Communication from the ASGE Technology Committee

TECHNOLOGY STATUS EVALUATION REPORT

Per-oral endoscopic myotomy (with video)

Prepared by: ASGE TECHNOLOGY COMMITTEE

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The American Society for Gastrointestinal Endoscopy (ASGE) Technology Committee provides reviews of existing, new, or emerging endoscopic technologies that have an impact on the practice of GI endoscopy. Evidence-based methodology is used by performing a MEDLINE literature search to identify pertinent clinical studies on the topic as well as a U.S. Food and Drug Administration Center for Devices and Radiological Health (MAUDE) database search to identify the reported complications of a given technology. Both are supplemented by accessing the related articles feature of PubMed and by scrutinizing pertinent references cited by the identified studies. Controlled clinical trials are emphasized, but in many cases, data from randomized, controlled trials are lacking. In such cases, large case series, preliminary clinical studies, and expert opinions are used. Technical data are gathered from traditional and Web-based publications, proprietary publications, and informal communications with pertinent vendors. Technology Status Evaluation Reports are drafted by 1 or 2 members of the ASGE Technology Committee, reviewed and edited by the Committee as a whole, and approved by the Governing Board of the ASGE. When financial guidance is indicated, the most recent coding data and list prices at the time of publication are provided. For this review, the MEDLINE database was searched through July 2015 for relevant articles by using the key words "per-oral endoscopic myotomy," "endoscopic myotomy," "POEM," "achalasia," "nutcracker esophagus," "jackhammer esophagus," "diffuse esophageal spasm," and "laparasocopic Heller myotomy." Technology Status Evaluation Reports are scientific reviews provided solely for educational and informational purposes. Technology Status Evaluation Reports are not rules and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment or payment for such treatment.

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BACKGROUND

Per-oral endoscopic myotomy (POEM) has emerged as a natural orifice transluminal endoscopic surgery (NOTES) procedure for the treatment of achalasia. The POEM procedure evolved from submucosal endoscopy with a mucosal protective flap in porcine models and the clinical experience with endoscopic submucosal dissection (ESD). In 2007, Pasricha et al[1] first described a novel approach for the endoscopic treatment of achalasia by creation of a submucosal tunnel followed by myotomy of the circular muscle of the lower esophageal sphincter in a porcine survival model. Inoue et al[2] subsequently performed the first successful human POEM procedure in 2008 and reported a case series in 2010. In the relatively short timeframe since, POEM has gained widespread adoption, with some centers reporting an experience of >200 cases.[3-5] The American Society for Gastrointestinal Endoscopy (ASGE) recently published a white paper summary[6] and a preservation and incorporation of valuable endoscopic innovations (PIVI) document[7] on POEM; both documents concluded that although there is a paucity of controlled data, the short-term to medium-term favorable outcomes reported in large series suggest that POEM is a promising alternative to surgery, with a similar safety and efficacy profile. This manuscript reviews the technology and currently practiced techniques for POEM.

TECHNOLOGY UNDER REVIEW

Preprocedure assessment and patient selection

Comprehensive preprocedure assessment of the patient is an essential prerequisite to a successful POEM procedure.[8] Foremost, an accurate clinical and manometric diagnosis of achalasia should be established. This usually involves clinical assessment, endoscopic evaluation of the

