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Per Oral Endoscopic Myotomy (POEM): Review of Current Techniques and Outcomes (Including Postoperative Reflux)

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Abstract Per oral endoscopic myotomy (POEM) is a novel surgical endoscopic treatment for achalasia. It is an incisionless procedure in which lower esophageal sphincter myotomy and distal esophageal myotomy are accomplished via the use of electrosurgery. The clinical results in terms of dysphagia relief and patient satisfaction have been excellent. The safety profile has also been superb. POEM seems, at least on preliminary short-term studies, to achieve results that are equivalent to LHM combined with a fundoplication. We will review in detail the emerging data on POEM.

Keywords Per oral endoscopic myotomy (POEM) · Achalasia · Gastroesophageal reflux disease (GERD) · Heller myotomy · Natural orifice transluminal endoscopic surgery (NOTES) · Submucosal endoscopy · Postoperative reflux

Introduction

Achalasia is an uncommon usually idiopathic esophageal motility disorder manifested predominantly by dysphagia to solids and liquids, but patients may also have chest pain, regurgitation, coughing, and malnutrition. Diagnosis is strongly suggested by an esophageal contrast study demonstrating a dilated esophagus tapering to a "bird's beak" with delayed contrast passage into the stomach, but is formally made by esophageal manometry showing incomplete relaxation of the lower esophageal sphincter (LES) and disturbed peristalsis of the esophageal body. Medical therapy is ineffective in achalasia and treatment is centered on ablation of the LES. Large-diameter balloon pneumatic dilation (PD) and laparoscopic Heller myotomy (LHM) are the current mainstays in achalasia therapy with botulinum toxin injection (BTI) properly reserved for the frail elderly. A recent seminal study demonstrated therapeutic equivalence between PD and LHM with Dor's fundoplication at 43 months post-intervention in terms of LES pressure and relief from dysphagia [1]. However, LHM remains the preferred therapy for achalasia because of the usually more durable response with myotomy, and perhaps a concern regarding the PD complication of perforation [2]. A systematic review and meta-analysis found LHM to offer better and more durable results than PD and BTI [3]. End-stage achalasia with a massively dilated esophagus often requires partial esophagectomy [4].

Per Oral Endoscopic Myotomy (POEM)

Ortega described a case series of 17 achalasia patients in 1980 who were subjected to a direct trans-mucosal LES myotomy with good clinical, radiologic, and manometric results, but there were no follow-up studies perhaps because of concerns regarding complications including perforation and mediastinitis [5]. With the advent of natural orifice transluminal endoscopic surgery (NOTES) in 2004, there has been an impetus to develop less invasive endoscopic alternatives to surgical procedures. This led to the concept of a submucosal tunnel closed by a mucosal

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flap as a technique for access to the mediastinum or the peritoneum that allows facile and secure closure [6]. Interventions on the muscularis could be performed at a distance from the mucosal entry point which is closed at the procedure termination. This approach was used in 2007 to perform a LES myotomy in a porcine survival model [7]. In 2008, Inoue utilized this technique of submucosal tunneling to perform the first human endoscopic LES myotomy for achalasia and termed it POEM, for 'per oral endoscopic myotomy' [8]. In the United States, Stavropoulos performed the first human POEM outside Japan in 2009 [9•]. There is a burgeoning international experience with more than 20 centers performing POEM at significant volumes. An international survey (IPOEMS) was performed describing the worldwide POEMS experience through July 2012 [10•]. This survey database was derived via participation of 16 out of the 19 international high-volume POEM centers as of that time.

