Communication from the ASGE Standards of Practice Committee

PRESERVATION AND INCORPORATION OF VALUABLE ENDOSCOPIC INNOVATIONS

The American Society for Gastrointestinal Endoscopy PIVI (Preservation and Incorporation of Valuable Endoscopic Innovations) on peroral endoscopic myotomy

GENERAL CLINICAL AREA OF THIS PRESERVATION AND INCORPORATION OF VALUABLE ENDOSCOPIC INNOVATIONS

The area covered is peroral endoscopic myotomy (POEM) for the treatment of achalasia.

BACKGROUND AND STATEMENT OF CLINICAL RELEVANCE

Achalasia is a motility disorder associated with degeneration of neurons in the wall of the esophagus. It is characterized by failure of relaxation of the lower esophageal sphincter (LES) and is commonly accompanied by a loss of esophageal peristalsis. Although achalasia remains relatively rare, heightened awareness of the disease and increasing use of high-resolution manometry have allowed this disorder to be more readily diagnosed and differentiated from other motility disorders of the esophagus. Nonsurgical therapy has traditionally involved pneumatic balloon dilation or endoscopic botulinum toxin injection. Although endoscopic therapies have had good short-term clinical response rates, the durability of treatment has been variable.[1,2] Surgical myotomy, although more invasive, has long been considered to provide more sustained relief of symptoms.[3] More recent data have suggested that serial endoscopic pneumatic dilation and surgical myotomy are comparable in efficacy.[4] POEM has emerged as a potential attractive option for the treatment of achalasia that offers a minimally invasive endoscopic approach to myotomy with the potential for a durable response to therapy.

SPECIFIC CLINICAL ISSUES ADDRESSED BY THIS PIVI

What performance characteristics are required for POEM to be considered a therapeutic option for the treatment for achalasia?

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THRESHOLDS RECOMMENDED FOR THIS PIVI

For endoscopic myotomy to be considered a therapeutic option for the treatment of achalasia, the procedure should have

(1) 80% or greater efficacy 12 months after the procedure, defined as an Eckardt score 3 or less with a dysphagia component of 2 or less and
(2) a 6% or lower serious adverse event rate and a 0.1% or lower mortality rate within 30 days after the procedure.

SUMMARY EXPLANATION OF THRESHOLDS FOR THIS PIVI

Achalasia is a rare esophageal motility disorder characterized by incomplete relaxation of the LES. Medical therapy has little effect on the treatment of this disorder. Endoscopic therapies have attempted to decrease LES pressure either with botulinum toxin injection or with disruption of the LES by using pneumatic balloon dilation. Operative intervention involves a surgical myotomy of the LES with or without a fundoplication to reduce the incidence of gastroesophageal reflux disease (GERD). A laparoscopic approach is the preferred method as this technique has been associated with better outcomes and faster recovery times compared with the open or thoracoscopic operations.[5]

POEM is a natural orifice transluminal endoscopic surgery approach to the traditional surgical myotomy. There is worldwide interest in this procedure as it holds promise for providing a highly efficacious and durable endoscopic approach for the treatment of achalasia with minimal morbidity and faster recovery times. The goal of this PIVI is to propose performance targets for POEM to be considered a therapeutic option for achalasia. Outcome data on POEM have been limited to those from several high-volume centers. Additional data regarding the procedure are emerging, although long-term data are lacking. To propose performance thresholds for POEM, the Committee thought that it was important to first consider the performance characteristics of alternate interventions including endoscopic botulinum toxin injection, pneumatic dilation, and Heller myotomy in addition to reviewing the current published literature on POEM. Much of the older literature is difficult to interpret because these studies predate the

TABLE 1. Severity of dysphagia assessed by the dysphagia score and the Eckardt score

Eckardt score	Weight loss, kg	Dysphagia	Retrosternal pain	Regurgitation
0	None	None	None	None
1	<5	Occasional	Occasional	Occasional
2	5-10	Daily	Daily	Daily
3	>10	Each meal	Each meal	Each meal

use of high-resolution manometry and inadvertently include patients with other spastic esophageal motility disorders. Endoscopic techniques vary from 1 study to another, and clinical endpoints used to measure efficacy are not standardized. With these limitations in mind, the Committee proposed clinical endpoints as well as efficacy targets for future research.

The most commonly used metric for evaluating achalasia therapies is the Eckardt score, with clinical success defined as a score of 3 or lower after the therapeutic intervention. The Eckardt score consists of 4 components including dysphagia, chest pain, regurgitation, and weight loss.[6] Each component is assigned a score from 0 to 3 based on the patient's self-reported response, resulting in a total score that can vary from 0 to 12 (Table 1). Although the Eckardt score is increasingly used to assess response to treatment, there are important limitations to the scoring system. Dysphagia is the predominant symptom that is targeted with achalasia treatment, yet a patient may have an Eckardt score of 3 and still experience dysphagia symptoms with each meal. Therefore, the committee thought that it was important to highlight the dysphagia component of the Eckardt score in addition to the overall score when assessing the efficacy of POEM. Some authors suggest that for patients undergoing POEM for end-stage achalasia/megaesophagus, a relative decrease in the Eckardt score may be a more attainable endpoint as these patients are unlikely to have complete symptom relief.[7] The definition for end-stage achalasia is controversial and has previously been defined by an esophageal lumen diameter greater than 6 cm or the presence of a distal esophageal angulation with a sigmoid-like configuration.[8] These cases must be evaluated on an individual basis.

Given the limitations of the Eckardt scoring system, some have proposed that objective data be used to measure the efficacy of achalasia treatment. The committee suggests that an objective study should be performed before the procedure and again 12 months after the procedure to provide objective confirmation of the efficacy of the procedure. Current data support the use of esophageal manometry or a timed-barium study to assess the response to achalasia therapy.[9] Interventions that result in more than a 50% manometric decrease in LES pressure, or a greater than 50% reduction in barium height 5 minutes after ingestion are considered successful. However, due to institutional regulations and/or a lack of insurance coverage, many centers have not been able to perform objective studies after POEM. Furthermore, many individuals refuse to undergo invasive procedures such as manometry if they are not experiencing persistent dysphagia symptoms and are not willing to pay for additional testing that is not covered by insurance. Other measurements such as functional lumen distensibility may provide objective data to guide response to therapy.[10] Recent data suggest that intraoperative evaluation of functional lumen distensibility can be used to assess the extent and completeness of the myotomy during POEM.[10,11]

Endoscopic pneumatic dilation and laparoscopic Heller myotomy (LHM) are considered first-line therapies for achalasia. Endoscopic botulinum toxin injection is moderately efficacious in the short term, with approximately 79% of patients experiencing symptom improvement when evaluated 4 weeks or less after the procedure.[1] However, this therapy lacks a sustained response, with 53% of individuals reporting symptom relief at 6 months and 41% reporting relief at 12 months.[1] Due to waning efficacy over time, many individuals often require repeat or alternative therapy.[2] Subsequent botulinum toxin injection is associated with decreased efficacy and has the potential to result in submucosal fibrosis, possibly making subsequent myotomy more difficult. Despite its favorable safety profile, botulinum toxin injection has been demonstrated to be less efficacious than both pneumatic dilation and LHM and is, therefore, generally reserved for patients considered to be at higher surgical risk. Pneumatic dilation has an 81% success rate at 6 months with a less than 2% perforation rate.[2] Lower rates of perforation from pneumatic dilation have been reported for high-volume centers, with many of these perforations managed conservatively or with endoscopic therapy and infrequently require operative intervention.[12] The previous dogma that pneumatic dilation is markedly less efficacious than surgical myotomy is no longer considered true. Earlier studies demonstrated less effectiveness of a single balloon dilation compared with Heller myotomy because the need for repeat pneumatic dilation was considered a failure of therapy. Recent studies using a stepwise dilation strategy (incrementally increasing balloon diameter from 30 mm to 35 mm to 40 mm at short intervals if there is a lack of response to a previous dilation) have demonstrated this technique to be similar to Heller myotomy in short-term efficacy.[4,13]