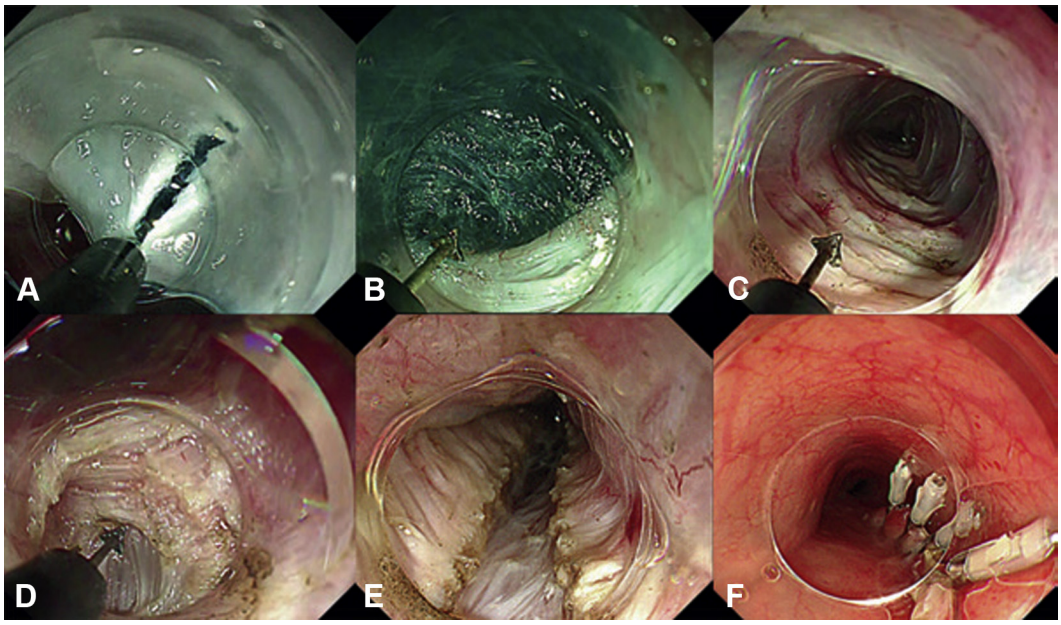

Figure 1. Steps of per-oral myotomy procedure. Mucosal incision **(A)**, submucosal dissection **(B)**, submucosal tunneling **(C)**, myotomy **(D, E)**, and mucosal closure **(F)**. Republished with permission.[12]

gastroesophageal junction (GEJ) to exclude pseudoachalasia, high-resolution manometry to identify the nature and subtype of the esophageal motor disorder, and a contrast esophagogram.[8,9] A CT scan of the chest may also provide additional information on esophageal configuration, relationship to adjacent structures, and the presence of ectopic varices.[9] Many centers also objectively validate symptoms by using a dysphagia questionnaire, usually the Eckardt score, to establish a preprocedure baseline.[10] Comorbidities such as prior thoracoabdominal radiation therapy, cirrhosis with portal hypertension, and prior endoscopic therapy for esophageal diseases (eg, ablation of Barrett's esophagus, EMR and/or ESD for esophageal neoplasia) may be contraindications to the procedure.[6]

Overview of the procedure

The POEM procedure generally involves 4 sequential steps: (1) mucosal incision, (2) submucosal tunneling, (3) myotomy, and (4) closure of the mucosal flap (Fig. 1), (Video 1, available online at www.giejournal.org).[2,6,11,12] A diagnostic endoscopy often is performed 2 to 3 days before the actual procedure to evaluate for retained food or mucosal pathology. Patients are placed on a liquid diet for a variable period of 1 to 5 days before the procedure.[8,12] Prophylactic antibiotics, most commonly a second-generation cephalosporin,[8] are administered routinely, and some centers administer preprocedure empiric antifungal therapy.[8,12]

The patient is positioned supine, and general anesthesia with endotracheal intubation is used. A cap-fitted, high-definition, diagnostic gastroscope, preferably with a dedicated water jet, is used for the procedure. Carbon dioxide (CO_2) is used for insufflation throughout the procedure. Before mucosal incision, the esophagus is lavaged with sterile saline solution, which, at some centers, is mixed with antibiotics or topical antimicrobial agents.[9] The site of mucosal entry usually is 10 to 15 cm proximal to the GEJ. After a submucosal cushion is created by using saline solution mixed with a dye (preferably indigo carmine), an approximately 2-cm longitudinal mucosal incision is made to facilitate entry into the submucosal space. Subsequently, a submucosal tunnel is created by using techniques similar to those of ESD. The plane of dissection is maintained close to the muscularis propria, and care is taken to avoid mucosal injury during the dissection. The submucosal tunnel is extended approximately 3 cm distal to the GEJ to ensure complete myotomy of the lower esophageal sphincter (LES). Once a submucosal working space has been created, a 6 to 10–cm long myotomy is performed, usually proximal to distal. Most commonly, only a selective myotomy of the circular muscle is performed. Subsequently, a careful inspection of the mucosa is performed to detect inadvertent mucosal tears. Endoscopic hemostatic clip closure or other endoscopic closure methods are then used to seal the site of mucosal entry.

A follow-up esophagogram that uses water-soluble contrast material is obtained the following day to evaluate for leaks and to guide timing of initiation of a liquid or pureed diet. Many centers routinely perform a second-look endoscopy 24 to 72 hours after the procedure.[8] The average length of hospital stay for postprocedure observation is 4 days in Japan and 1 to 2 days in the United States and Europe.[12]

Technique variations

The 2 major variations in technique relate to the orientation (anterior vs posterior) and to the depth of myotomy (circular vs complete). In a survey study,[8] 14 of 16 centers favored the anterior approach (11-3 o'clock) as per the original description by Inoue et al,[2] with only 2 centers using a posterior approach (5-6 o'clock).[13,14] Most centers perform a selective circular muscle myotomy, whereas a few perform a complete (circular and longitudinal) myotomy.[12,13]

DEVICES USED FOR POEM

Many of the devices that are used for ESD also are used for POEM. The ASGE recently published a technology document on ESD that comprehensively details all the devices approved for ESD in the United States.[15] In general, devices such as hemostatic forceps, clips, and injection needles are similar to those used for ESD. Devices and related issues that are specific to POEM are detailed in the following.