Technique

Equipment required to perform POEM is readily available (Fig. 1). The general sequence of POEM is (1) submucosal injection, mucosal entry, (2) creation of the submucosal tunnel with subsequent, (3) distal esophageal circular muscle dissection, (4) LES myotomy, and (5) closure of the mucosal incision, which is illustrated in Fig. 2. The patient is on clear liquids for a minimum of a day and the esophagus is cleared of residual debris and liquid antibiotic is infused over the esophageal mucosa to reduce risk of mediastinal contamination during POEM. A high-definition diagnostic gastroscope with a fitted distal transparent cap is used for the procedure. A submucosal injection of a dilute indigo-carmine solution is initiated 10–15 cm proximal to the LES to create a mucosal bleb (Fig. 3). Then a 2- to 3-cm mucosal incision (usually in the right lateral wall of the esophagus either anteriorly at 1–2 o'clock or posteriorly at 5 o'clock) is made via an electrosurgical ESD knife (either Olympus triangular tip knife or ERBE T-type hybrid knife) and the gastroscope is inserted in the submucosal space (Fig. 4). The tunnel is extended by careful dissection using ESD technique with repeated injection and electrosurgical dissection (although tunnel formation using balloon dilation has also been described (Fig. 5) [9•]. It is paramount to proceed slowly and not disrupt the mucosa as the tunnel is created. A long submucosal tunnel is created along the right wall of the esophagus and then extended beyond the LES about 2–4 cm into the submucosa of the cardia along the lesser curvature. The esophageal myotomy is begun about 3 cm distal to the mucosal incision site. The muscle is dissected until the plane between the longitudinal and circular muscle layers is delineated (Fig. 6). Then, the circular muscle fibers are hooked with the electrosurgical knife and the circular myotomy is continued distally until it is extended about 2 cm distally into the cardia (cardiomyotomy) (Fig. 7). A porcine POEM study supports this extension in significantly lowering LES pressure and this has been supported by the LHM literature [11, 12]. Hemostasis is performed via the coagulation mode of the electrosurgical device or by a dedicated coagulation grasper. After hemostasis and complete circular layer myotomy including the LES is accomplished within the tunnel, the tunnel is closed at the mucosal incision site; usually by endoclips (Fig. 8). This is the ingenuity of the submucosal tunnel technique as myotomy is accomplished and the tunnel is "sealed" from the esophageal lumen using the mucosal flap to ensure secure closure.