The main advantage of LHM has been the durability of response with a single operation compared with the need for multiple endoscopic procedures with pneumatic dilation. Failure rates of LHM defined as persistent or frequent dysphagia symptoms have been reported as high as 23%, but are closer to 10% in larger prospective series. However, this represents a more invasive approach compared with endoscopic therapies with increased morbidity and often requires a concomitant, an antireflux maneuver to limit postoperative GERD. As many as 10% to 15% of patients who have undergone therapy will have progressive esophageal dilation and subsequently fulfill criteria for end-stage achalasia.[7]

For POEM to be considered a viable therapeutic option, the risks of the procedure should not exceed the risks associated with LHM. Thus, we propose that the rate of serious adverse events with POEM should be 6% or lower and the mortality rate 0.1% or lower. These rates are based on systematic review of the available literature on LHM and consensus opinion.[1] Serious adverse events should be defined to include extraluminal gas that results in hemodynamic compromise, mediastinal sepsis, peritonitis, clinically significant bleeding, tunnel dehiscence, need for reoperation or additional invasive intervention, readmission to the hospital within 30 days, and prolonged hospitalization of more than 7 days. Additional surgery- and anesthesia-related adverse events (ie, deep venous thrombosis, aspiration pneumonia) should be equivalent to those of LHM. Insufflation-related pneumothorax, pneumomediastinum, and pneumoperitoneum that require needle decompression are considered mild adverse events. Subcutaneous emphysema is commonly noted during the procedure and is not considered a true adverse event.

METHODOLOGY USED FOR THIS PIVI

Focused clinical questions were used for directed literature review and analysis. A comprehensive data search was performed to answer focused clinical questions by using a National Library of Medicine PubMed search engine from January 1980 to March 2014. Single or limited case reports were excluded, and in cases of replicated sequential series, only the most recent publication (highest case number) was used. Studies were excluded if combined data were reported.

Expert consensus was also used.

Focused clinical questions were the following:

1. What are the performance characteristics (efficacy, durability, and safety) of endoscopic botulinum toxin injection for achalasia?
2. What are the performance characteristics of pneumatic dilation for achalasia?
3. What are the data comparing endoscopic botulinum toxin injection with pneumatic dilation for achalasia?
4. What are the performance characteristics of thoracoscopic myotomy for achalasia?
5. What are the performance characteristics of laparoscopic myotomy for achalasia?
6. What are the data comparing pneumatic dilation with laparoscopic myotomy for achalasia?
7. What are the published performance characteristics of POEM?

LITERATURE REVIEW RESULTS/SUMMARY

1. What are the performance characteristics of endoscopic botulinum toxin injection for achalasia?

The use of endoscopic botulinum toxin injection for the management of achalasia was previously summarized.[1] There have been 9 published, prospective, cohort/case-control series from 1996 to 2003 for a total of 315 patients, with a mean follow-up of 18 months. The dose of botulinum toxin in these studies varies from 25 units to 100 units. Injection of more than 100 units of botulinum toxin has not been more effective.[14] Four studies reported symptom improvement 6 months after botulinum toxin injection, with an overall response of 53% (range 44%-57%).[15-18] Six studies reported symptoms more than 12 months after botulinum toxin injection with an average response of 41% (range 10%-55%).[18-23] Almost half of the patients (47%) required repeat treatment with botulinum toxin injection. One randomized, controlled trial demonstrated superiority of 2 planned treatments of 100 units of botulinum toxin 1 month apart compared with a single treatment with 200 units of botulinum toxin (81% vs 57%), yet 30% of patients still required additional therapy.[14] Elderly patients and those with a baseline LES pressure less than 50% higher than normal have been shown to have improved response to botulinum toxin injection.[22] As botulinum toxin therapy has been demonstrated to be less efficacious than both pneumatic dilation and LHM for the treatment of achalasia, it is generally reserved for patients considered to be poor surgical candidates.[24]

2. What are the performance characteristics of pneumatic dilation for achalasia?

Pneumatic dilation has been studied extensively for the treatment of achalasia with results recently summarized.[25] Trial size, outcome measures, dilation technique, and follow-up are variable and have not been standardized. In a recent randomized, controlled trial of pneumatic dilation versus Heller myotomy therapeutic success of dilation, as measured by a decrease in Eckardt score to 3 or lower, was 90% at 1 year and 86% after 2 years.[4] Although techniques are highly variable, the graded dilation technique initially described by Kadakia et al,[26] which involves progressing sequentially from a 30-mm to 35-mm to 40-mm balloon until a response occurs, resulted in a success rate

TABLE 2. Representative studies of pneumatic dilation for achalasia

Study	Design	No.	Technique	Follow-up duration	Outcome measures	Results	Perforation rate, %
Boeckxstaens, 2011[4]	RCT	95	≥2 dilations, initial 30 mm, 35 mm at 1-3 wk, then 40 mm if still symptomatic	24 mo	Eckardt score (0-12)	90% at 1 y; 86% at 2 y	4
Leyden, 2014[2]	Systematic review pneumatic dilation vs botulinum toxin	178		12 mo	Symptom remission rates at 1, 6, 12 mo	Initial: 86% (82/95) 6 mo: 81% (46/57) 12 mo: 73% (55/75)	1.6
Dobrucali, 2004[28]	Case series	43	Initial 30 mm, 35 mm if still symptomatic	5 y	Symptom questionnaire	80% at 1 y, 54% at 5 y	2.3
Chan, 2004[29]	Case series	66	30, 35, or 40 mm at discretion of operator	19 y	Eckardt score 0-1	86% at 12 wk, 74% at 5 y, 62% at 10 y	4.5
Vela, 2004[30]	Case series	111	30, 35, 40 mm in sequence and depending on response	Mean, 7 mo; range, 1-62 mo	Symptom score for dysphagia and regurgitation ≤3 on 5-point scale	86%	2
Wehrmann, 1995[31]	Case series	40	30 or 35 mm initially	4-6 wk	Stark symptom score decrease ≥3 points on scale of 14	88%	2
Abid, 1994[32]	Case series	36	35 or 40 mm	Mean: 27 mo	25-point symptom score	88% good to excellent based on decrease in symptom score	6.6
Kadakia, 1993[26]	Case series	29	Graded dilation 30, 35, 40 mm based on symptoms	NA	Clinical symptoms	93% with graded dilation	0

NA, Not available.

of 93%.[27] This has now become the preferred approach to pneumatic dilation, as the overall response to graded dilation appears to be 70% to 90% at 1 year (Table 2).[27] Conversely, the success rate of a single dilation is only 68% at 1 year.[1] The response rate appears to deteriorate over time ranging from 44% to 73% at 6 years after dilation.[33,34] The perforation rate is now approximately 2% with rates as low as 0.37% in experienced centers.[13]

Given the variable response to pneumatic dilation, attempts have been made to determine predictors of response. These include age older than 45 years, male sex, nondilated esophagus before dilation, LES pressure less than 10 mm Hg after dilation, and Chicago Classification type II pattern of achalasia.[13]

3. What are the data comparing endoscopic botulinum toxin injection with pneumatic dilation for achalasia?

A Cochrane analysis found 7 high-quality randomized, controlled trials for achalasia comparing botulinum toxin injection with pneumatic dilation.[2] However, the studies used different approaches for both botulinum toxin injection (doses ranging from 60 to 100 units, being administered as either scheduled or unscheduled injections) and pneumatic dilation techniques (balloon sizes of 30, 35, and 40 mm, starting with different size balloons, scheduled or unscheduled repeat dilations). The general outcomes measured were symptoms and LES pressure, but with different scales and at different time points. Only 5 studies were included in the analysis for initial response to treatment, 3 studies provided data at 6 months, and 4 studies provided data at 12 months. Studies also varied in how they defined remission at 12 months, and not all studies repeated esophageal manometry. Most of the studies were single blind (to patient), but none were double blind. There were variable inclusion criteria, as some studies included patients who had previously undergone pneumatic dilation. Adverse events were recorded, with none in the botulinum toxin group and 3 perforations in 188 pneumatic dilation procedures (1.6%).

