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Per-oral endoscopic myotomy: Major advance in achalasia treatment and in endoscopic surgery

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Abstract

Per-oral endoscopic myotomy (POEM) represents a natural orifice endoscopic surgery (NOTES) approach to laparoscopy Heller myotomy (LHM). POEM is arguably the most successful clinical application of NOTES. The growth of POEM from a single center in 2008 to approximately 60 centers worldwide in 2014 with several thousand procedures having been performed attests to the success of POEM. Initial efficacy, safety and acid reflux data suggest at least equivalence of POEM to LHM, the previous gold standard for achalasia therapy. Adjunctive techniques used in the West include impedance planimetry for real-time intraprocedural luminal assessment and endoscopic suturing for challenging mucosal defect closures during POEM. The impact of POEM extends beyond the realm of esophageal motility disorders as it is rapidly popularizing endoscopic submucosal dissection in the West and spawning offshoots that use the submucosal tunnel technique for a host of new indications ranging from resection of tumors to pyloromyotomy for gastroparesis.

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Key words: Per oral endoscopic myotomy; Achalasia; Natural orifice transluminal endoscopic surgery; Submucosal tunnel endoscopic resection; Submucosal tunnel endoscopy; Endoscopic suturing; Endoscopic myotomy; Endoscopic submucosal dissection; EndoFLIP

Core tip: Per-oral endoscopic myotomy (POEM) is a novel endosurgical therapy for achalasia. POEM developed as an offshoot of early natural orifice endoscopic surgery (NOTES) approach investigation, but, now, is arguably the most successful clinical application of NOTES. The clinical results of POEM therapy in terms of dysphagia relief and safety have been excellent. The impact of POEM is extending far beyond the narrow domain of esophageal motility disorders. As the first successful clinical application of submucosal endoscopy it is now spawning many other NOTES interventions utilizing a submucosal tunnel approach including submucosal tunnel endoscopic resection of submucosal and mucosal lesions and per oral pyloromyotomy for gastroparesis.

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INTRODUCTION

Achalasia is a rarely encountered motor disorder of the esophagus, which is usually of unclear etiology. Most patients have dysphagia to solids and liquids and others may have chest pain, regurgitation, and coughing.

Barium esophageal contrast study usually shows a dilated esophagus tapering to a “bird’s beak” with delayed contrast passage into the stomach, but diagnosis is confirmed by esophageal manometry showing infrequent or no relaxation of the lower esophageal sphincter (LES) and a variety of abnormalities in 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) reserved for the frail elderly. A recent pivotal article noted equivalent results between PD and LHM with Dor’s fundoplication at 43 mo post-therapy as noted by LES pressure measurements and dysphagia scores^[1]. LHM is still considered the best therapy for achalasia because of its durable response and the possibility of perforation with PD^[2]. A systematic review and meta-analysis noted LHM to yield superior and more durable results than PD and BTI^[3]. End stage achalasia with a hugely dilated esophagus may necessitate partial esophagectomy (recently performed *via* laparoscopy)^[4].

HISTORICAL BACKGROUND

Ortega described a case series of 17 achalasia patients in 1981 described a direct trans-mucosal lower esophageal sphincter myotomy and good clinical, radiologic and manometric results; there were no confirmatory work perhaps related to complications such as perforation and mediastinitis^[5]. Natural orifice transluminal endoscopic surgery (NOTES) came to the fore in 2004 and there has been a push to design endoscopic less traumatic alternatives to traditional transcutaneous surgical interventions. Thus the concept of a submucosal tunnel closed by a mucosal flap with access to the mediastinum or the peritoneum was formulated^[6]. Interventions on the esophageal muscularis could be performed at a distance from a mucosal entry point, which is then closed at the procedure termination. The concept was implicated in 2007 to perform a LES myotomy in a porcine survival model^[7]. In 2008, Inoue used the technique of submucosal tunneling to perform the first human endoscopic LES myotomy for achalasia and coined the term POEM for per oral endoscopic myotomy^[8]. Our group performed the first human POEM outside Japan in 2009^[9]. There is a rapidly increasing international experience with over fifty centers now performing POEM. An international survey (IPOEMS) was performed describing the global POEM experience through July 2012^[10].

INDICATIONS AND CONTRAINDICATIONS

Patients considered for POEM therapy must have a high-quality (preferably high resolution) esophageal manometry to define their specific motor abnormality as this will dictate both their eligibility for POEM and spe-

cifics of the procedure. POEM is performed predominantly for achalasia, but this technique has also been successfully applied in diffuse esophageal spasm, nutcracker and jackhammer esophagus^[11,12]. The international survey (IPOEMS) revealed that 28% of the 841 reported POEMs performed by the 16 reporting centers, were performed for hypertensive esophageal motor disorders including DES, hypertensive LES, nutcracker and jackhammer esophagus^[10]. The consensus from IPOEMS and other studies is that POEM has significant efficacy in nutcracker esophagus, hypertensive LES, DES and type III (spastic) achalasia^[10-13]. POEM seems to be more helpful in diminishing dysphagia than the chest pain associated with these disorders^[13]. POEM may be ideally suited in the treatment of patients with hypertensive esophageal motor disorders other than achalasia because in those disorders often a longer myotomy is required than can be achieved *via* the laparoscopic approach.