Endoscopes and caps

Most endoscopists perform POEM by using a flexible, high-definition, diagnostic gastroscope with a dedicated water-jet channel (GIF-HQ 190/GIF-H180J; Olympus Corporation, Center Valley, Pa or EG2990i/EG2990k; Pentax Medical Corporation, Montvale, NJ). As with ESD, the endoscope is fitted with a soft, flexible cap at the distal end to facilitate submucosal dissection. A straight or oblique cap is most commonly used, depending on operator preference.[8] Some authors recommend securing the cap with tape to prevent dislodgement in the submucosal tunnel.[9]

Injection devices

Submucosal injection of saline solution admixed with dye usually is performed through an injection needle and/or spray catheter. During submucosal dissection, this requires an exchange of accessories between the needle-knife and the injection device. To minimize these exchanges, a modified water pump that enables on-demand jet injection of saline solution through a separate bottle activated by a foot pump has been described.[16] Another strategy is to use the hybrid knife (ERBE USA; Marietta, Ga) to create a needleless initial submucosal lift and for subsequent injection during submucosal dissection. The hybrid knife has a central capillary within the cutting knife that facilitates injection by a 120-μm water jet when combined with the foot-pedal activated water jet system (ERBEJET 2 system; ERBE USA). The ERBEJET2 system has been described in a previous ASGE technology document on ESD.[15]

Needle-knives

The most commonly used needle-knives for all aspects of POEM are the triangle-tip knife (TT knife, KD-640L; Olympus Corporation) or the T-type hybrid knife (ERBE USA) (Table 1, Fig. 2).[8] The TT knife has a conductive triangular tip at the end of a 4.5-mm cutting knife.[15] The T-type hybrid knife has a conductive 1.6 mm–diameter disk-shaped electrode at the tip of a 5-mm cutting knife.

TABLE 1. Specifications of needle-knives commonly used in per-oral endoscopic myotomy

Specification	Triangular tip knife*	Hybrid knife†
Tip type	T type	T type
Needle length	4.5 mm	5 mm
Minimum channel size	2.8 mm	2.3
Water jet	No	Yes†
List price	$709	$488

*Olympus America, Center Valley, Pa.
†Requires the use of ERBEJET 2 Water-jet system; ERBE USA, Marietta, Ga.

Electrosurgical generator settings

A detailed review of electrosurgical units and settings for ESD is presented in the ASGE Technology Committee review of ESD[15] and the ASGE Technology Status Evaluation Report on the electrosurgical generator unit (ESU).[17] For POEM, as with ESD, whereas other newer-generation electrosurgical units may be used, specific settings for various aspects of the procedure have been most commonly reported with the ERBE VIO 300D unit (ERBE, USA) (Table 2). For the initial mucosal incision, dry cut mode (50 W, effect 2-3) or Endocut I (effect 2-4, cut duration 1-3 ms, cut interval 1-3 milliseconds) are suggested.[2,9,15] Endocut is a proprietary mode that alternates a pure cutting current with soft coagulation mode; initially there is a high power output for successful initiation of the cut, and the power is then modulated based on tissue impedance.[15] The use of Endocut mode for mucosal incision in POEM is similar to the step of initial mucosal incision in ESD. Submucosal dissection for creation of the tunnel and minor hemostasis in POEM is performed by using a no-touch technique that uses the spray coagulation mode (30-50 W, effect 1-2), which is different than in ESD.[2,9,15] Spray coagulation offers a contact-free, efficient surface coagulation with low penetration depth. There is an automatic dosing of power within the preselected settings. Myotomy also can be performed by using spray coagulation (30-50 W, effect 1-2), especially when there is bleeding from perforating vessels.[2] Care should be taken with using this mode at the GEJ to avoid mucosal injury in the narrow working space. Endocut also is used for myotomy with similar settings as for the initial mucosal incision. Hemostasis of larger vessels in the submucosal space is performed by using a soft coagulation mode (80 W, effect 5).[9]

Carbon dioxide

Because the POEM procedure involves working in the submucosal space in close proximity to the mediastinum

Figure 2. Needle-knives commonly used in per-oral endoscopic myotomy procedures. **A,** Triangular tip knife (KD-640L; Olympus America, Center Valley, Pa). **B,** Hybrid knife 20150-060; ERBE USA, Marietta, Ga. Images courtesy of Olympus America and ERBE USA, respectively.