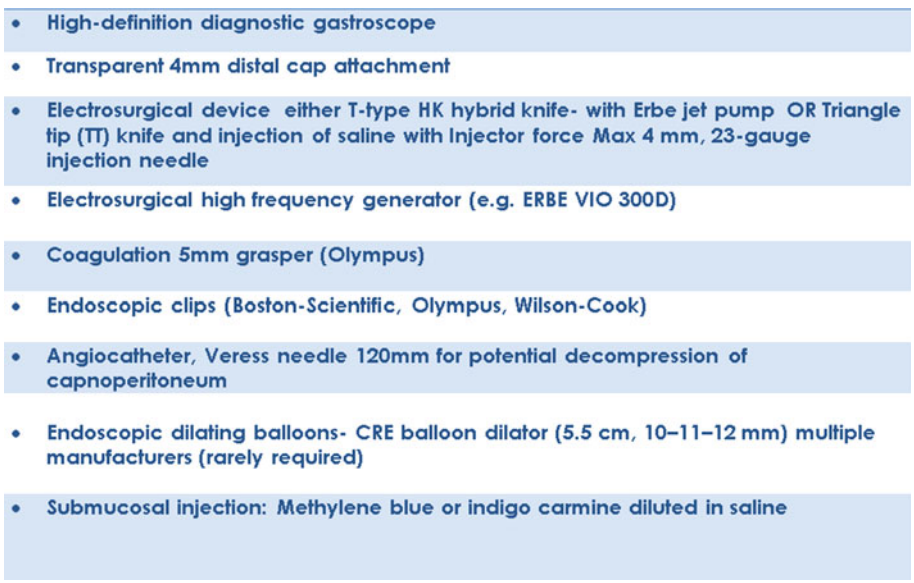

Fig. 1 Equipment used in POEM

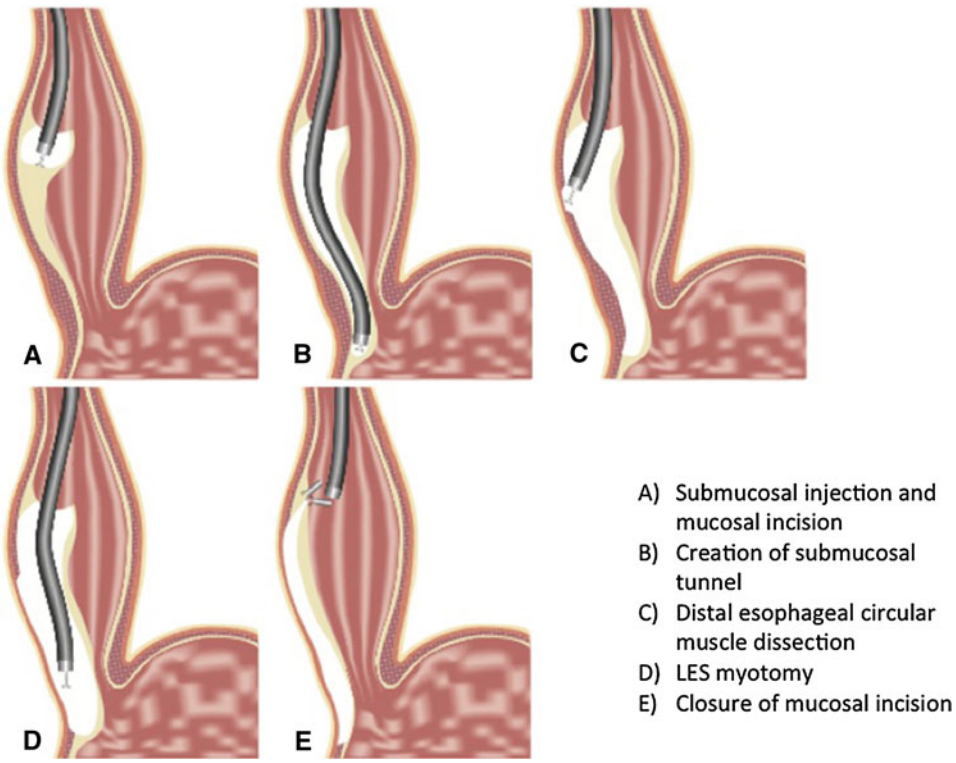

Fig. 2 Graphic illustration demonstrating the five critical steps in performing POEM (© Winthrop University Hospital, 2012)

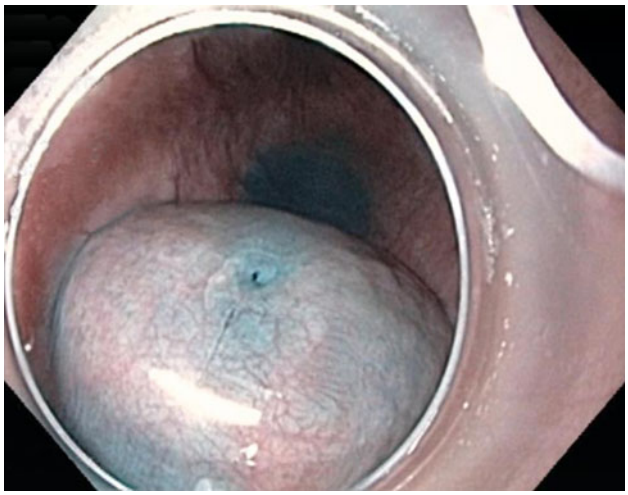

Fig. 3 A submucosal injection is used to expand the submucosal space and create a bleb

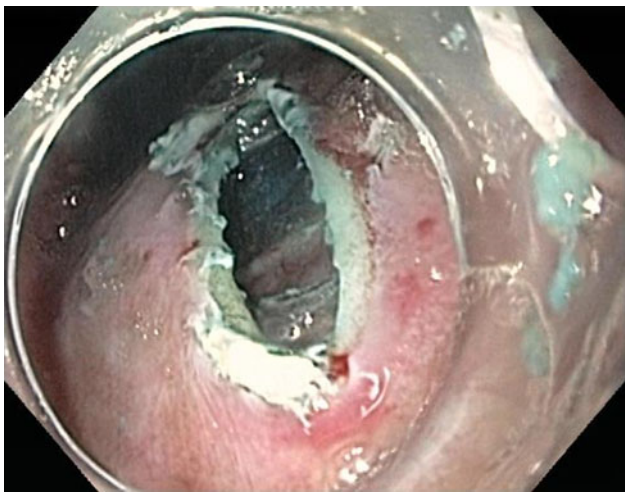

Fig. 4 An electrosurgical knife is use to create a mucosal incision

It should be noted that there are variations among POEM operators in terms of background (surgeons vs. gastroenterologists), technique, (myotomy length/mucosal incision orientation/myotomy depth) and practice setting (O.R. vs. endoscopy suite) [10•]. Individual centers have evolved their techniques over time. For example, we initially employed balloon dilation rather than the currently used endoscopic submucosal dissection (ESD) devices to create the submucosal tunnel mainly due to unavailability of these ESD devices in the U.S. in 2009 [9•]. The Shanghai POEM group had significant issues with barotrauma (cutaneous emphysema, pneumothorax) possibly related to their early use of air insufflation during the procedure and this diminished significantly with the dedicated use of carbon dioxide which is now standard for all POEM centers [13•]. The Shanghai group (the highest volume group in the world currently) compared the hybrid knife (ERBE) with the triangular tip knife (Olympus) for POEM in a small randomized trial reported in abstract form and found the former to be associated with shorter procedure time, easier hemostasis, and less need to switch instruments [14].