Experienced POEM operators can also now successfully treat patients with prior Heller myotomy and previous endoscopic intervention including botulinum injection and pneumatic dilation^[14,15]. Forty-three percent of subjects in the IPOEMS database had prior intervention (BTI, PD, LHM)^[10]. The consensus was that that the cases were more technically challenging, but there was similar good efficacy with few adverse events as the total subjects group. Subsequent smaller reported studies are consistent with these findings^[14,15].

POEM has been performed throughout the age spectrum^[10,16]. Most experienced operators will consider POEM in the gamut of achalasia subtypes, achalasia with “sigmoid” esophagus and medically fragile patients. POEM has been performed in post-gastric bypass patients with achalasia^[17]. POEM contraindications by consensus include severe pulmonary disease, esophageal irradiation, esophageal malignancy, bleeding disorders including coagulopathy and recent esophageal surgery or endoscopic intervention including endoscopic mucosal resection and endoscopic submucosal dissection (ESD)^[10].

POEM TECHNIQUE

POEM was developed from a technique devised to access the mediastinum in NOTES^[6]. POEM features the creation of a submucosal tunnel enabling the LES myotomy to be performed away from the mucosal entry site. The procedure requires equipment employed in ESD with capability for dissection, cutting, coagulation and infusion of volume-expanders within the submucosal space. POEM is performed with general anesthesia with the patient usually in the supine position. Carbon dioxide is used for insufflation utilizing a high-definition forward-viewing gastroscope with accessory water jet for irrigation with an attached clear cap. The esophageal submucosal space is expanded with injection of an indigo carmine-saline mixture^[18]. The submucosal tunnel is typically initiated 10-15 cm above the gastroesophageal junction (GEJ).