TABLE 2. Reported settings for ERBE VIO 300D electrosurgical unit* for different stages of per-oral endoscopic myotomy[6,9,12,15]

POEM stage	Electrosurgical unit
Mucosal incision	Dry cut 50 W, E 2-3 Endocut I E 2-4, cut duration 1-3, cut interval 1-3
Submucosal tunneling	Spray coagulation 30-50 W, E 1-2
Myotomy	Spray coagulation 30-50 W, E 1-2 Endocut I E 2-4, cut duration 1-3, cut interval 1-3
Minor hemostasis	Spray coagulation 30-50 W, E 1-2
Major hemostasis†	Soft coagulation 80 W, E5

POEM, Per-oral endoscopic myotomy; *E,* effect.
*ERBE USA, Marietta, Ga.
†Requires use of coagulation grasper (Olympus America, Center Valley, Pa).

and the peritoneum, there is a substantial risk of tracking of gas into these spaces, leading to insufflation-related adverse events, which are the most commonly reported adverse events associated with POEM.[6] Radiologic evidence of pneumomediastinum and pneumoperitoneum was present in greater than 50% of patients in a study in which CT scans were routinely performed after POEM.[18] In a retrospective study that compared outcomes, when room air was used as the insufflation agent early in the POEM experience, and CO_2 was used later, there was a higher incidence of symptomatic insufflation-related adverse events with the use of room air.[19]

The rapid diffusion capacity of CO_2 makes it an attractive alternative to room air for the POEM procedure to minimize the risk of mediastinal emphysema, tension pneumothorax, and pneumomediastinum.[20] Therefore, CO_2 is now almost universally used in POEM procedures.[6,12] CO_2 insufflators and regulators and the use of CO_2 in endoscopy have been described in recent ASGE Technology documents.[20,21] Two other important aspects related to insufflation deserve specific mention with regard to the POEM procedure: a lower flow rate of CO_2 is preferred, and the operator should make a conscious effort to minimize insufflation while working in the submucosal tunnel.[4,6,12] In a retrospective study (n = 100), the incidence of tension pneumoperitoneum was 37% with the use of CO_2 insufflation when a higher flow rate was used, compared with no cases of pneumoperitoneum with a lower flow rate.[22] Therefore, a judicious use of insufflation, combined with a lower flow rate of CO_2 is recommended to minimize insufflation-related adverse events.[12] An underwater POEM technique in which water is infused instead of gas recently has been described in 2 patients.[23]

Evaluation of GEJ distensibility

Objective measurement of GEJ distensibility is being increasingly used and has been reported to be a predictor of postoperative outcomes after POEM and laparascopic Heller myotomy (LHM).[24] Distensibility of the GEJ is measured by using the Endoluminal Functional Lumen Imaging system and probes (EndoFLIP, EF-325N, EF-325R; Crospon USA, Carlsbad, Calif). The probe is a 240-cm catheter with a 14-cm balloon at the distal end; the balloon is compliant to a maximal diameter of 25 mm. The system uses impedance planimetry to calculate the cross-sectional area of the balloon at each of the 16 electrode pairs, which are separated by a distance of 5 mm. Therefore, the probe provides an assessment of luminal geometry over an 8-cm area. Catheter-based pressure measurements also are reported. GEJ distensibility index is calculated as the minimum cross-sectional area divided by the intraballoon pressure. In POEM, most authors describe obtaining preprocedure baseline measurements after induction of anesthesia and subsequent postprocedure measurements after completion of myotomy.[24-26] Distensibility index also may be predictive of the likelihood of developing postoperative gastroesophageal reflux.[24]

Mucosal closure devices

The most common method for closure of the mucosal incision after completion of the myotomy is the use of standard endoscopic clips. In a large case-series (n = 500), all mucosal incisions were closed successfully with standard endoscopic clips.[3] Other reported techniques of mucosal closure are the use of the over-the-scope closure device (Ovesco Endoscopy USA, Los Gatos, Calif) and endoscopic suturing with the OverStitch endoscopic suturing system (Apollo Endosurgery Inc, Austin, Tex).[27-30]

Over-the-scope closure use has been reported when closure with endoscopic clips was technically challenging because of a gaping proximal edge or because of inverted edges.[27,30] Placement of fully covered self-expandable metal stents or endoscopic suturing has been undertaken for inadvertent perforations during POEM.[28-31]

OUTCOMES AND COMPARATIVE DATA

Achalasia

The majority of POEM procedures worldwide have been performed in patients with achalasia without a sigmoid esophagus.[2,6] Outcomes data are largely in the form of case series and 1 international multicenter prospective study; a standardized reporting framework for outcomes has not been established. Objective parameters of technical success include a timed barium esophagogram, manometric measurements such as change in LES pressure and integrated relaxation pressure, and the GEJ distensibility index.[12] The Eckardt score usually is used to assess clinical response; a successful outcome is commonly defined as a postoperative Eckardt score of <3.[7,10]