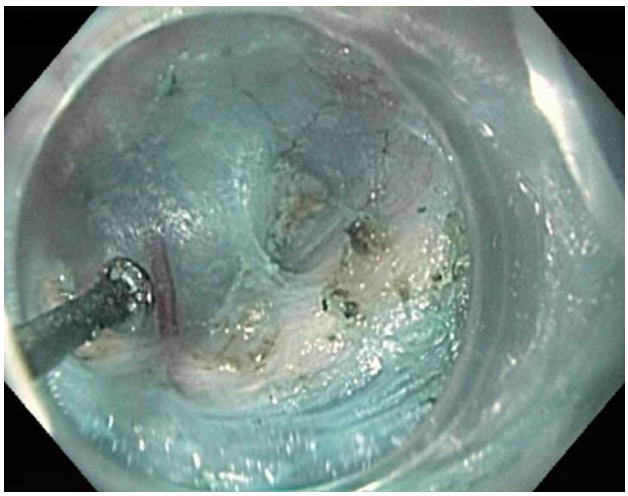

Fig. 5 The hybrid-knife is used to create the submucosal tunnel via sequential submucosal injection and submucosal dissection

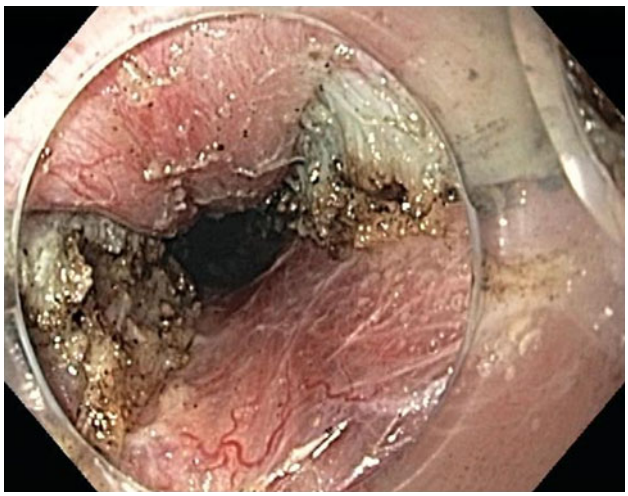

Fig. 7 This represents a completed myotomy with the cut edges of the muscle visible

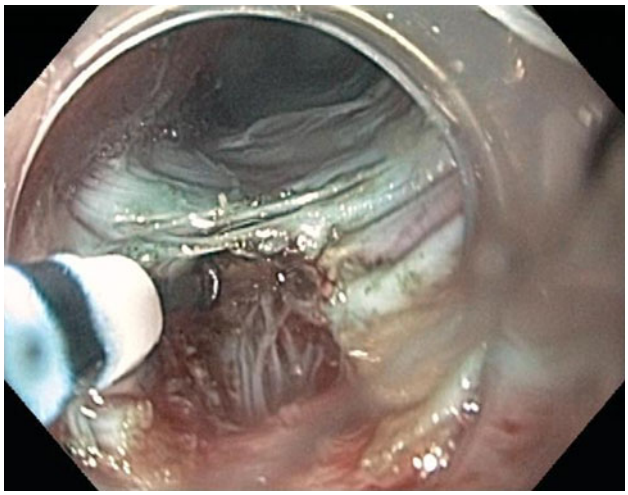

Fig. 6 The hybrid knife is used to initiate the myotomy. An incision of the circular layer has been performed exposing the longitudinal layer of the esophageal muscularis propria