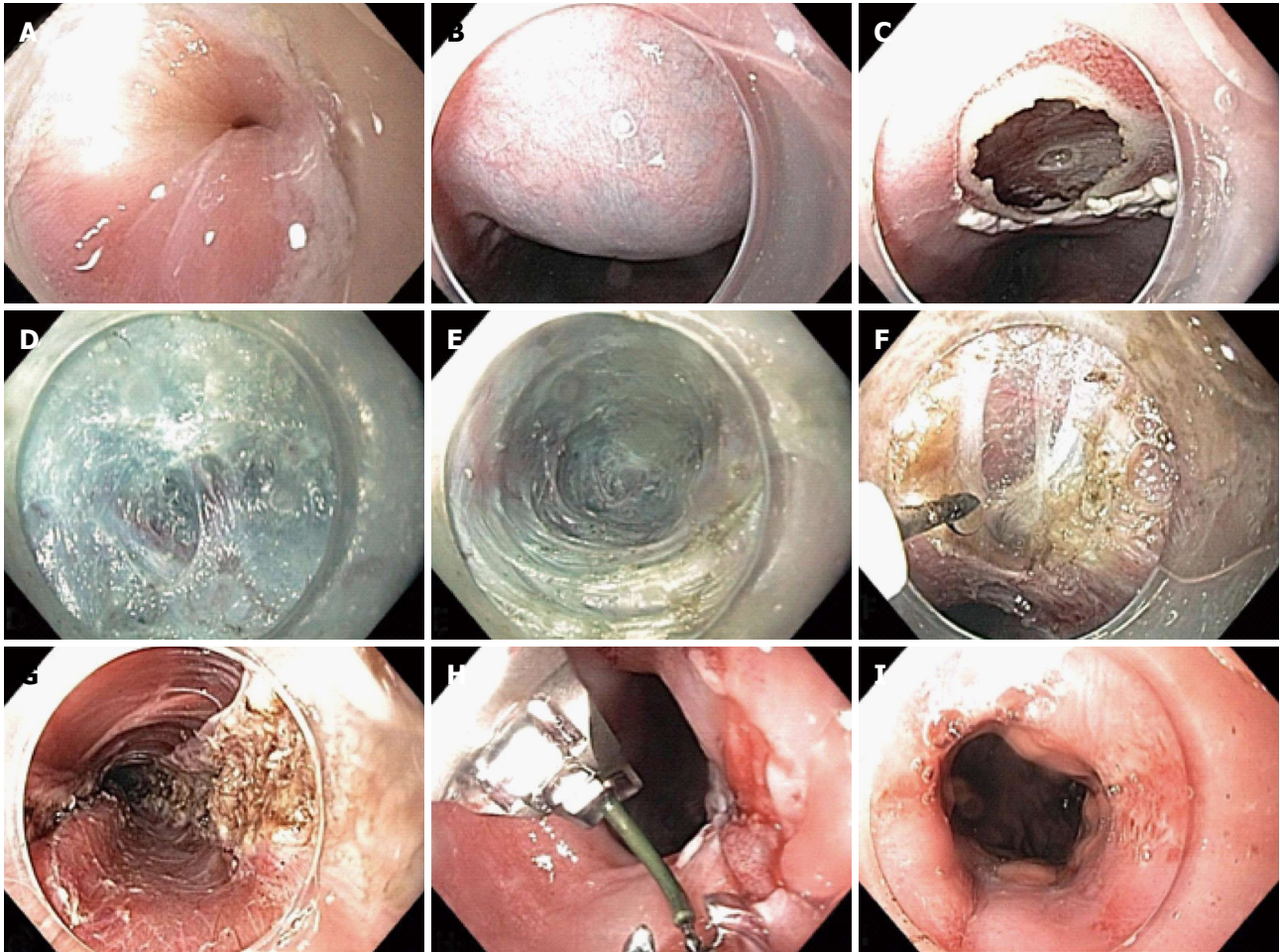


Figure 1 Per-oral endoscopic myotomy technique. A: Prior to per-oral endoscopic myotomy (POEM), there is evidence of a tightly puckered lower esophageal sphincter (LES); B: Submucosal injection is performed with saline stained with indigo carmine; C: Mucosotomy is performed along the right anterior wall of the esophagus; D: Submucosal dissection is performed with hybrid knife; E: Submucosal tunnel is extended into the gastric cardia; F: Myotomy is initiated 2 cm below site of mucosotomy; G: Final full thickness myotomy is seen as endoscope is withdrawn from the submucosal tunnel; H: Mucosotomy is closed with an endoscopic suturing device; I: After POEM, the LES appears patulous.



Figure 2 OverStitch endoscopic suturing system (Courtesy of Apollo Endosurgery, Austin Texas).

The submucosal space is entered by the gastroscope after a small electrosurgical cut and subsequently a submucosal tunnel is dissected using ESD technique for creation of a conduit to the GEJ and the lower esophageal sphincter. The submucosal tunnel is extended into

the gastric cardia 2-3 cm distal to the GEJ. Delineation of the GEJ while in the tunnel is done in a variety of ways including monitoring endoscope insertion length, visually noting changes in tunnel diameter and vascularity, tactile feedback and even transillumination viewed by a second endoscope^[19]. Then the myotomy is performed starting 2-3 centimeters distal to the mucosal entry point. The final critical step is closure of the tunnel at the mucosal entry point. Figure 1 demonstrates the critical steps in the POEM technique. We have presented a detailed explanation of the technique in video format elsewhere (*VJGIEN*, 2013)^[20]. Patients typically have a post-procedural contrast study to exclude complications such as perforations and may be discharged the following day if clinically well including ingestion of clear liquids. Antibiotics are given during the POEM and continued for several days after discharge.