A meta-analysis of the 5 randomized, controlled trials comparing single-dose botulinum toxin injection with

single pneumatic dilation revealed no significant difference in remission within the first 4 weeks, but the remission rates were approximately 1.6 and 1.9 times higher with pneumatic dilation at 6 and 12 months, respectively.[2] The same conclusions were made from another meta-analysis that included 5 studies.[35] There are also other studies showing improvement with combined botulinum toxin injection and pneumatic dilation versus pneumatic dilation alone.[36]

4. What are the performance characteristics of thoracoscopic myotomy for achalasia?

There have been 17 studies with a total of 306 thoracoscopic myotomy cases published from 1992 to 2004. There are multiple publications of the same series from the same institution with variable outcomes and numbers. There were 4 case reports, 11 retrospective case series (7 comparative, 3 single technique; 10 single institution, 1 multiple institution), and 1 Markov model. There were no prospective or randomized studies. Supplemental Table 1 (available online at www.giejournal.org) summarizes the data from representative studies. The largest series and noncomparative studies show good feasibility and high efficacy (>80%).[5,65,67,69-73] All studies comparing thoracoscopic myotomy with laparoscopic myotomy with fundoplication demonstrated longer operating times, longer hospital stays, a trend to higher open conversion rates, and poorer dysphagia relief, with higher postoperative GERD for thoracoscopic myotomy.[5,65,69,71-73] A Markov model with published and institutional utilities showed thoracoscopic myotomy to have the lowest quality-adjusted life-years score among all therapeutic options, including LHM with fundoplication, pneumatic dilation, and endoscopic botulinum toxin injection.[37]

The overall quality of published evidence is very low with relatively small numbers. However, the data show marked inferiority of thoracoscopic myotomy compared with a laparoscopic approach in all parameters. This has led to the procedure being more or less abandoned in the literature and in the clinical treatment of achalasia.

5. What are the performance characteristics of laparoscopic myotomy for achalasia?

A literature review identified 38 studies from 1999 to 2012 with a total of 1289 patients (Table 3). Most publications were from the United States, Canada, and Italy. There were 3 multicenter, prospective studies and 1 multicenter, retrospective study. All other studies were single-institution studies. Of these, 19 studies were prospective series and 15 were retrospective. Mean follow-up was 34.5 months (range 5-125 months).

Outcome measures used in these studies varied widely. Although the Eckardt score is now increasingly used, many studies focused on symptom prevalence as measured with symptom scores or by questionnaire. Some studies measured results with objective tests such as barium swallow, esophageal manometry, or pH testing. Other studies used quality-of-life measures such as the SF-36 or GI quality-of-life tests such as the GERD-health related quality of life or GERD Symptom Assessment Scale.

The mortality rate was nil in almost every series. The failure rate, defined as persistent and/or frequent dysphagia, ranged from 2.2% to 23% (mean, 10.9%). Mucosal perforation rates ranged from 2.1% to 23.9% (mean, 7.4%) and were typically more frequent in patients who underwent previous endoscopic therapy with botulinum toxin injection or pneumatic dilation. Satisfaction rates were typically high and, in many series, higher than the observed success rate, which suggests some degree of subjective improvement despite frequent dysphagia. This finding suggests that dysphagia scores and objective studies may more accurately reflect the efficacy of an intervention than global satisfaction scores.

Almost all procedures in these series include some type of fundoplication, with Dor and Toupet being the most common. The evidence shows that the incidence of postoperative acid reflux, as measured by pH studies, is significantly higher without fundoplication. Furthermore, Dor fundoplication was found to be less effective that Toupet or Nissen fundoplication in controlling postoperative reflux, but Toupet and Nissen fundoplication was associated with higher rates of postoperative dysphagia.

LHM remains the criterion standard for the surgical treatment of achalasia. The failure rate of the procedure is approximately 10%, even in large series with prospectively collected data. Mucosal perforation remains an observed adverse event in many series and is readily repaired with laparoscopic suture closure with fundoplication or with endoscopic therapy. Fundoplication at the time of the surgical myotomy is the standard in most series, although the type of fundoplication used varies.

6. What are the data comparing pneumatic dilation with laparoscopic myotomy for achalasia?

For many years, surgical myotomy was considered superior to pneumatic dilation for achalasia.[37-41] In a large retrospective, nonrandomized cohort study of 1461 patients, 80.8% underwent pneumatic dilation, whereas 19.2% underwent Heller myotomy.[41] There was no difference between the 2 groups with respect to the need for subsequent surgical myotomy or esophagectomy. Differences in risk were observed only when subsequent pneumatic dilation was included as an adverse outcome. Given that pneumatic dilation is often performed as a staged procedure, starting with a 30 mm diameter balloon and progressing sequentially to 35 mm and 40 mm if symptoms persist, the need for a second or third pneumatic dilation should no longer be viewed as an adverse event. Rather, patients electing to undergo pneumatic dilation should be counseled that sequential dilations are often necessary. In this study, patients that were treated with pneumatic

dilation were no different from those treated with surgical myotomy with respect to subsequent physician visits, time to use of histamine-2 receptor blockers, proton pump inhibitors, or prokinetic medications.[41]

To date, there have been 9 retrospective cohort studies comparing surgical myotomy and endoscopic dilation for achalasia. These were previously summarized in a meta-analysis by Campos et al.[1] When taken collectively, these 9 studies appear to favor surgery over endoscopic dilation. However, most of these studies used alternate methods of dilation, including rigid and mercury-weighted bougies, and, in some series, the dilation was insufficient, limited to 20 mm. Because most of these endoscopic techniques are considered inadequate by today's standards, the conclusion that surgical management of achalasia is superior to endoscopic management may be premature, especially with improved understanding and refinement of the graded pneumatic dilation technique.

There have been only 3 prospective, randomized trials of pneumatic dilation compared with surgical myotomy. Csendes et al[42] described 81 patients who were randomized to either pneumatic dilation or surgical myotomy. There were fewer treatment failures in the surgery group, but, once again, the need for a second pneumatic dilation was considered a treatment failure. The study was limited by methodological problems, including the use of a Mosher bag for dilation.

Kostic et al[43] randomly assigned 51 patients to either pneumatic dilation or surgical myotomy. In this study, 2 balloon dilations were allowed as initial therapy if needed within the first 7 to 10 days. However, treatment failure was thought to exist if a patient required an additional dilation at 3 months or longer after initial therapy. Once again, there were more treatment failures in the endoscopic arm.