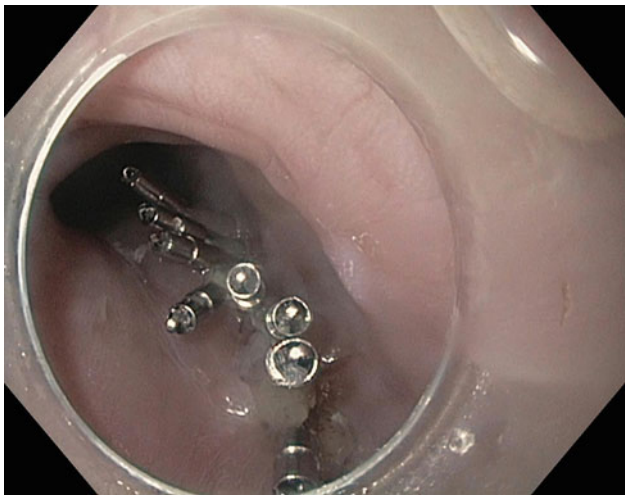

Fig. 8 The mucosal incision site is closed with endoclips

The human LES is a complex entity that includes weaker thinner clasp (circular) component located on the gastric lesser curvature centered at 2 o'clock if the most anterior point from the endoscopist's perspective is defined as 12 o'clock, and an oblique sling fiber component centered on the left posterior lateral wall of the LES at 8 o'clock which drapes over the anterior and posterior walls at 5 and 11 o'clock, respectively [15] (Fig. 9). The sling fibers represent a significant barrier to reflux. LHM may include partial transection of the sling fibers since myotomy orientation is along the anterior esophageal and gastric walls at about 11 o'clock. This may contribute to a high rate of reflux after LHM. On the other hand, the POEM orientation in the right lateral wall of the esophagus may result in cutting almost exclusively clasp fibers and preserving the sling fibers which may result in less severe reflux compared to LHM.

The gastroesophageal (GE) junction may be difficult to delineate within the submucosal tunnel. Identification of the GE junction is essential to ensure adequate extension of the tunnel and the myotomy into the gastric cardia. The identification of the thicker LES circular muscle layer or aberrant longitudinal muscle bundles of the gastric cardia may be helpful, but a more useful indicator may be the more capacious gastric cardia submucosa with more and larger vessels compared to the esophageal submucosa. Additional useful indicators are visualization of the palisading vessels on the mucosal flap, blue hue on the gastric cardia mucosa on retroflexed endoluminal view, and use of the markings on the endoscope to ensure a distance from

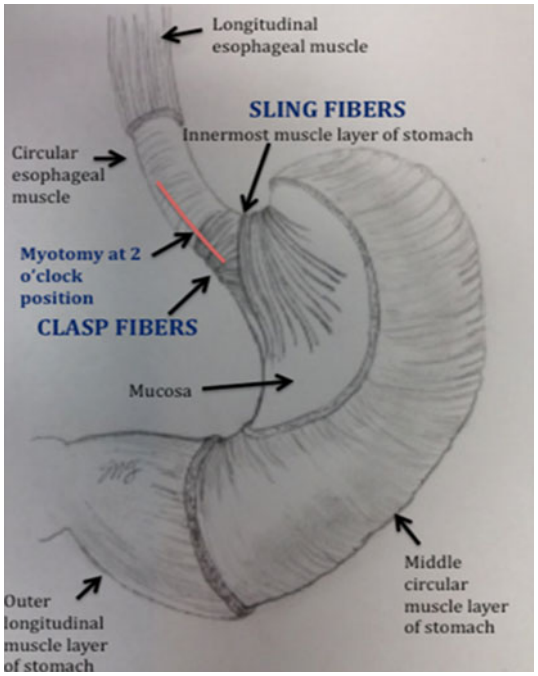

Fig. 9 Human LES anatomy in relation to POEM myotomy orientation (© Stavros N. Stavropoulos, Winthrop University Hospital, 2012)

the incisors that corresponds to an appropriate depth of insertion to reach 3–4 cm into the cardia [10•]. Most POEM operators prefer partial LES myotomy with dissection of the circular layer and attempted preservation of the longitudinal layer. However, the outer longitudinal layer is generally flimsy and easily disrupted by the endoscope. A few centers (Shanghai, Mineola) favor a complete LES myotomy of both layers similar to that performed during a surgical Heller myotomy [10•]. von Renteln et al. [16] changed from a partial (circular) to complete myotomy for the last 7 of 16 patients in their published study. Patients with a complete myotomy had significantly better esophageal emptying of contrast after POEM [16]. However, these are very limited retrospective data. Data based on much larger numbers but still retrospective should be forthcoming from the Shanghai group (personal communication with the authors). A porcine model study noted that full thickness myotomy did not decrease LES pressure more than a partial myotomy, but the lack of significant drop in post-myotomy LES pressure in all groups raises concerns about technique [11]. Technical assessment of the adequacy of the endoscopic myotomy includes visual assessment of the LES at the tunnel and within the lumen of the esophagus, and more objectively by using the EndoFlip^{TM} device which measures distensibility at the gastroesophageal junction [17].

Initial POEM operators limited the length of their esophageal myotomies to <6 cm [8, 9•]. Inoue subsequently increased his myotomy length to 8–10 cm, which was consistent with LHM literature, and the other centers followed suit [18]. The length of the myotomy can possibly be geared to the esophageal manometry findings. High resolution manometry (HRM) is useful in differentiating among the different subtypes of achalasia and related motility disorders [18]. For example, a longer myotomy could be effective for spastic disorders of the esophageal body [achalasia Type III Chicago classification, diffuse esophageal spasm (DES)] as reviewed below.