TECHNIQUE VARIATIONS

Individual POEM operators have generally evolved in

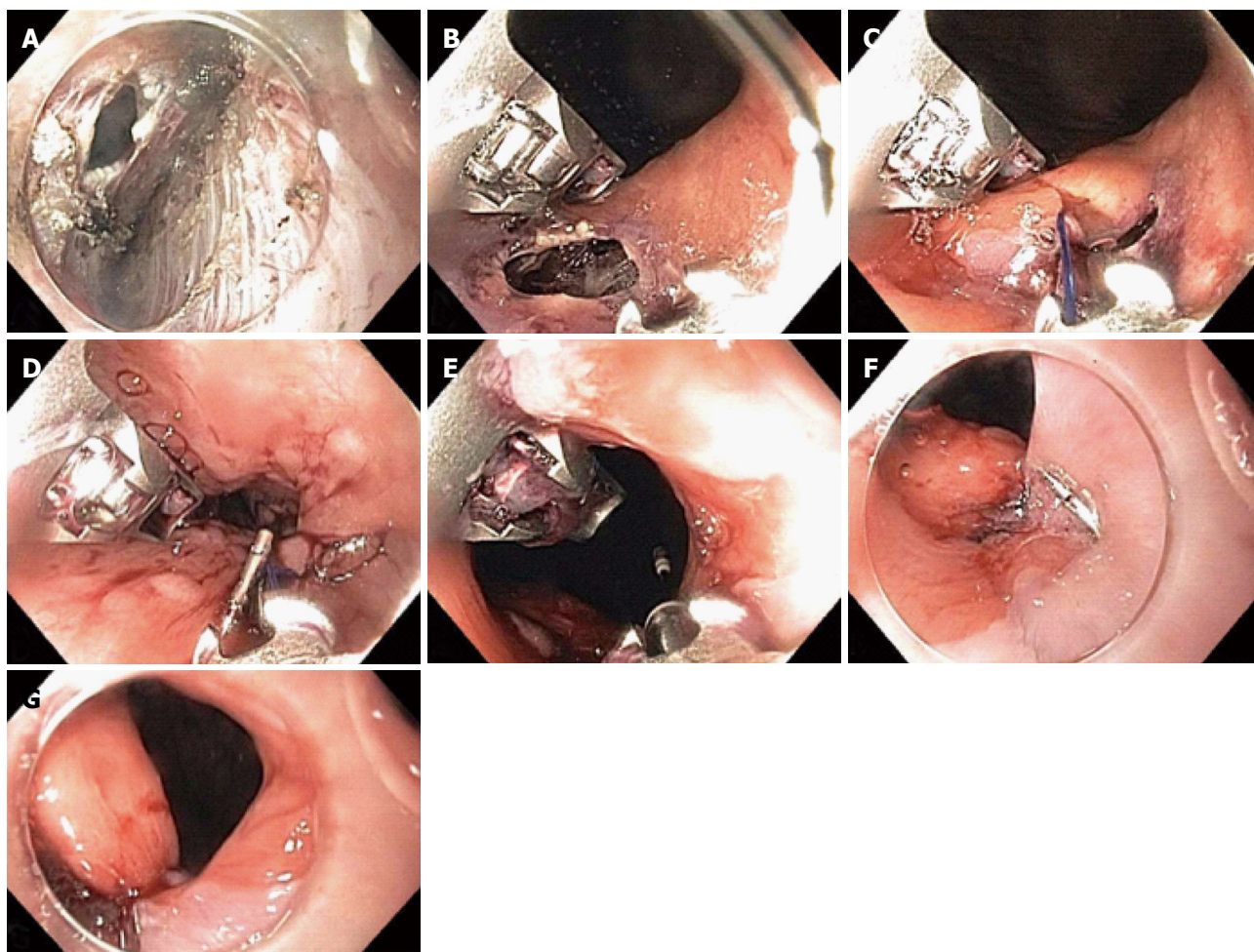


Figure 3 Closure of gastroesophageal junction mucosal perforation with endoscopic suturing device. A: Inadvertent mucosal perforation at the gastroesophageal junction (GEJ) seen within the submucosal tunnel; B: Inadvertent mucosal perforation at the GEJ seen endoluminally; C: Endoscopic suture-initial "bite"; D: Suture closure; E: Cinch T-tag is deployed; F: Endoscopic suturing achieved secure closure of the perforation; G: Patulous lower esophageal sphincter.

their techniques. The Shanghai group has converted to carbon dioxide after frequent serious complications with room air, and this group touts the hybrid (inject/cautery) ESD knife for faster dissection during POEM^[21,22]. Inoue prefers the triangular tip knife and initially performed more modest length circular muscle myotomies^[16]. Our group initially employed balloon dilation in tunnel creation (lack of ESD knives in the US before 2011), but now electrocautery dissection is exclusively used and we are more comfortable with extended length circular and longitudinal full-thickness muscle dissection^[9,23]. Most centers employ clips for closure of the mucosal defect at the tunnel initiation. We have used an endoscopic suture device (OverStitch™ Endoscopic Suturing System; Apollo Endosurgery Austin, Texas) (Figure 2) for our recent cases and this is also invaluable for inadvertent mucosal tunnel perforation^[24]. Figure 3 demonstrates a mucosal flap injury at the GEJ closed effectively with the endoscopic suturing device without concern for delayed leak in the patient. In our series when we compared the last 25 consecutive mucosotomy closures using endoclips and endoscopic suturing, there was no statistically significant difference in mean closure time (clips 8.8 min

vs suture 10.1 min, $P = 0.1$), complications or mean cost (clips \$915.84 *vs* suturing \$818, $P = 0.2$) (unpublished data) Closure has also been described with an over-the-scope clip and fibrin glue^[25,26].

There are POEM controversies regarding the orientation and extent of LES dissection. The human LES has several components that include a weaker clasp (circular) fiber part on the lesser curvature of the stomach centered at 2 o'clock (using the convention of 12 o'clock being the most anterior point) and a sling (oblique) fiber part on the left posterior lateral wall of the LES at 7 o'clock and draping over the anterior and posterior walls at 5 and 11 o'clock respectively^[27]. These sling fibers are a significant barrier to reflux. Laparoscopic Heller Myotomy is often performed anteriorly at 11-12 o'clock and thus partially transects the sling fibers at 11 o'clock and thus GERD is common after LHM. Currently, most POEM operators reportedly perform myotomy at 2 o'clock, which may theoretically minimize post-procedure reflux, but be less efficacious as LES disruption is the main goal in achalasia surgery. We and others (Shanghai group) that employ a predominant 5 o'clock position for the myotomy may have less dysphagia because of sling