In the largest single-institution series published to date, Inoue et al[3] reported outcomes on 500 consecutive patients; short-term (2 month) outcomes were reported in all patients, and 58% of patients had a 3-year follow-up. The median operating time was 90 minutes (interquartile range [IQR] 71-120 minutes), median myotomy length was 14 cm (IQR 12-16 cm), and median duration of hospital stay was 4 days (IQR 4-5 days). The median Eckardt score decreased from 6 (range 5-8) preoperatively to 1 (range 0-2) at 2 months and 1 (range 1-2) at 3 years ($P < .01$). There also was a significant decrease in the median LES pressure (baseline 25 mm Hg [range 18-35 mm Hg] vs 13 mm Hg [range 11-16 mm Hg] at 2 months and 12 [range 10-15 mm Hg] at 3 years).

The ASGE PIVI document set a threshold efficacy of 80% at ≥12 months after the procedure (Eckardt score ≤3, with a dysphagia component of ≤2 and a ≤6% serious adverse event rate and a ≤0.1% 30-day mortality rate) and noted that the reported efficacy of POEM ranged from 82% to 100% in this timeframe.[7] A comprehensive listing of reported efficacy from all published case series of >10 patients (2010-2014) noted that efficacy in studies that assessed symptoms objectively with an Eckardt score ranged from 89% to 100%.[12]

An international, prospective, multicenter (5 centers in Europe and North America) study (n = 70) with a mean follow-up of 10 months reported treatment success in 97% (95% confidence interval [CI], 89-99) at 3 months; pretreatment Eckardt scores decreased from 7 to 1 ($P < .01$), and mean LES pressure decreased from 28 to 9 mm Hg ($P < .01$).[32] Sustained treatment success was somewhat lower at 6 months (89%) and 12 months (82%).

Two large meta-analyses reported a significant decrease in Eckardt scores and LES pressures after POEM. In the first analysis (1045 patients from 29 studies), there was a significant reduction in Eckardt scores (overall effect size -7.9; $P < .01$) and LES pressures (overall effect size -7.3; $P < .01$). The other pooled analysis (1122 patients from 22 studies) noted a decrease in Eckardt scores from 6.8 ± 1.2 to 1.2 ± 0.6, a pooled estimate of LES pressure improvement of 66% (>50% considered a successful outcome), and 80% improvement in the timed barium esophagogram.[33]

Three studies that objectively assessed change in quality of life after POEM by using the short form (SF-36) questionnaire reported a statistically significant improvement in quality of life, compared with a baseline.[34-36] Patients also demonstrated a significant improvement in pain scores, social functioning, emotional well-being, and role limitations related to physical and emotional health.[36]

Comparative studies

There are no randomized trials comparing POEM to other treatment modalities for achalasia. Several mostly retrospective, single-institution studies have compared outcomes between LHM and POEM for achalasia.[36-41] In a retrospective, comparative analysis, the authors noted that POEM (n = 37) was associated with a shorter operating time (120 vs 149 minutes; $P < .01$), length of hospital stay (1.1 vs 2.2 days; $P < .01$), and greater improvement in short-term (1 month) Eckardt scores (0.8 vs 1.8; $P < .01$), compared with LHM (n = 64).[39] Postoperative morbidity, 6-month Eckardt scores, LES pressure measurements, and incidence of GERD were similar between the 2 groups. Other studies have reported shorter operating times and recovery and comparable efficacy and incidence of postoperative GERD between the 2 procedures.[36-41] Two ongoing, randomized, controlled trials comparing POEM with LHM are expected to report results in the next few years.

Comparative studies on technique variations

There are no comparative trials on outcomes relative to the orientation or length of the myotomy. Comparative data on circular versus full-thickness myotomy also are limited. A retrospective study that compared full-thickness (n = 103) to circular-muscle myotomy (n = 131) reported similar efficacy and adverse event rates but slightly shorter operative time (42 vs 49 minutes; $P = .02$) with full-thickness myotomy.[13] A double-endoscope method has been described to better define the degree of extension of the submucosal tunnel into the cardia.[42] In a randomized trial, the double-endoscope method, as compared with the conventional single-endoscope technique, resulted in significant extension of the gastric myotomy length but similar clinical success and adverse event rates.[43]

Another variation in the technique is the use of the triangular tip versus hybrid-knife. A retrospective comparative analysis noted a shorter POEM procedure time with a hybrid knife versus a triangular tip knife (53.0 ± 17.2 vs 67.6 ± 28.4 minutes; $P = .02$) but similar clinical outcomes and adverse event rates.[44] A randomized, prospective, controlled trial, comparing the hybrid knife with the water-jet system and the triangular tip knife with the conventional injection technique, reported significantly decreased procedure times with the hybrid knife (22.9 ± 6.7 vs 35.9 ± 11.7 minutes; $P < .01$), with no differences in clinical outcomes or adverse event rates.[19]

Efficacy of POEM in achalasia subgroups

As experience increases, patients at extremes of age and those with late-stage sigmoid esophagus are undergoing POEM.