Finally, Boeckxstaens et al[4] reported the results of a European multicenter, prospective, randomized trial comparing pneumatic dilation with LHM with Dor fundoplication. The initial dilations were with a 35-mm balloon. There were 4 perforations in the first 13 patients who underwent pneumatic dilation, so the protocol was amended to initiate pneumatic dilation at 30 mm and advanced sequentially through 35 mm to 40 mm if the Eckardt score was still higher than 3. All patients underwent at least 2 dilations. This is the first study to treat pneumatic dilation as a stepwise procedure, with treatment failure defined as symptom recurrence after all treatments (endoscopic or surgical) were completed. Treatment was considered a failure if the patient had an Eckardt score higher than 3. Primary failure was defined as failure after the initial 30- through 40-mm dilations. If symptoms recurred in the follow-up period, a second series of dilations was allowed, beginning with 35 mm. If the Eckardt score was higher than 3 within 2 years of the second dilation, the treatment was considered a failure because of symptom recurrence. If symptoms recurred again 2 years after the second series of dilations, a third series of dilations was allowed. In both the intention-to-treat analysis and the per-protocol analysis, there was no difference between the 2 groups in the primary outcome of therapeutic success, defined as a reduction in the Eckardt score to 3 or lower. Secondary outcomes (quality of life, LES pressure, and esophageal emptying) were similar in both groups. There were 4 additional perforations in the subsequent 82 patients in the pneumatic group after the protocol was amended to begin with the 30-mm balloon. There were 12 mucosal tears in the surgery group, which were recognized immediately and repaired at the index surgery, only 1 of which required conversion to open surgery. There were no deaths reported.

As long-term data have accumulated, it is becoming increasingly clear that pneumatic dilation, performed as a staged procedure, provides outcomes equivalent to those of surgical myotomy.[4,44] An emerging paradigm is that pneumatic dilation should be considered first, with surgery being reserved for failures.[45] Surgical myotomy has been demonstrated to be safe and effective as a salvage procedure for failed pneumatic dilations, and previous pneumatic dilation does not adversely affect surgical outcome.[46-48] These questions should be addressed by randomized, prospective trials, including the use of POEM, with sufficient power to detect a difference in outcomes.

7. What are the published performance characteristics of POEM?

Current published POEM efficacy data from the literature are summarized in Table 4.[49-58] Replicated sequential series publications were eliminated so that only the last dated publication or largest series from each institution is included. All studies used a dysphagia score as the primary efficacy measure. Short-term clinical success was achieved in 82% to 100% of patients. All studies included pre- and post-POEM LES pressure measurements. All but 1 study reported a decrease in baseline LES pressure of more than 50%.[54] Four studies provided data on timed barium emptying after POEM, with 2 institutions reporting the percentage emptying at 5 minutes and 2 centers reporting the height of barium at 1, 2, and 5 minutes.[60,53,56,58] Clinical success was determined by efficacy measures assessed at 6 weeks to 12 months after POEM, depending on the series. Patient follow-up after POEM ranged from a 3-month minimum follow-up to a mean follow-up of 12.5 months. Only 4 series had an average follow-up of more than 6 months.[49,55-57] Consequently, data on the durability of the procedure are somewhat limited. Early patients have now completed 5 years of follow-up in the centers with the longest experience. However, it should be noted that efficacy in these initial patients may differ from that in subsequent patients due to refinement of technique because initial myotomy lengths were shorter compared with the current standard of 8 to 10 cm along with increased operator experience.[6] The study with the lowest short-term efficacy was a European multicenter trial that reported a 97% success rate at

TABLE 3. Representative studies of laparoscopic surgical myotomy for achalasia

Study	Design	No. of pts	Approach	F-U, mo	Outcome	Results
Gockel et al., 2012[87]	Prospective SI	74	LHM-D	12	Eckardt, GQLI	Eckardt score decreased from 7 to 2; 1 pleural effusion.
Rawlings et al, 2012[70]	Prospective multicenter	60	LHM-D or T	12	Likert, pH, SF-36	Mean operating time: LHM-D vs LHM-T (159 min vs 160 min). Abnormal pH in 10 of 24 (LHM-D) and 4 of 19 (LHM-T). SF-36 improved in 7/10 domains (LHM-T) and 5/10 domains (LHM-D).
Carter, 2011[88]	Retro SI	165	LHM-D	62	Likert	Dysphagia weekly or less, 78%. Satisfaction 3.7/4. Postoperative dilation, 18%. Reoperation, 4%. Heartburn more than once a week, 12%.
Parise, 2011[89]	Retro SI	137	LHM-D	65	Sx prevalence	Dysphagia resolved in 94.78% of pts. 3 mucosal perforations; 0 mortality. Heartburn 10.9% of pts. 1.5% reoperation rate.
Salvador, 2010[90]	Prospective SI	246	LHM-D	31	Sx score	Sx score of 18.5 decreased to 0; in 27/241 pts treatment failed (and were dilated); 9.1% pH positive for acid.
Rosemurgy, 2010[91]	Prospective SI	505	LHM ± D	31	Sx score	95% Sx < 1x/wk, 86% outcome; satisfying or better; 92% would undergo myotomy again.
Finley, 2010[92]	Prospective SI	261	LHM ± D	36.4	Von Trappen score	Increase in late dysphagia in botulinum toxin pts; less late regurgitation in pts dilated preoperatively.
Snyder, 2009[93]	Retro SI	134	LHM ± D	22	GSAS, SF-36, Sx score	90.4% report Sx resolved or improved. 23.9% perforation rate; 14% failure rate. Increase in pts with reflux Sx.
Rebecchi, 2008[94]	Prospective SI	144	LHM-D vs N	125	Sx, manometry, pH	2.8% vs 0% GERD (Dor vs Nissen); 2.8% vs 15% dysphagia (Dor vs Nissen).
Zaninotto, 2008[95]	Prospective SI	407	LHM-D	30	Sx score	82% symptom-free at 10 y; 9.6% failure rate; 8.5% reflux by pH probe.
Schuchert, 2008[96]	Retro SI	194	LHM-T or D	31.6	Sx score	4% failure rate; 4% perforation rate.
Wright, 2007[97]	Retro SI	115	LHM-D vs T	45	Sx score	Less dysphagia in the extended myotomy/Toupet group; 9/52 (17%) reinterventions in the Dor group; 3/63 (5%) in the EM/Toupet group.
Youssef, 2007[98]	Retro SI	100	LHM ± D	40	SF-36, Sx score	92% satisfied; 23% failure rate.
Smith et al, 2006[38]	Prospective SI	205	LHM-T vs D	21	Sx score	17.2% failure rate; preoperative endoscopic treatment had higher rate of failure; 4 esophageal (2.0%) and 10 gastric perforations (4.9%).
Horgan, 2005[99]	Retro multicenter	62	LHM-D	22	Sx score	Dysphagia score decreased from 2.9 to 0.3; 10% failure rate; 16% perforation rate; 16% reflux Sx placed on proton pump inhibitor.
Khajanchee et al, 2005[69]	Prospective SI	121	LHM-T	9	Sx score	84.3% relief of dysphagia (9% failure rate); 33.3% postoperative reflux on pH studies; 31.7% pts with preoperative GERD with postoperative heartburn
Rossetti, 2005[100]	Prospective SI	195	LHM-N	83	Questionnaires	91.8% relief of dysphagia (2.2% failure rate); 4 leaks (2.1%)
Raftopoulous, 2004[101]	Prospective multicenter	88	LHM-T or D	25	Sx score	Sx scores all statistically improved; 2.9% perforation rate; 9.8% failure rate; 13.7% reflux rate (Sx).
Zaninotto, 2001[102]	Prospective SI	142	LHM-D	26	Sx score	10.6% failure rate; 6.7% postoperative reflux on pH studies; 4.1% perforation rate
Patti et al, 1999[79]	Prospective multicenter	133	LHM-T or D	28	Sx score, manometry, pH	4.5% perforation rate; 11% failure rate; 17% reflux on pH studies.

pts, Patients; *F-U*, follow-up; *Retro SI*, retrospective case series from a single institution; *LHM-T, SI*, single institution; *LHM-D, Sx*, symptoms; *GQLI*, Gastrointestinal Quality of Life Index; *LHM-N*, *LHM ± D*, *GSAS*, GERD Symptom Assessment Scale; *LHM ± T*; *GERD-HRQL*, GERD-health related quality of life.