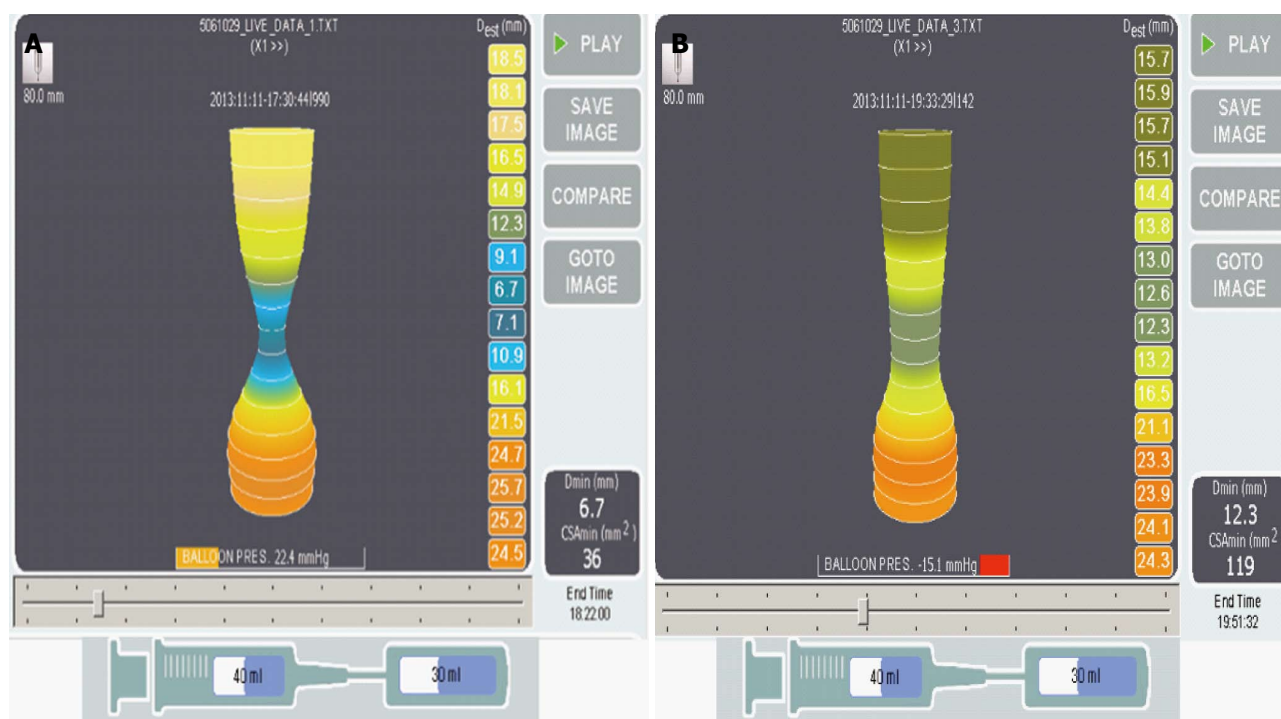


Figure 4 EndoFLIP Images before and after per-oral endoscopic myotomy. Seventy-seven years old man with achalasia for 4 years, prior Botox × 1, esophageal diameter of 5 cm, non-sigmoid, underwent per-oral endoscopic myotomy (POEM), 8 cm posterior myotomy. A: EndoFLIP performed immediately prior to POEM; B: immediately after POEM at 30 mL balloon volume shows an excellent response with increase of the minimal diameter at the gastroesophageal junction (GEJ) (Dmin) from 6.7 to 12.3 cm and increase in cross-sectional diameter at the GEJ (cross-sectional area) from 36 to 119 mm².

fiber resection but could theoretically have more GERD. We believe most post-POEM patients with GERD will do well with medical therapy. A lesser controversy with a similar theme is whether to dissect the weaker longitudinal muscle component of the LES along with the LES circular muscle. Additional resection of this longitudinal muscle may promote post-POEM reflux, but a study on this issue found no difference between POEM patients who had the additional resection and those that did not in terms of dysphagia relief and GERD^[28].

ENDOFLIP

The adequacy of the POEM can be grossly assessed by visualization and passage of the gastroscope. Our group and other assess the esophagogastric junction distensibility quantitatively with the EndoFLIP system intraoperatively to confirm that an adequate myotomy has been performed^[29]. The endoluminal functional lumen imaging probe (EndoFLIP®)(Crospon Ltd., Galway, Ireland) device is a balloon-tipped catheter that measures shape and compliance of the GEJ using impedance planimetry. It determines minimal luminal diameter and cross-sectional area (CSA) at the level of the LES. Real time quantitative assessment of GEJ distensibility can be calculated by dividing CSA by the balloon pressure that is also recorded by the device. This may assist in confirming that adequate myotomy has been achieved and possibly predict degree of dysphagia relief. A recent study by Rohof and colleagues demonstrated that GEJ distensibility more closely

correlated with symptomatic recurrence after interventions for achalasia than manometry^[30]. In our series, there was a patient who required additional LES dissection in another plane based on this data^[23]. Using EndoFLIP intraoperative assessment in 43 POEMs at a 30 mL balloon inflation, there was a mean 3.5 fold increase in GEJ distensibility^[31]. Figure 4 demonstrates nearly a two fold increase in Dmin diameter as well as three fold increase in cross-sectional area after myotomy. In a small but provocative study, intraoperative Endoflip measurements suggested that LHM requires more of a proximal esophageal myotomy to reduce GEJ distensibility than POEM^[32].

EFFICACY AND SAFETY

The global results of POEM have been superb with dysphagia efficacy (using Eckardt score) in > 90% of subjects and no reported mortality in > 1000 patients^[10,13,31,33-40] (Table 1). More limited data from these studies and smaller ones suggest significant diminution of LES pressure after POEM. Only a small number of studies have reported efficacy based on objective assessment of esophageal emptying by timed barium esophagram. However, their results confirm the high efficacy of the procedure (Table 1). We have performed > 130 cases with similar efficacy and safety.