Clinical Results

The IPOEMS survey and published case series of various designs cover a large proportion of the POEM experience to date [10•, 19•, 20, 21•, 22•, 23–26, 27•, 28•, 29•, 30]. Therapeutic endpoints were dysphagia relief and the more global Eckardt score; some centers reported esophageal manometry. Reported POEM clinical results were excellent with all ten reporting centers in the IPOEMS survey noting an improvement in dysphagia and a diminution of Eckardt scores [10•]. The clinical response rate for both this survey and the published case series was 90–100 % [10•, 19•, 20, 21•, 22•, 23–26, 27•, 28•, 29•, 30] (Table 1). The available data on manometry clearly demonstrate functional LES ablation. The therapeutic success is remarkable with the caveat, however, of limited numbers and brief follow-up.

The reported POEM efficacy is made more impressive in view of the significant proportion of subjects who had prior history of failed achalasia therapy (PD, BTI, LHM). The IPOEMS database of 841 patients included 26, 57, and 276 subjects, respectively, that had prior failed Heller, BTI, or PD (43 % of the total!) [10•]. The consensus among the experienced operators was that prior therapy (especially BTI) made POEM more challenging, but prior experience and diligence could result in similar success as in the general achalasia cohort [10•]. The Portland group published a series of 40 patients with esophageal motility disorders who had undergone POEM, demonstrating similar efficacy and safety between groups who had and had not had prior endoscopic intervention [31•]. Although POEM can present special challenges in the failed surgical Heller myotomy patient due to the presence of adhesions, alteration of GE junction anatomy and frequent presence of a concomitant anterior or posterior fundoplication have limited reported numbers in published case series that demonstrate its success. In fact, the Shanghai group reported 90 % success with POEM after failed LHM in a series of 12 patients [32•].

There are limited data regarding POEM in patients with severe sigmoidization and megaesophagus ("end-stage achalasia"). Inoue reported successful POEM in three

Table 1 POEM efficacy and GERD in published case series (abstracts and articles)

Site	Yokohama Japan [19•]	Yokohama Japan [20]	Hamburg Frankfurt Zurich Montreal MCT [21•][a]	Shanghai China [22•][a]	Rome Italy [23][a]	Dusseldorf Germany [24][a]	Nagasaki Japan [25]	Hong Kong [26]	Mineola New York [27•][a]	Portland Oregon [28•]	Chicago Illinois [29•]	Korea [30]
n	17	236	69	205	52	21	28	16	45	18	18	13
Follow-up (months)	5	11	3	8.5	3	9[b]	3	3	9.5	≥6	≥6	6.9[b]
POEM clinical success (%)	100	99	96	97	92	95	100	100	95	94	89	100
Pre–post mean LES (mmHg)	52.4	26.8	27.4	–	40.8	46	71.2	43.6	45	45	19	30.3
	19.8	12.6	9.2		16.1	22	21	29.8	15	16.8	9	15.3
	$p = 0.0001$	$p < 0.001$	$p < 0.001$		$p < 0.05$	$p = 0.003$	$p < 0.05$	$p = 0.005$	$p = 0.0001$	$p = 0.009$	$p < 0.001$	$p = 0.007$
Pre–post mean Eckardt score	10.3	6.36	7.6	0	7.8	6.62	6.7	5.5	7.8	6	7	6.4
	1.3	1.45	1.2		1	1.39	0.7	0	0.4	0	1	0.4
	$p = 0.0003$	$p = 0.003$	$p < 0.001$		$p < 0.05$	$p < 0.001$	$p < 0.05$	$p = 0.001$	$p = 0.0001$	$p = 0.002$	$p < 0.001$	$p = 0.001$
GERD symptoms (%)	6 %	10.5 %	20 %	–	7 %	31 %	21.4 %	6 %	20 %	44 %	22 %	0 %
			7/35		2/30	5/16						
Endoscopic evidence of GERD	6 %	–	18 %	–	–	–	39.3 %	20 %	43 %	28%	33 %	–
	1/17		7/38				11/28	3/15	6/14	4/14	5/15	
+pH study	–	–	–	–	–	–	–	–	36 %	46 %	–	–
									5/14	6/13		

[a] Abstract

[b] Mean

patients with grade III (>6 cm) on his initial 17 patient series. Our group is the only other group to report performing POEM on 12 patients with megaesophagus (grade III 6–8 cm and grade IV >8 cm) and seven patients with sigmoid esophagus [27•]. Our results reveal these patients have now completed ≥6 months follow-up with Eckardt score remaining ≤3. Inoue showed good treatment response in his initial series with five sigmoid achalasia patients and later reported successful POEM in 16/105 patients with sigmoid achalasia [19•, 33]. Six centers in the IPOEM survey performed POEM in patients with severe sigmoidization and consider POEM not contraindicated in such patients [10•]. In general, most patients with severe end-stage achalasia (megaesophagus and/or severe sigmoidization) have been found to respond poorly to conventional achalasia treatments including Heller myotomy, and often require esophagectomy. POEM could be used as an initial minimally invasive treatment option in these patients, with esophagectomy reserved for those with inadequate response.