TABLE 4. POEM outcomes from published series

Site(s)	Yokohama, Japan[49]	Portland, Ore[50]	Hamburg, Frankfurt, Germany[51]	Rome, Italy[52]	Chicago, Ill[53]
No. of pts	236*	18	16	11	18
F-U, mo	11†	6	3	3	6‡
POEM success rate, % of pts	99	94	94	91	88.9§
Reason for POEM failure	Retreatment with pneumatic dilation in 1 case, retreatment with POEM in 1 case	Failure to empty esophagus at 5 min in timed barium study in 1 case	1 retreatment with pneumatic dilation	Submucosal fibrosis; pneumatic dilation performed in 1 case	Retreatment with salvage laparoscopic Heller myotomy in 2 cases
Pre/post mean LES resting pressure (mm Hg), *P* value	26.8/12.6 ($P < .001$)	45§/16.8§ ($P = .009$)	27.2/11.8 ($P < .001$)	45.1/16.9 ($P < .001$)	19/9§ ($P < .001$)
Pre/post mean timed barium esophagram		% emptying at 5 minutes: 48%§ (range 4-100%)/100%§ (range 80-100%) ($P = .001$)			1 min: 17/7 cm 2 min: 16/5 cm 5 min: 14/0 cm ($P \leq .001$)§
Pre/post mean Eckardt score,‡ *P* value	6.36/1.45 ($P = .003$)	—/0§	8.8/1.4 ($P < .001$)	7.1/1.1 ($P = .0001$)	7/1§ ($P < .001$)
GERD symptoms, %	44	6	0	0	22
GERD: endoscopic evidence (erosions)	4/14 (28%) esophagitis (all grade 1 in the Savory-Miller classification)	18/105 (17%) esophagitis	1/16 (6%) erosive esophagitis LA classification A	0	5/15 (33%) esophagitis LA classification: A, 2/15 (13%) B, 2/15 (13%) C, 1/15 (7%)
Esophageal pH data	—	6/13 (46%)	—	—	—

pts, Patients; *F-U*, follow-up; *POEM*, peroral endoscopic myotomy; *LES*, lower esophageal sphincter.
Failure generally defined as need to use alternative achalasia treatments and/or failure to meet the criterion or criteria for successful treatment, including technical failure/inability to complete the procedure, failure to achieve appropriate symptom improvement (eg, Eckardt score ≤ 3), and recurrence of symptoms during the follow-up provided by these studies.
*Total number obtained by personal communication with lead author.
†Mean.
‡Non-Eckardt dysphagia score.
§Median.

3 months, but only an 82% success rate at 1 year.[55] It has been hypothesized that inherent to the multicenter design of the study, some centers may have had limited previous experience with POEM and that a learning curve effect may account for the reduced efficacy compared with other single-center studies.[59] Table 5 summarizes the reported adverse events in published series and abstracts.

There are limited published retrospective comparative data for POEM and LHM.[53,60] These preliminary data suggest at least equivalence of the 2 procedures in terms of procedure duration, morbidity, and efficacy. A nonrandomized study of 12 patients undergoing POEM compared with 17 patients undergoing LHM found similar postoperative anatomic and functional outcomes as measured by timed-barium study.[53] Another nonrandomized study of 37 patients undergoing POEM compared with 65 patients undergoing LHM found similar Eckardt scores at 6 months after intervention with similar morbidity; however, those undergoing POEM had a shorter hospitalization than those undergoing LHM (1.1 days vs 2.2 days; $P < .0001$).[60] There are no prospective, randomized, controlled trials comparing POEM with LHM or any other treatment for achalasia.

Unlike LHM, which is nearly always accompanied by an antireflux operation, POEM does not involve an antireflux procedure; therefore, concerns have been raised regarding

TABLE 4. Continued

Hong Kong, China[54]	International multicenter study[55]	Nagasaki, Japan[56]	Seoul, South Korea[57]	Amsterdam, the Netherlands[58]
16	70	28	13	10
3	12	16	6.9[†]	3
100	82	100	100	100
—	5 retreatment with pneumatic dilation 3 cases retreatment with salvage laparoscopic Heller myotomy	—	—	—
43.6/29.8 ($P <$ .005)	27.6/8.9	71.2/21	30.3/15.3	20.5/6.8
	—	Qualitative: shorter passage in all	—	1 min: 11.7/ 3.2 cm 2 min: 10.9/ 2.7 cm 5 min: 10.1/ 2.3 cm 9/10 pts (90%): >50% reduction in height 40% pts: complete emptying
5.5/0[‡]	6.9/1	6.7/0.7	6.4/0.4	8/1
6	3 mo: 1.5% daily symptoms, 31.3% occasional symptoms 6 mo: 6.6% daily; 23.4% occasional 12 months: 7.8% daily; 29.4% occasional	6/28	—	30
—	(42%) LA class A, 29.2% B, 12.3%	(11/28) 39.3% LA class M, 2/28 A, 7/28 B, 1/28 C, 1/28	—	6/10 (60%) LA class A, 3/10 (30%) B, 3/10 (30%)
3/15 (20%)	—	—	—	Only 1 pt reported (positive)

GERD and associated long-term sequelae (ie, Barrett's esophagus, esophageal cancer).

AREAS FOR RESEARCH

The most important issue is to determine how POEM compares to LHM with fundoplication and endoscopic pneumatic dilation. Appropriately designed and powered prospective, randomized, controlled trials are lacking and need to be conducted to effectively compare POEM with other treatment modalities for achalasia. POEM should not only meet the thresholds recommended by this document, but also should demonstrate noninferiority to LHM and endoscopic therapies based on these prospective trials.

Few centers have been performing POEM for more than 5 years, and long-term data on the efficacy of the procedure will be forthcoming. It is unclear whether POEM is more effective for certain Chicago Classification manometric subtypes of achalasia. In addition, there are a number of research areas relevant to this PIVI. Preliminary experience with the intraoperative evaluation of functional lumen distensibility appears promising for assessing the extent and completeness of the myotomy during POEM. Additional experience is needed to confirm

TABLE 5. Adverse events reported in published POEM series and abstracts

	Yokohama, Japan[7,49,81]	Rome, Italy[52,82,83]	International Multicenter Study[55]	Shanghai, China[61,84]	Portland, Ore[50]	Chicago, Ill[53]	Hong Kong[54]	Mineola, NY[85,86]	Nagasaki, Japan[56]	South Korea[57]
No. of cases	236	52	70	205	18	18	16	66	28	13
Pneumo-/capnoperitoneum	1*	17*	8*	47†	1*	7*		9*		
Pneumo-/capnomediastinum		10		12‡/35§						
Pneumo-/capnothorax	1‖			3‡,‖/14§,‖	1‖					
Aspiration pneumonia	1						1			
Subcutaneous emphysema		4	6	27‡/66§		1	2			
Mucosal flap injury	3	4	2		2			6	1	
Accidental full-thickness muscle perforation					1					
Peritonitis	1									
Mucosal ulceration			2							
Submucosal hematoma	1									
Delayed bleeding				1					2	
Other pulmonary adverse events				58 pleural effusion (2 chest tube), 59 atelectasis				1 atelectasis		
Leak/perforation						1				
Other adverse events				1 seizure, 1 Submucosal fistula		1 atrial fibrillation 1 Urinary retention		1 atrial fibrillation		
Esophageal stricture				1						
Dehiscence at tunnel entry				1						