GERD as defined by symptoms and available pH and endoscopy data is the most prevalent adverse event after POEM, though prevalence varied widely^[10,13,23,31,35-38,40]. In the European multicenter POEM study, esophagitis

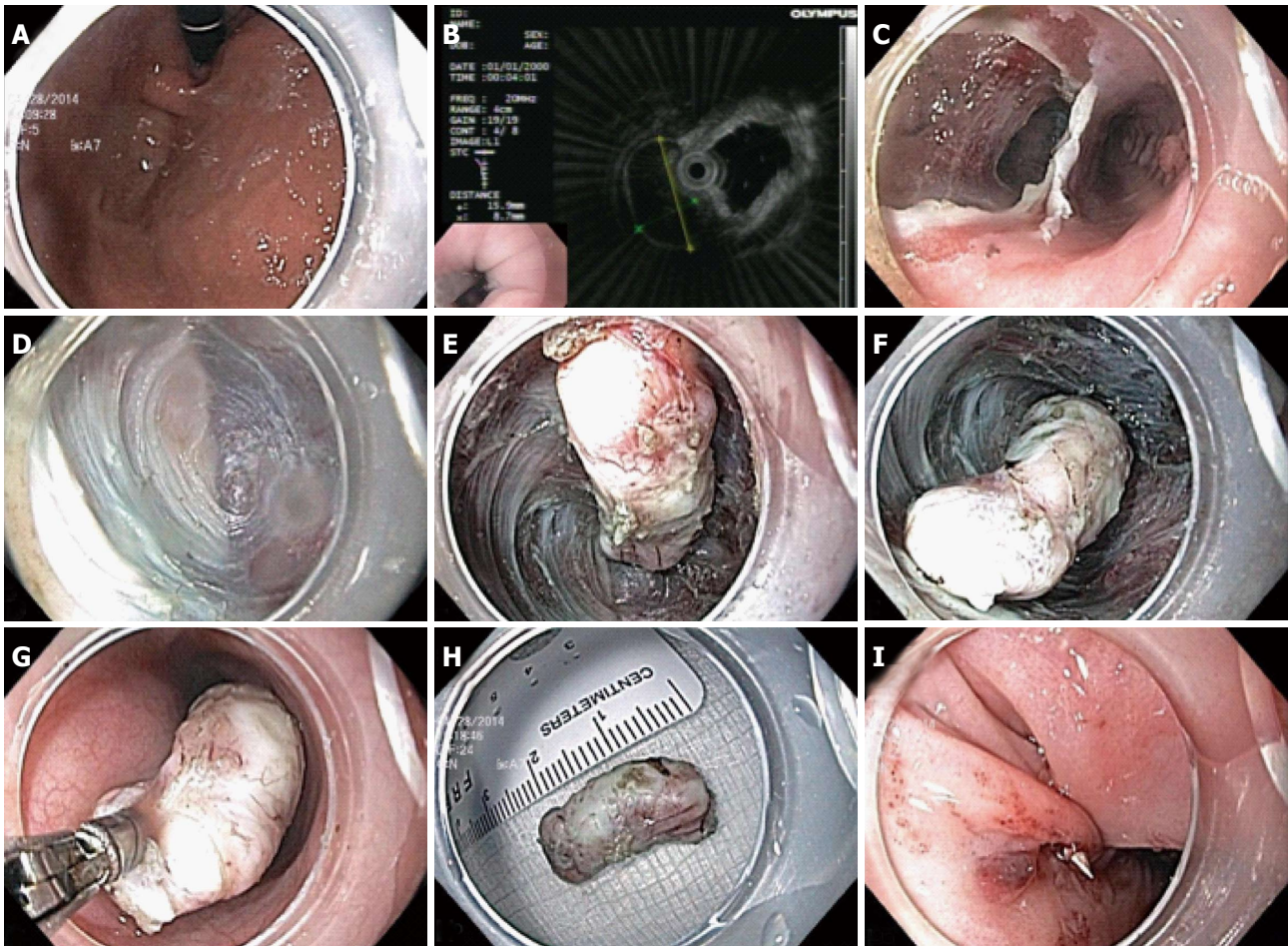


Figure 5 Submucosal tunneling endoscopic resection technique. A: Gastroesophageal junction lesion seen on retroflexion during endoscopy; B: Endoscopic ultrasound probe demonstrates hypoechoic muscularis propria based lesion; C: Creation of submucosal tunnel parallel to esophageal lumen; D: Endoscopic submucosal dissection (ESD) with submucosal tunnel; E-F: Freeing of submucosal lesion via ESD; G: Removal of submucosal lesion from tunnel with biopsy forceps; H: 2.5 cm leiomyoma; I: Endoscopic sutured closure of mucosal entrance to tunnel.

was noted in 42% of subjects though was usually mild^[38]. A small study suggested almost 40% of POEM subjects had abnormal acid exposure on pH testing, but this was similar to LHM subjects^[41]. Insufflation related complications are less common with CO₂ insufflation^[42]. Damage to overlying esophageal mucosa seems to be the common technical concern for the POEM operator. Modest rents can usually be remedied with clips or endoscopic suturing^[24]. Bleeding in the tunnel is unusual but may require reentry for hemostasis^[26].