Pediatric achalasia. LHM is considered definitive therapy for pediatric achalasia. However, successful use of POEM has been reported in children in several small case series. A study of 27 patients (age range 6-17 years) reported that the procedure was successfully performed in all but 1 patient, and over a follow-up of 2 years, the treatment was successful in all patients, with no serious adverse events.[45] Other smaller series with <10 patients also reported favorable outcomes with no adverse events.[46-49]

Sigmoid esophagus and/or megaesophagus. POEM is technically challenging in these patients because of the dilation and tortuosity of the esophagus and the associated submucosal fibrosis from long-standing achalasia. In a retrospective study of 32 patients with sigmoid esophagus, POEM was feasible in all patients and remained effective in 97% of cases at a mean follow-up of 30 months.[50] Procedure times were longer, and the procedure was expectedly more challenging technically, compared with POEM in other populations, but there were no serious adverse events. One advantage of POEM is that it does not preclude a subsequent esophagectomy because the risk of adhesions is low. Given the procedural complexities in patients with sigmoid esophagus, it is particularly recommended that endoscopic myotomy in this subgroup be performed by endoscopists well-experienced in POEM.[14]

Achalasia with prior treatment. *Botulinum* toxin injections and pneumatic balloon dilation often are performed as endotherapy for achalasia. However, *Botulinum* toxin injections, and, to some extent, pneumatic balloon dilation, can induce submucosal fibrosis, which can make the POEM procedure more challenging. Two studies that specifically compared outcomes in patients with and without prior endoscopic treatment reported similar outcomes and adverse events in both groups; there was no significant difference in operating times.[51,52] In general, POEM is considered equally effective and safe in patients with achalasia treated with *Botulinum* toxin injections or pneumatic dilation, compared with treatment-naïve patients.[4,6,12,53]

POEM in patients with recurrence of symptoms after LHM has been reported in small case series (5-12 patients) with a follow-up of 5 to 18 months. In expert hands, POEM was effective in this subgroup of patients, with no increase in adverse events, and this is currently an accepted indication in higher-volume centers.[8,41,54,55] Some authors have reported that a posterior POEM approach in these patients provides the opportunity to perform a myotomy while avoiding the scarring and fibrosis induced by the prior anterior surgical myotomy.[54]

Efficacy of POEM in spastic esophageal disorders

These disorders include type III achalasia, diffuse esophageal spasm, and hypercontractile (jackhammer) esophagus. The efficacy of POEM for these indications appears to be lower compared with achalasia, but comparable with, or better than, LHM in this difficult-to-treat subgroup of patients.[56-58] In a multicenter, retrospective study of POEM for type III achalasia, compared with LHM, clinical response was significantly higher in the POEM group than LHM at 1 institution (98% vs 81%; $P = .01$), although follow-up was shorter in the POEM group (8.6 vs 21.5 months; $P < .01$).[58] The same multicenter group also reported outcomes in 73 patients with spastic disorders; overall response was 93% at a median follow-up of 8 months, and improvement of pain was noted in 87%.[56] The efficacy of POEM for dysphagia in spastic disorders was lower (71%) in other studies.[57]

SAFETY

Since its introduction, approximately 5000 POEM procedures have been performed worldwide. The reported rates of serious adverse events associated with the procedure are low. However, the majority of these studies have been from centers that have pioneered the procedure. Adverse event reporting among studies is heterogeneous; some authors have suggested the adoption of an adverse event classification and reporting method for more accurate assessment of outcomes.[12]

The most common adverse events in POEM are insufflation-related events, bleeding, and mucosal perforation.[12] Less-common events include mediastinitis, peritonitis, aspiration pneumonia, and pleural effusions. The overall serious adverse event rate in the largest single-center series (n = 500) was 3.2%; all were managed conservatively with no perioperative mortality.

Insufflation-related adverse events

These include pneumoperitoneum, pneumomediastinum, and subcutaneous emphysema and account for the most common adverse events associated with POEM.