*Requiring 18-gauge needle decompression.
†No intervention.
‡Intraoperative.
§Postoperative.
‖Chest tube placement.

whether this technique can predict response rates to POEM and to determine whether there are other predictors of a successful outcome. POEM is also being used to treat various spastic disorders of the esophagus (ie, diffuse esophageal spasm), and the efficacy of endoscopic myotomy for these disorders has not been well defined. It also remains to be seen whether previous failed endoscopic botulinum toxin injection or pneumatic dilation affects the performance characteristics of POEM because many centers currently exclude these patients from undergoing endoscopic myotomy. The ideal strategy for salvage therapy after a failed POEM procedure has not been detailed.

Cost-effectiveness studies need to be performed related to the performance characteristics of POEM and the need for salvage therapy compared with LHM and a graded approach to pneumatic dilation. Quality-of-life studies before and after POEM are needed. In addition, long-term rates of GERD or reflux-related diseases, including erosive esophagitis, Barrett's esophagus, and esophageal adenocarcinoma, are unknown. Additional quality metrics focusing on outcomes and adverse events need to be identified and validated.

TRAINING ISSUES/ESTABLISHMENT OF COMPETENCY

There are limited published data on the optimal methods for training in POEM.[51,52,54,61-63] Swanstrom et al[59] analyzed the learning curve for their first 40 POEM procedures as measured by the rate of accidental mucosotomies and duration of the procedure per centimeter length of myotomy. The learning curve appears to become

less steep at around 20 procedures, which is in accord with what the majority of practitioners have estimated for POEM training and with published learning curves on LHM.[64,65]

Most early POEM adopters have had previous experience with endoscopic submucosal dissection, but few had previous human natural orifice transluminal endoscopic surgery experience.[64] Hands-on preclinical training is strongly recommended.[66] Most POEM operators have undergone training in a live animal or human cadaver model with a mean of 46 hours of preclinical training.[64] An expert proctor for initial human cases is recommended, with the majority of practitioners having availed themselves of one for a median of 2 proctored cases per center (range 1-7). Most of the early adopters of POEM support a formal center accreditation for POEM, POEM operator certification, and mandatory reporting of severe adverse events to an independent monitoring body.[64] This broad agreement among early adopters regarding stringent accreditation requirements despite their disparate backgrounds (surgeons and gastroenterologists with wide geographic distribution spanning Asia, Europe, and North America) underscores the fact that POEM is an invasive endoscopic surgical procedure that requires appropriate training and preparation, and rigorous accreditation and monitoring of outcomes to ensure safety and efficacy.

FACTORS CONSIDERED BY THE PIVI COMMITTEE IN ESTABLISHING THE THRESHOLD

The factors considered included performance characteristics of alternative therapeutic options for achalasia, specifically with regard to efficacy, durability, and safety.

Other issues addressed by the committee

GERD after POEM is an evolving issue. It has been theorized that POEM may be associated with a lower incidence of reflux than LHM because POEM does not involve dissection of the periesophageal ligaments, such as the phrenoesophageal membrane, that are important in maintaining an antireflux valve function. Initial POEM series indicated very low rates of reflux symptoms (< 10%) in patients after POEM.[7,51] The surprisingly low rate of GERD in these initial reports may have been partly due to possible intrinsic differences between American and Asian achalasia patients (eg, body mass index, eating habits) that may affect the post-POEM incidence of GERD.[50] An additional reason for the very low GERD rates in these initial reports may have been that assessment was mainly by reflux symptom scores rather than objective endoscopic or pH assessment. From the LHM literature, symptoms are known to correlate poorly with reflux in achalasia patients.[67] Recently, reports appeared that included post-POEM evaluation for reflux using objective data, such as EGD, to assess for erosive esophagitis, and pH studies.[50,53] Not surprisingly, by objective assessment, the rate of GERD after POEM was found to be significantly higher than the rate reported based on symptom assessment alone. In recent series, erosive esophagitis was found in 28% to 43% of those post-POEM, and objective documentation of acid reflux was found in 20% to 46% of those who underwent an ambulatory pH study after POEM.[50,53,54] Overall, the severity of the reflux has been mild and easily controlled medically. The rate of reflux appears similar to that after LHM with fundoplication. The incidence of GERD in a surgical myotomy patient without fundoplication is between 55% and 100% but decreases to 21% to 42% with the addition of Toupet or Dor fundoplication.[66-70]

The rates of GERD or reflux-related diseases including esophagitis, Barrett's esophagus, and esophageal cancer after POEM are not well defined. Given the fact that symptoms correlate poorly with reflux in achalasia patients, endoscopic follow-up should be considered 6 to 12 months after the procedure to assess for reflux-related esophagitis. Longitudinal endoscopic follow-up for reflux-related diseases should be performed.

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All authors disclosed no financial relationships relevant to this publication.

Abbreviations: LES, lower esophageal sphincter; LHM, laparoscopic Heller myotomy; POEM, peroral endoscopic myotomy.

REFERENCES

1. Campos GM, Vittinghoff E, Rabl C, et al. Endoscopic and surgical treatments for achalasia: a systematic review and meta-analysis. Ann Surg 2009;249:45-57.
2. Leyden JE, Moss AC, MacMathuna P. Endoscopic pneumatic dilation versus botulinum toxin injection in the management of primary achalasia. Cochrane Database Syst Rev 2014;12:CD005046.
3. Stefanidis D, Richardson W, Farrell TM, et al. SAGES guidelines for the surgical treatment of esophageal achalasia. Surg Endosc 2012;26:296-311.
4. Boeckxstaens GE, Annese V, des Varannes SB, et al. Pneumatic dilation versus laparoscopic Heller's myotomy for idiopathic achalasia. N Engl J Med 2011;364:1807-16.
5. Stewart KC, Finley RJ, Clifton JC, et al. Thoracoscopic versus laparoscopic modified Heller Myotomy for achalasia: efficacy and safety in 87 patients. J Am Coll Surg 1999;189:164-9.
6. Eckardt VF, Aignherr C, Bernhard G. Predictors of outcome in patients with achalasia treated by pneumatic dilatation. Gastroenterol 1992;103:1732-8.
7. Inoue H, Minami H, Kobayashi Y, et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia. Endoscopy 2010;42:265-71.
8. Vaezi MF, Pandolfino JE, Vela MF. ACG clinical guideline: diagnosis and management of achalasia. Am J Gastroenterol 2013;108:1238-49.
9. Rohof WO, Lei A, Boeckxstaens GE. Esophageal stasis on a timed barium esophagogram predicts recurrent symptoms in patients with long-standing achalasia. Am J Gastroenterol 2013;108:49-55.