Comparison to laparoscopic Heller myotomy

There is a lack of long-term efficacy of POEM generally and in relation to LHM or PD. There are no randomized controlled trials comparing POEM to LHM. One prospective series compared 18 POEM and 21 LHM subjects and noted no difference in operative time, myotomy length, relief of dysphagia or complications (each group had one perforation), but the POEM subjects had less postoperative pain and quicker return to work^[43]. However, another group comparing 34 POEM to 64 LHM subjects found the POEM group to have less operative time, lower postoperative Eckardt scores, lower LES

pressures, less length of stay and less dysphagia at six month follow-up^[41]. A third series comparing 70 POEM and 110 LHM subjects found lower Eckardt and LES scores in the POEM group with no significant difference in erosive esophagitis^[44]. More such comparative studies with longer follow-up are expected.

FUTURE PERSPECTIVES

There is current intense investigation in comparing POEM and LHM for achalasia, but long term data for POEM is lacking^[13,41]. The available comparison bodes well for POEM with relative shorter operative times and hospital stays, lower cost and greater patient satisfaction^[36]. Diminishing efficacy of POEM with time is a concern, but more studies are needed^[38]. There is controversy regarding POEM operator background and training as well as credentialing. The apparent success of POEM has fueled some of this debate. Most POEM operators in the US and the world are surgeons^[10]. Yet our group and others feature gastroenterologists with an impressive track record^[23]. The Inoue group feels that extensive animal model practice is paramount for POEM success^[45]. Two

Table 1 Overview of peroral endoscopic myotomy efficacy and gastro-esophageal reflux disease data

Location primary investigator	Patients (n)	Mean age (yr)	Eckardt score (pre/post)	LES pressure (pre/post) (mmHg)	Follow-up (mo)	Timed barium esophagram	Efficacy	Objective GERD evidence n (%)
Costamagna <i>et al</i> ^[34] , Rome, Italy	11	41 (23-68)	7.1/1.1	45.1/16.9	3		100%	
Swanstrom <i>et al</i> ^[35] , Portland, Oregon	18	59 (22-88)	6/0	45/16.8	6	Median emptying at 5 min 15/16: 80%-100% emptying 1/16 less than 80% emptying	94%	Esophagitis (Grade 1 Savory-Miller classification) 4/14 (28) +pH study 6/13 (46)
Chiu <i>et al</i> ^[35] , Hong Kong, China	16	47 (22-87)	5.5/0	43.6/29.8	3		100%	+pH study 3/15 (20)
Hungness <i>et al</i> ^[36] , Chicago, Illinois	18	38 (22-69)	7/1	19/9	63	Median height 1 min 7 cm (0-15 cm) 2 min 5 (0-13 cm) 5 min 0 (0-9 cm) (P < 0.001)	89%	Esophagitis Los Angeles (LA) class A 2/15 (13.3) B 2/15 (13.3) C 1/15 (6.7)
Minami <i>et al</i> ^[37] , Nagasaki, Japan	28	52 (19-84)	6.7/0.7	71.2/21	16 ³		100%	Esophagitis (11/28) 39.3% LA class M 2/28 A 7/28 B 1/28 C 1/28
Von Renteln <i>et al</i> ^[38] , European MCT	70	45	6.9/1	27.6/8.9	12		82%	Esophagitis (42) LA class A 29.2% B 12.3%
Stavropoulos <i>et al</i> ^[31] , Mineola, New York ¹	100	52 (17-93)	7.8/0.2	44.2/17.6	13.3 ²	Mean emptying at 5 min 31/42: 100% emptying 41/42: > 50% emptying	98%	Esophagitis 17/53 (32) +pH study 17/52 (33)
Onimaru <i>et al</i> ^[39] , Yokohama, Japan ¹	300	45 (3-87)	6.13/1.33	27.3/13.4	12		98%	
Verlaan <i>et al</i> ^[40] , Amsterdam, Netherlands	10	43	8/1	20.5/6.8	3	Median height 1 min 3.2 cm (IQR 0.5-6.5) (P = 0.005) 2 min 2.7 cm (IQR 0.4-5.2) (P = 0.005) 5 min 2.3 cm (IQR 0-3.2) (P = 0.005)	100%	Esophagitis (60%) LA class A 3/10 (30) B 3/10 (30)

¹Abstract; ²Mean; ³Median, remainder are minimum follow-up. GERD: Gastroesophageal reflux disease; LES: Lower esophageal sphincter; IQR: Interquartile range.

American “learning curve” studies were small and yielded somewhat conflicting results^[46,47].