Looking at indications for POEM other than classic achalasia, the IPOEMS respondents were mixed as to the success of POEM for type III achalasia, but there was consensus that POEM was generally less effective for DES than for classic achalasia, and that POEM was useful for nutcracker esophagus and hypercontractile LES [10•]. Of the IPOEMS subjects 22 % were classified as DES, hypercontractile LES, and nutcracker esophagus, and 6/16 centers perform longer myotomies for DES subjects [10•]. POEM for DES has been reported elsewhere [34–36]. The Portland group published similar findings in their series of 40 patients with esophageal motility disorders who had undergone POEM, demonstrating POEM more efficacious for nutcracker esophagus and hypertensive LES than DES [31•].

Adverse Events

POEM has a superlative safety record with now over 1,000 (841 in IPOEMS alone) procedures performed with no reported mortality and few major serious complications. The Shanghai group as mentioned had significant issues with pneumoperitoneum, pneumothorax, and subcutaneous emphysema, but these resolved with change of technique including dedicated carbon dioxide use [13•]. There were about 3 % severe non-fatal adverse events in the IPOEMS database [10•]. These included bleeding within the submucosal tunnel and pneumothorax. Minor technical adverse events with minimal clinical impact included capnoperitoneum, necessitating intraprocedural venting, and accidental perforation of the mucosal flap requiring intraprocedural closure with clips. The published case series also noted a low complication rate [19•, 21•, 22•, 23–26, 27•, 28•, 29•, 30, 31•, 32•, 33–41] (Table 2). The severe morbidity and mortality incidence of POEM so far is better than the 6.2 and 0.8 % incidence, respectively, noted in a meta-analysis of LHM studies [3]. The infrequent POEM complications are striking in view of the large proportion of extended indication subjects and the extremes of age, with a number of medically fragile subjects. However, it should be noted that these results reflect series from expert centers with operators with the high level of expertise required to be pioneers in adopting POEM. As the technique spreads to later adopters, some of which may not be as experienced in the techniques of endoscopic surgery, the incidence and severity of adverse events may increase to some degree.

Gastroesophageal reflux disease (GERD)

GERD is the most prevalent untoward result of POEM. GERD was not frequent in two initial series [16, 19•]. This may be related to intrinsic differences in study groups (e.g., Asian vs. Western patients) and/or GERD assessment based on symptoms rather the more objective endoscopy and pH study data. In the Portland group, 6/13 post-POEM patients had increased acid exposure via esophageal pH testing and 1 additional patient had minimal esophagitis on endoscopy yielding 50 % overall rate of objective evidence of GERD [28•]. However, the GERD was deemed mild and was controlled with PPI therapy. The Hungness et al. [29•] group had 4/18 patients with esophagitis on endoscopy. Post-POEM GERD symptoms were common in the international database with 8/13 centers reporting a rate >14 % [10•]. Of centers performing endoscopy, 8/11 reported >20 % esophagitis rate and the 4 centers performing pH studies noted a acid reflux rate ranging from 0 to 38 % [10•]. Endoscopic evidence of GERD was noted in ~20 % of subjects in a European MCT [21•]. Our group had 6/14 patients with esophagitis on endoscopy and 5/14 patients with positive pH (Table 1).

These data suggest that the rate of GERD after POEM may be similar to the rate after a Dor fundoplication (25–40 %) and somewhat higher than the rate after a Toupet fundoplication (20–30 %) (using data from high quality prospective randomized LHM trials) [42, 43].