10. Rohof WO, Hirsch DP, Kessing BF, et al. Efficacy of treatment for patients with achalasia depends on the distensibility of the esophagogastric junction. Gastroenterology 2012;143:328-35.
11. Rieder E, Swanstrom LL, Perretta S, et al. Intraoperative assessment of esophagogastric junction distensibility during per oral endoscopic myotomy (POEM) for esophageal motility disorders. Surg Endosc 2013;27:400-5.
12. Lynch KL, Pandolfino JE, Howden CW, et al. Major complications of pneumatic dilation and Heller myotomy for achalasia: single-center experience and systematic review of the literature. Am J Gastroenterol 2012;107:1817-25.
13. Rohof WO, Salvador R, Annese V, et al. Outcomes of treatment for achalasia depend on manometric subtype. Gastroenterology 2013;144:718-25.
14. Annese V, Bassotti G, Coccia G, et al. A multicentre randomised study of intrasphincteric botulinum toxin in patients with oesophageal achalasia. GISMAD Achalasia Study Group. Gut 2000;46:597-600.
15. Pasricha PJ, Rai R, Ravich WJ, et al. Botulinum toxin for achalasia: long-term outcome and predictors of response. Gastroenterology 1996;110:1410-5.
16. Cuilliere C, Ducrotte P, Zerbib F, et al. Achalasia: outcome of patients treated with intrasphincteric injection of botulinum toxin. Gut 1997;41:87-92.
17. Gordon JM, Eaker EY. Prospective study of esophageal botulinum toxin injection in high-risk achalasia patients. Am J Gastroenterol 1997;92:1812-7.
18. Kolbasnik J, Waterfall WE, Fachnie B, et al. Long-term efficacy of Botulinum toxin in classical achalasia: a prospective study. Am J Gastroenterol 1999;94:3434-9.
19. Fishman VM, Parkman HP, Schiano TD, et al. Symptomatic improvement in achalasia after botulinum toxin injection of the lower esophageal sphincter. Am J Gastroenterol 1996;91:1724-30.
20. Wehrmann T, Kokabpick H, Jacobi V, et al. Long-term results of endoscopic injection of botulinum toxin in elderly achalasic patients with tortuous megaesophagus or epiphrenic diverticulum. Endoscopy 1999;31:352-8.
21. D'Onofrio V, Miletto P, Leandro G, et al. Long-term follow-up of achalasia patients treated with botulinum toxin. Dig Liver Dis 2002;34:105-10.
22. Neubrand M, Scheurlen C, Schepke M, et al. Long-term results and prognostic factors in the treatment of achalasia with botulinum toxin. Endoscopy 2002;34:519-23.
23. Martinek J, Siroky M, Plottova Z, et al. Treatment of patients with achalasia with botulinum toxin: a multicenter prospective cohort study. Dis Esophagus 2003;16:204-9.
24. Zaninotto G, Annese V, Costantini M, et al. Randomized controlled trial of botulinum toxin versus laparoscopic Heller myotomy for esophageal achalasia. Ann Surg 2004;239:364-70.
25. Katzka DA, Castell DO. Review article: an analysis of the efficacy, perforation rates and methods used in pneumatic dilation for achalasia. Aliment Pharmacol Ther 2011;34:832-9.
26. Kadakia SC, Wong RK. Graded pneumatic dilation using Rigiflex achalasia dilators in patients with primary esophageal achalasia. Am J Gastroenterol 1993;88:34-8.
27. Pehlivanov N, Pasricha PJ. Achalasia: botox, dilatation or laparoscopic surgery in 2006. Neurogastroenterol Motil 2006;18:799-804.
28. Dobrucali A, Erzin Y, Tuncer M, Dirican A. Long-term results of graded pneumatic dilatation under endoscopic guidance in patients with primary esophageal achalasia. World J Gastroenterol 2004;10:3322-7.
29. Chan KC, Wong SK, Lee DW, et al. Short-term and long-term results of endoscopic balloon dilation for achalasia: 12 years' experience. Endoscopy 2004;36:690-4.
30. Vela MF, Richter JE, Wachsberger D, et al. Complexities of managing achalasia at a tertiary referral center: use of pneumatic dilatation, Heller myotomy, and botulinum toxin injection. Am J Gastroenterol 2004;99:1029-36.
31. Wehrmann T, Jacobi V, Jung M, et al. Pneumatic dilation in achalasia with a low-compliance balloon: results of a 5-year prospective evaluation. Gastrointest Endosc 1995;42:31-6.
32. Abid S, Champion G, Richter JE, et al. Treatment of achalasia: the best of both worlds. Am J Gastroenterol 1994;89:979-85.
33. Hulselmans M, Vanuytsel T, Degreef T, et al. Long-term outcome of pneumatic dilation in the treatment of achalasia. Clin Gastroenterol Hepatol 2010;8:30-5.
34. Vela MF, Richter JE, Khandwala F, et al. The long-term efficacy of pneumatic dilatation and Heller myotomy for the treatment of achalasia. Clin Gastroenterol Hepatol 2006;4:580-7.
35. Wang L, Li YM, Li L. Meta-analysis of randomized and controlled treatment trials for achalasia. Dig Dis Sci 2009;54:2303-11.
36. Mikaeli J, Bishehsari F, Montazeri G, et al. Injection of botulinum toxin before pneumatic dilatation in achalasia treatment: a randomized-controlled trial. Aliment Pharmacol Ther 2006;24:983-9.
37. Urbach DR, Hansen PD, Khajanchee YS, et al. A decision analysis of the optimal initial approach to achalasia: laparoscopic Heller myotomy with partial fundoplication, thoracoscopic Heller myotomy, pneumatic dilatation, or botulinum toxin injection. J Gastrointest Surg 2001;5:192-205.
38. Smith CD, Stival A, Howell DL, et al. Endoscopic therapy for achalasia before Heller myotomy results in worse outcomes than Heller myotomy alone. Ann Surg 2006;243:579-84.
39. Lopushinsky SR, Urbach DR. Pneumatic dilatation and surgical myotomy for achalasia. JAMA 2006;296:2227-33.
40. Francis DL, Katzka DA. Achalasia: update on the disease and its treatment. Gastroenterology 2010;139:369-74.
41. Anselmino M, Perdikis G, Hinder RA, et al. Heller myotomy is superior to dilatation for the treatment of early achalasia. Arch Surg 1997;132:233-40.
42. Csendes A, Braghetto I, Henriquez A, et al. Late results of a prospective randomised study comparing forceful dilatation and oesophagomyotomy in patients with achalasia. Gut 1989;30:299-304.
43. Kostic S, Kjellin A, Ruth M, et al. Pneumatic dilatation or laparoscopic cardiomyotomy in the management of newly diagnosed idiopathic achalasia. Results of a randomized controlled trial. World J Surg 2007;31:470-8.
44. Parkman HP, Reynolds JC, Ouyang A, et al. Pneumatic dilatation or esophagomyotomy treatment for idiopathic achalasia: clinical outcomes and cost analysis. Dig Dis Sci 1993;38:75-85.
45. Fellows IW, Ogilvie AL, Atkinson M. Pneumatic dilatation in achalasia. Gut 1983;24:1020-3.
46. Ponce J, Juan M, Garrigues V, et al. Efficacy and safety of cardiomyotomy in patients with achalasia after failure of pneumatic dilatation. Dig Dis Sci 1999;44:2277-82.
47. Beckingham IJ, Callanan M, Louw JA, et al. Laparoscopic cardiomyotomy for achalasia after failed balloon dilatation. Surg Endosc 1999;13:493-6.
48. Dolan K, Zafirellis K, Fountoulakis A, et al. Does pneumatic dilatation affect the outcome of laparoscopic cardiomyotomy? Surg Endosc 2002;16:84-7.
49. Eleftheriadis N, Inoue H, Ikeda H, et al. Training in peroral endoscopic myotomy (POEM) for esophageal achalasia. Ther Clin Risk Manag 2012;8:329-42.
50. Swanstrom LL, Kurian A, Dunst CM, et al. Long-term outcomes of an endoscopic myotomy for achalasia: the POEM procedure. Ann Surg 2012;256:659-67.
51. von Renteln D, Inoue H, Minami H, et al. Peroral endoscopic myotomy for the treatment of achalasia: a prospective single center study. Am J Gastroenterol 2012;107:411-7.
52. Costamagna G, Marchese M, Familiari P, et al. Peroral endoscopic myotomy (POEM) for oesophageal achalasia: preliminary results in humans. Dig Liver Dis 2012;44:827-32.
53. Hungness ES, Teitelbaum EN, Santos BF, et al. Comparison of perioperative outcomes between peroral esophageal myotomy (POEM) and laparoscopic Heller myotomy. J Gastrointest Surg 2013;17:228-35.