The reported incidence of insufflation-related adverse events varies widely,[12] but in meta-analyses, these events were noted in 20% to 30% of patients after the procedures.[33,59] In a study of 108 POEM procedures, in which a postprocedure CT scan was performed routinely, radiologic evidence of pneumomediastinum and/or peritoneum was noted in 53% of patients; however, there was no correlation between this finding and development of clinical symptoms or adverse events.[18] Subcutaneous emphysema occurs in 10% to 15%, but patients usually are asymptomatic. Small, asymptomatic pleural effusions are relatively common (about 40%) and do not require intervention.[4] The incidence of pneumothorax ranges from 6% to 11%.[33,59]

Bleeding

Bleeding can occur during the procedure or postoperatively into the submucosal tunnel and can be severe, causing hematemesis, retrosternal pain, and hemorrhagic shock.[60] Fortunately, clinically significant postoperative bleeding is rare. The incidence was noted to be 1.1% in the meta-analysis of 1122 patients undergoing POEM[33] and among large case series, the delayed postoperative bleeding incidence was uniformly <1%.[3,5,22,57,60] Minor intraprocedural bleeding is common and is managed by using techniques similar to ESD with the needle-knife or coagulation grasper (Olympus America, Center Valley Pa).

For severe postprocedure bleeding, endoscopic reevaluation of the submucosal tunnel and hemostasis of active bleeding sites have been reported.[60] This can be very challenging because of the presence of blood in the submucosal tunnel. In these situations, the use of a Sengstaken-Blakemore tube (Bard Medical, Covington, Ga) for hemostasis via esophageal tamponade also has been reported.[60] However, given that after POEM, only the mucosal layer exists as a defense from a full-thickness tear, a Sengstaken-Blakemore tube should be used with extreme caution.[12]

Mucosal perforation

Inadvertent mucosal perforation during the procedure may be relatively common but reporting of intraprocedural mucosal breaks that were successfully treated is varied. In a comprehensive review of all studies with >10 patients, the rate of intraprocedural mucosal perforation was generally <10%, but varied from 0% to 25%, dependent on operator experience.[12] Almost all mucosal perforations were repaired endoscopically and did not require surgical intervention. Esophageal leaks after POEM are rare; the incidence was 0.3% in a pooled analysis.[33]

GERD

GERD is commonly noted after POEM, because this procedure, unlike LHM, is usually not combined with a fundoplication. The reported incidence of GERD varies substantially, but this has been objectively evaluated in only a few studies. In systematic reviews and/or meta-analyses, the incidence of GERD and/or erosive esophagitis ranged from 11% to 19%.[33,59,61,62] Of the studies that reported objective data after POEM, esophagitis was noted in 20% to 59% (predominantly Los Angeles Classification grade A/B) and abnormal acid exposure on ambulatory pH monitoring in 31% to 51%.[14,57,63] A retrospective study compared patients who underwent LHM and Dor or Toupet fundoplication (n = 64) with POEM (n = 37); 24-hour pH testing was available in 48% of LHM patients and 76% of POEM patients.[39] Symptoms of heartburn, reflux, and abnormal acid exposure were similar between the groups.

Ease of use

POEM is a complex procedure that requires the operator to have expertise in flexible endoscopy, NOTES, and in the management of esophageal motility disorders. Many of the early adopters of the POEM procedure were endoscopists with extensive ESD experience or experienced thoracic surgeons with surgical expertise in performing LHM. POEM is unique in that it is a complex procedure for a relatively rare disease, which limits more widespread adoption. The parameters to assess competency in performing POEM have not been established.

Training for POEM and learning curve

The optimal training paradigm and measures of operator proficiency need to be defined. Before performing POEM clinically, the operator should have a clear understanding of the principles of the procedure, anatomical considerations, and in-depth knowledge of devices and ESU settings. There is also general consensus that ex vivo training is critical, especially in Western settings where ESD experience is not widely prevalent, and that an experienced operator should proctor initial clinical cases. In the IPOEMS survey, all gastroenterologists performing POEM reported at least some experience with ESD, and most surgeons had NOTES experience.[8] Preclinical training included ex vivo porcine models, live animal survival and nonsurvival models, and cadavers. The mean preclinical training time in this survey was 46 hours (range 12-154 hours).

Three U.S. studies have reported on learning curves for POEM. The most common surrogate measure of proficiency reported is total procedure time. A cumulative sum analysis on 93 consecutive POEM procedures performed by 1 experienced gastroenterologist noted that efficiency was achieved after 40 procedures and mastery after 60 procedures.[64] In multivariate analyses, operator experience was an independent predictor of procedure time. In this study, clinical outcomes or rate of incidental mucosal injury did not differ by operator experience. A single-center, prospective analysis of the initial 40 POEM procedures reported a decrease in procedure duration, time per centimeter of myotomy, and rate of inadvertent mucosal injury with increasing experience of the operator,

with a plateau noted at around 20 cases.[65] In a report of the POEM experience of 2 surgeons who performed the procedures (n = 36) conjointly, mean operating time did not decrease, but other measures of efficiency such as inadvertent mucosal injury and number of clips decreased with experience.[65] Of note, mean dysphagia scores at 1-year of follow-up decreased with increased operator experience.