POEM appears to be associated with far less GERD than LHM without fundoplication. This may be because POEM avoids dissection of the phrenoesophageal membrane and other structures that contribute to the anti-reflux barrier, and typically POEM entails only the dissection of the clasp fibers in the LES region with preservation of the sling fibers that maintain the angle of His. Thus, avoiding disruption of the normal suspensory elements of the hiatus

Table 2 POEM complications in published case series (abstracts and articles)

	Yokohama Japan [19•, 33, 37]	Rome Italy [23, 38, 39][a]	Hamburg Frankfurt Amsterdam Zürich Montreal MCT [21•, 40][a]	Shanghai China [13•, 22•][a]	Portland Oregon [28•]	Chicago Illinois [29•]	Hong Kong [26]	Dusseldorf Germany [24][a]	Mineola New York [27•, 41][a]	Nagasaki Japan [25]	Korea [30]	Total studies (18)
No. of cases	236	52	69	205	18	18	16	21	45	28	13	721
Pneumo/ capnoperitoneum	1[b]	17[b]	8[b]	47[c]	1[b]	7[b]			9[b]			43 (6 %)[b]
Pneumo/ capnomediastinum		10		12[d]/35[e]				1				58 (8 %)
Pneumo/capnothorax	1[f]			3[f,d]/14[f,e]	1[f]							19 (2.6 %)
Aspiration pneumonia	1						1					2 (0.3 %)
Subcutaneous emphysema		4	6	27[d]/66[e]		1	2					106 (14.7 %)
Mucosal flap injury	3	4	2		2			1	6	1		19 (2.6 %)
Accidental full thickness muscle perforation					1							1 (0.1 %)
Peritonitis	1											1 (0.1 %)
Mucosal ulceration			2									2 (0.3%)
Submucosal hematoma	1											1 (0.1 %)
Delayed Bleeding				1						2		3 (0.2 %)
Other pulmonary adverse events				58 pleural effusion (2 chest tube) 59 atelectasis					1 atelectasis			117 (16.3 %)
Leak/perforation						1						1 (0.2 %)
Other adverse events				1 seizure 1 submucosal fistula		1 atrial fibrillation 1 urinary retention			1 atrial fibrillation			5 (0.7 %)
Esophageal stricture				1								1 (0.1 %)
Dehiscence at tunnel entry				1								1 (0.1 %)

[a] Abstract

[b] Requiring 18-gauge needle decompression

[c] No intervention

[d] Intraoperative

[e] Postoperative

[f] Chest tube placement

minimizes GERD after POEM in relation to LHM, where these structures are usually dissected [28•, 44].

It is paramount to follow post-POEM patients for the indefinite future with periodic surveillance endoscopies even in the absence of dysphagia or GERD symptoms, as there is a concern for Barrett's esophagus, stricture, and esophageal cancer. Successful achalasia therapy such as POEM may mitigate against the development of esophageal malignancy, but this remains conjectural [45].

POEM Versus LHM

The published POEM efficacy and safety data reviewed in Tables 1 and 2 demonstrate excellent outcomes, which is encouraging. In fact, there are limited retrospective data comparing recent consecutive LHMs to the initial POEM experience at centers in Germany, US, and India, suggesting at least equivalence between the two procedures in terms of procedure duration, morbidity, and efficacy [29•, 46•, 47•]. In the study published in full by Hungness et al. [29•], POEM had a significantly shorter duration and less blood loss than LHM with otherwise similar short-term outcomes. Although these findings are not from prospective randomized controlled trials, these results are very encouraging, since equivalence at this point, with POEM being at a beginning stage and LHM at a developed stage, suggests that in the future POEM may displace LHM as a first-line treatment for achalasia.

Training/Program Initiation

Achalasia is a relatively uncommon disease, and thus centers contemplating POEM should anticipate an adequate volume to ensure experience and ultimate expertise. In addition, there should be multidisciplinary collaboration, including between gastroenterology and surgery. IRB approval is mandatory as POEM is a novel procedure without long-term follow-up. Training in POEM has yet to be standardized, but likely would consist of proctoring by experts, course attendance, and animal model work [20]. A recent study has reported on a learning curve that appears to flatten after 20 POEM procedures [31•].

Conclusions

Heller myotomy has been the standard for achalasia therapy for a century, but its reign as the gold standard is now threatened [48]. POEM has emerged as much less invasive alternative for the achalasia patient with short-term results that are equivalent to or better than LHM. The cogent advantages of POEM include aesthetic lack of external scars, somewhat more rapid recovery time, no disruption of external ligamentous elements of the LES, and conceivably easier repeat intervention for dysphagia or GERD issues. There are controversies regarding post-POEM GERD, implementation/credentialing issues, and the need for long-term data, but, overall, the future of POEM appears bright.

Compliance with Ethics Guidelines

Conflict of Interest Stavros N. Stavropoulos has received honoraria from ERBE and Boston Scientific. David Friedel and Rani Modayil declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with animal subjects performed by any of the authors. With regard to the authors' research cited in this paper, all procedures were followed in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2000 and 2008.

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