causes irreversible esophageal dysfunction [20]. It will be important for all centers performing POEM to conduct routine preoperative and postoperative high-resolution manometry on all surgical myotomy patients (both POEM and Heller myotomy) to elucidate whether these operations result in differential effects on esophageal and EGJ physiology.

Postprocedure gastroesophageal reflux

As with LHM, postprocedural GER rates after POEM procedure are a topic of close interest. A number of things make this subject not easily characterized.

Table 3

Outcomes from recent POEM series with longer term follow-up

Series	Patients	Follow-up interval (mo)	Clinical success % (ie, Eckardt \leq 3)	Eckardt score (pre/post)	4-Second IRP (pre/post)	Objective GER
Werner et al [12], 2015	80	29	78.5	8/2	31.9/10.1	NR (37% symptomatic)
Chen et al [36], 2015	45	24	100	6/1	24.9/11.1	NR
Inoue et al [29], 2015	500	>36 (61 patients)	88.5	6/1	25.4/11.7 ^a	24% ^b
Hungness et al [28], 2016	112	24	92	7/1	31/12	40% (27/68)

Abbreviations: GER, gastroesophageal reflux; IRP, integrated relaxation pressure; NR, not reported; POEM, per-oral esophageal myotomy.

^aReported as "lower esophageal pressure."

^bReflux esophagitis > LA grade A in 45 of 191 at 1 to 2 years of follow-up.

First, the mechanism by which GER is prevented anatomically and physiologically is complex. Second, alteration of that mechanism via myotomy, hiatal disruption/repair, dissection/alteration of the angle of His, and so on, and its impact on GER is not well-understood. Third, the correlation and significance of abnormal lower esophageal pH with endoscopic evidence of esophagitis and clinical symptoms of reflux/heartburn is still being characterized. Finally, the long-term effect of subclinical GER after myotomy has yet to be defined.

Several observational studies have looked at post-POEM GER using a combination of subjective questionnaires to assess symptoms, and endoscopy and pH testing to objectively assess lower esophageal acid exposure. The majority of these studies have a mean follow-up of less than 12 months, with high attrition for objective testing. The longest post-POEM GER outcome data to date are from Inoue and colleagues [29], also with only 15% objective follow-up data at 3 years. They showed subjective symptoms in 21% of patients and objective esophagitis (LA grade A or greater) in 56%. Abnormal pH testing in post-POEM patients has been reported in the 40% to 60% range, including data from our own group [28,30,31]. Predictors of increased rates of GER include postprocedure IRP, obesity, and preexisting hiatal hernia [28,32].

It is worth noting that 2 recent randomized controlled trials involving LHM with partial fundoplication have demonstrated comparable postoperative GER rates (33% and 34%, respectively) with that of POEM [33,34].

Owing to the increased risk of postoperative GER, patients with hiatal hernia or obesity may be better served by LHM with concomitant hiatal hernia repair or Roux-en-Y gastric bypass, respectively. However, POEM is a reasonable initial option in obese achalasia patients unwilling to proceed with bariatric surgery, because it leaves that option open for the future without necessitating complicated revisional foregut surgery. We recommend routine assessment with a validated GER symptom score and a 24-hour pH study off PPIs in all patients at 6 to 12 months after POEM, regardless of the presence of symptoms; as well, continued future surveillance should be promoted, the details of which still need to be defined.

SUMMARY

POEM replicates the controlled surgical myotomy of a traditional laparoscopic Heller operation, while eliminating the need for skin incisions or entering the abdomen. Two-year and longer outcome data demonstrate durable symptomatic improvement of achalasia after POEM to approximately 90%, with an incidence of GER in approximately one-third. Complications after POEM are comparable or even better than LHM with risk of adverse events approximately 14%, and the chance of requiring additional surgery for complications around 0.2%. As experience and outcome data are gained, especially from prospective, randomized trials, there is potential for POEM to represent a paradigm shift in the management of idiopathic achalasia and other esophageal motor disorders. Although many referring providers and patients will likely opt for this less invasive approach, surgeons must be cautious and analytical

when it comes to the adoption of this, and other, new techniques. Comprehensive preoperative evaluation by a multidisciplinary team of gastroenterologists and surgeons is essential to confirming candidacy for POEM, as well as appropriately counseling patients on expected postoperative outcomes, the lack of long-term outcome data, and the need for long-term surveillance.

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