Establishing a POEM program

The Natural Orifice Consortium for Assessment and Research (NOSCAR) white paper on POEM detailed the suggested steps for establishing an institutional POEM program.[6] The most important aspect is to develop a multidisciplinary team that includes interventional endoscopists, surgeons, and physicians with expertise in treating esophageal motility disorders. Because this procedure is relatively recent, institutional review board oversight and assessment of outcomes at each institution are recommended. Other aspects include obtaining appropriate institutional administrative approvals and credentialing and establishing a dedicated team of procedure nurses and technologists. As with other complex procedures, a preprocedure checklist and a standardized postprocedure protocol may be beneficial.[66] Having access to industry representatives to train staff and troubleshoot equipment also is recommended.

Logistics

Setting. Most centers perform POEM in the operating room, and almost all use general anesthesia with endotracheal intubation and neuromuscular paralysis with the patient in the supine position.[8,12] POEM procedures performed with the patient under intravenous sedation were associated with increased procedural times and adverse events in a retrospective study.[67] In a survey study, a quarter of respondents reported performing POEM in the endoscopy suite.[8] A single-center series (n = 60) of POEM performed in the endoscopy suite reported procedure times and outcomes that were similar to other reports from high-volume centers.[68]

Operating time. It is critical to allot adequate time and resources for successful outcomes with POEM as with ESD. This can be challenging in busy endoscopy practices. Expectedly, reported operating times vary greatly. The mean (± standard deviation) procedure time in published studies ranges from 29.4 ± 9.2 minutes to 155.8 ± 12.8 minutes.[61] In the International Per-Oral Endoscopic Myotomy Survey (IPOEMS), respondents reported allocating 1 to 3 hours, with the most common being 2 hours.[8]

FINANCIAL CONSIDERATIONS

Currently, there is no Current Procedural Terminology (CPT) code for POEM. In the IPOEMS, most U.S. centers reported using the *unlisted esophageal procedure* code (43499),[8] and some use EGD with injection of any substance and tissue ablation or thoracoscopic myotomy (32665). Unless a thoracoscopy is actually performed, the 43499 unlisted esophageal procedure code is more appropriate. Any reimbursement, however, is variable and payer dependent. It is important to provide a detailed indication and explanation of the procedure in the report to help the payer to review the request for extra payment and establish coverage and pricing. Payers often find it helpful to review copies of paid invoices.

FUTURE DIRECTIONS

The POEM procedure has rapidly gained acceptance worldwide and is changing the treatment paradigm for achalasia. However, several procedural aspects and outcomes need further study. Three important ongoing clinical trials are expected to report results in 2018 to 2019. Among them is a multicenter, randomized, noninferiority trial of POEM versus LHM for the primary treatment of achalasia (NCT01601678). There are also ongoing trials of POEM versus pneumatic dilation (NCT01793922) and anterior versus posterior myotomy approaches (NCT02454335). Prospective multicenter studies that objectively assess postprocedure abnormal acid exposure and rates of long-term GERD after POEM also are needed. Outcomes of POEM for nonachalasia indications and for extended indications such as megaesophagus and/or sigmoid esophagus should be evaluated in controlled studies. In addition, randomized trials on technical variations such as the orientation and depth of myotomy also are needed.

One of the challenges in comparing outcomes between centers is the lack of standardization in outcome and adverse event reporting. In this regard, a POEM-specific, concise, adverse event classification that can be adopted widely has been suggested.[12] Quality benchmarks and parameters of proficiency need to be established, and the learning curves to achieve proficiency also need to be further defined.

SUMMARY

POEM has emerged as a viable option for the treatment of achalasia and other spastic esophageal disorders. The POEM procedure involves sequential steps of mucosal incision, submucosal dissection and tunnel creation, myotomy, and subsequent closure of the mucosal incision. The optimal orientation (anterior vs posterior), depth (circular vs full thickness), and length of myotomy require further study. Several emerging technologies may provide information to help customize the procedural approach to an individual patient. The procedure is effective in >90% of achalasia patients, and the rate of serious adverse events is

generally <5%. There is a paucity of controlled data; however, several ongoing randomized clinical trials are underway. POEM is a complex procedure for a relatively rare disease, which makes for a steep learning curve. The optimal training paradigm and benchmarks of proficiency have not been established. Establishing a POEM program requires multidisciplinary collaboration, and institutional administrative and review board approval are recommended.

DISCLOSURES

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Abbreviations: ASGE, American Society for Gastrointestinal Endoscopy; CO_2, carbon dioxide; ESD, endoscopic submucosal dissection; ESU, electrosurgical generator unit; GEJ, gastroesophageal junction; LES, lower esophageal sphincter; LHM, laparascopic Heller myotomy; NOTES, natural orifice transluminal endoscopic surgery; PIVI, preservation and incorporation of valuable endoscopic innovations; POEM, per-oral endoscopic myotomy.

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