POEM OFFSHOOTS: OTHER RAPIDLY GROWING APPLICATIONS OF THE SUBMUCOSAL TUNNEL

POEM was derived from earlier NOTES experiments^[5], but currently POEM is more clinically advanced and more widely adopted than any other NOTES procedure. NOSCART has recently completed a comprehensive “White Paper” on POEM as a demonstration of this procedure’s prominence^[48]. More currently relevant is that the success of POEM has spurred interest and development in ESD; especially in the US^[49]. Arguably POEM has contributed more to ESD adoption in the US in the past few years than over 10 years of presentations and publications by

Japanese and other Asian endoscopists. However, the impact of POEM extends even further. POEM offers a controlled standardized setting for gastroenterologists to familiarize themselves with previously taboo spaces such as the mediastinum and peritoneum and become adept in fundamentals of NOTES such as managing insufflation (capnoperitoneum, capnomediastinum) and achieving secure closure of full thickness breeches of the GI lumen. Thus, the success of POEM has inspired other NOTES offshoots such as submucosal tunneling endoscopic resection (STER) to achieve full-thickness en bloc resection of muscularis based subepithelial tumors (Figure 5). Guidelines recommend resection of many of these tumors when they are larger than 2-3 cm, particularly if they are suspected to be gastrointestinal stromal tumors or if they are causing symptoms, increasing in size on surveillance or have high risk features on biopsy, endoscopic ultrasound (EUS) or computed tomography.

Table 2 Characteristics of United States single center submucosal tunneling endoscopic resection series *n* (%)

Characteristics	Value
STER cases (<i>n</i>)	7
Time period	9/2013-4/2014
Mean age (yr)	52 (47-62)
Gender	3 males; 4 females
ASA classification	
II	6 (86)
III	1 (14)
Location of lesion	4 GE junction; 2 esophagus; 1 gastric cardia
General anesthesia	100%
Procedure time (min)	53 (23-80)
Closure technique	2 clips (29); 5 endoscopic suture (71)
Histopathology	6 leiomyoma (86); 1 GIST (2/50 hpf) (14)
Mean size (cm)	1.5 (1-2.7)
<i>En bloc</i> resection	100%
Length of hospital stay (d)	2.3 (1-4)
Follow-up	100% no recurrence
Complications	1 mucosotomy required clipping 1 stricture at submucosal tunnel site responded to balloon dilation at 4 wk

GE: Gastroesophageal; STER: Submucosal tunneling endoscopic resection; ASA: American Society of Anesthesiologists.

Surgery can be difficult requiring resection of large portions of an organ such as partial gastrectomy or esophagectomy even for small tumors, especially those located in the esophagus, GE junction, pylorus or other challenging locations. For low risk lesions ≤ 2 cm, often endoscopic/endosonographic life-long surveillance is pursued. This overall approach generates a large burden of surgery and endoscopy for subepithelial tumors (SETs) less than 5 cm, the majority of which represent low risk lesions. STER may allow minimally invasive resection of submucosal tumors less than 3-4 cm and is especially appropriate for tumors in challenging locations for the surgeon including the GE junction, esophagus and gastric cardia. It offers a less invasive approach to resection for tumors requiring resection. For small tumors that were destined for surveillance it offers definitive histologic diagnosis (which not infrequently eludes standard endoscopic sampling such as EUS-guided fine needle aspiration). Furthermore, by achieving *en bloc* resection of these small low risk tumors it allows definitive histologic confirmation (including mitotic rate) of their benign nature and eliminates the need for life-long surveillance. It is not surprising that the initial reports of this technique originated at the two most prominent Asian POEM centers. Inoue *et al*^[50] from Yokohama, and Li *et al*^[51] from Shanghai reported their respective initial successes utilizing submucosal tunneling to safely and effectively achieve endoscopic resection of muscularis propria based submucosal tumors in a small series of patients. The Shanghai group subsequently reported their series of 290 patients with follow-up for 4 years showing no residual tumor, local tumor recurrence or distant metastasis^[52]. Our group performed the first STER in the US in September 2012. Our small series of patients also supports that STER is a safe and feasible method for removing muscularis propria based SETs^[53]

(Table 2).

The principle of the submucosal tunnel technique has been adapted to perform wide resections of mucosal lesions (early cancers) in the esophagus. In a series of five patients, *en bloc* resection of superficial esophageal cancer was achieved in all without evidence of recurrence or complications including dysphagia at follow-up between 3-13 mo^[54]. In a larger series of 25 superficial esophageal cancers, 92% *en bloc* resection was achieved with two patients having intramucosal carcinoma recurrence requiring further treatment at mean follow-up 22 mo^[55].

There is a report from a small series employing submucosal tunnel endoscopy under conscious sedation to safely and effectively explore the peritoneal and thoracic cavities through transgastric peritoneoscopy^[56].

Lastly, peroral pyloromyotomy (POP) using a tunneled approach very similar to that used to cut the lower esophageal sphincter in POEM, has been proposed as a potential therapy for gastroparesis^[57]. Studies are in progress at a number of centers. If POP proves effective for even a subset of gastroparesis patients, it may have a large impact on the therapy of this challenging disease.

CONCLUSION

In conclusion, POEM has the potential to be the preferred modality for achalasia and related esophageal motor disorders when personnel and logistics allow. Many questions remain regarding POEM, but its future is bright. The impact of POEM is extending far beyond the narrow domain of esophageal motility disorders. As the first successful clinical application of submucosal endoscopy it is now spawning many other NOTES interventions utilizing a submucosal tunnel approach.

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