54. Chiu PW, Wu JC, Teoh AY, et al. Peroral endoscopic myotomy for treatment of achalasia: from bench to bedside (with video). Gastrointest Endosc 2013;77:29-38.
55. Von Renteln D, Fuchs KH, Fockens P, et al. Peroral endoscopic myotomy for the treatment of achalasia: an international prospective multicenter study. Gastroenterology 2013;145:309-11.e3.
56. Minami H, Isomoto H, Yamaguchi N, et al. Peroral endoscopic myotomy for esophageal achalasia: clinical impact of 28 cases. Dig Endosc 2014;26:43-51.
57. Lee BH, Shim KY, Hong SJ, et al. Peroral endoscopic myotomy for treatment of achalasia: initial results of a Korean study. Clin Endosc 2013;46:161-7.
58. Verlaan T, Rohof WO, Bredenoord AJ, et al. Effect of peroral endoscopic myotomy on esophagogastric junction physiology in patients with achalasia. Gastrointest Endosc 2013;78:39-44.
59. Swanstrom LL. Poetry is in the air: first multi-institutional results of the per-oral endoscopic myotomy procedure for achalasia. Gastroenterology 2013;145:272-3.
60. Bhayani NH, Kurian AA, Dunst CM, et al. A comparative study on comprehensive, objective outcomes of laparoscopic Heller myotomy with per-oral endoscopic myotomy (POEM) for achalasia. Ann Surg 2014;259:1098-103.
61. Kurian AA, Dunst CM, Sharata A, et al. Peroral endoscopic esophageal myotomy: defining the learning curve. Gastrointest Endosc 2013;77:719-25.
62. Ren Z, Zhong Y, Zhou P, et al. Perioperative management and treatment for complications during and after peroral endoscopic myotomy (POEM) for esophageal achalasia (EA) (data from 119 cases). Surg Endosc 2012;26:3267-72.
63. Teitelbaum EN, Soper NJ, Arafat FO, et al. Analysis of a learning curve and predictors of intraoperative difficulty for peroral esophageal myotomy (POEM). J Gastrointest Surg 2014;18:92-8.
64. Stavropoulos SN, Modayil RJ, Friedel D, et al. The International Per Oral Endoscopic Myotomy Survey (IPOEMS): a snapshot of the global POEM experience. Surg Endosc 2013;27:3322-38.
65. Zheng B, Rieder E, Cassera MA, et al. Quantifying mental workloads of surgeons performing natural orifice transluminal endoscopic surgery (NOTES) procedures. Surg Endosc 2012;26:1352-8.
66. Stavropoulos SN, Desilets DJ, Fuchs KH, et al. Per-oral endoscopic myotomy white paper summary. Gastrointest Endosc 2014;80:1-15.
67. Gholoum S, Feldman LS, Andrew CG, et al. Relationship between subjective and objective outcome measures after Heller myotomy and Dor fundoplication for achalasia. Surg Endosc 2006;20:214-9.
68. Falkenback D, Johansson J, Oberg S, et al. Heller's esophagomyotomy with or without a 360 degrees floppy Nissen fundoplication for achalasia. Long-term results from a prospective randomized study. Dis Esophagus 2003;16:284-90.
69. Khajanchee YS, Kanneganti S, Leatherwood AE, et al. Laparoscopic Heller myotomy with Toupet fundoplication: outcomes predictors in 121 consecutive patients. Arch Surg 2005;140:827-33; discussion 833-4.
70. Rawlings A, Soper NJ, Oelschlager B, et al. Laparoscopic Dor versus Toupet fundoplication following Heller myotomy for achalasia: results of a multicenter, prospective, randomized-controlled trial. Surg Endosc 2012;26:18-26.
71. Raftopoulos Y, Landreneau RJ, Hayetian F, et al. Factors affecting quality of life after minimally invasive Heller myotomy for achalasia. J Gastrointest Surg 2004;8:233-9.
72. Lee JM, Wang CH, Huang PM, et al. Enduring effects of thoracoscopic Heller myotomy for treating achalasia. World J Surg 2004;28:55-8.
73. Kesler KA, Tarvin SE, Brooks JA, et al. Thoracoscopy-assisted Heller myotomy for the treatment of achalasia: results of a minimally invasive technique. Ann Thorac Surg 2004;77:385-91; discussion 91-2.
74. Codispoti M, Soon SY, Pugh G, et al. Clinical results of thoracoscopic Heller's myotomy in the treatment of achalasia. Eur J Cardiothorac Surg 2003;24:620-4.
75. Ramacciato G, Mercantini P, Amodio PM, et al. The laparoscopic approach with antireflux surgery is superior to the thoracoscopic approach for the treatment of esophageal achalasia. Experience of a single surgical unit. Surg Endosc 2002;16:1431-7.
76. Bloomston M, Boyce W, Mamel J, et al. Videoscopic Heller myotomy for achalasia–results beyond short-term follow-up. J Surg Res 2000;92:150-6.
77. Cade R. Heller's myotomy: thoracoscopic or laparoscopic? Dis Esophagus 2000;13:279-81.
78. Maher JW, Conklin J, Heitshusen DS. Thoracoscopic esophagomyotomy for achalasia: preoperative patterns of acid reflux and long-term follow-up. Surgery 2001;130:570-6; discussion 576-7.
79. Patti MG, Pellegrini CA, Horgan S, et al. Minimally invasive surgery for achalasia: an 8-year experience with 168 patients. Ann Surg 1999;230:587-93; discussion 593-4.
80. Cuschieri A. Endoscopic oesophageal myotomy for specific motility disorders and non-cardiac chest pain. Endosc Surg Allied Technol 1993;1:280-7.
81. Yoshida A, Inoue H, Ikeda H, et al. Clinical results of POEM (per oral endoscopic myotomy) for esophageal achalasia in 161 consecutive cases [abstract]. Gastrointest Endosc 2012;75:AB212.
82. Familiari P, Marchese M, Boskoski I, et al. PerOral Endoscopic Myotomy (POEM) for oesophageal achalasia. Preliminary results on 22 patients. Endoscopy 2012;44:A10-1.
83. Familiari P, Marchese M, Martino M, et al. PerOral Endoscopic Myotomy (POEM) for OEsophageal Achalasia. Outcomes of first 52 patients with mid-term follow-up [abstract]. Gastrointest Endosc 2013;77:AB351.
84. Zhou PH, Yao L, Zhang YQ, et al. PerOral Endoscopic Myotomy (POEM) for esophageal achalasia: 205 cases report [abstract]. Gastrointest Endosc 2012;75:AB132-3.
85. Stavropoulos SN, Modayil R, Brathwaite C, et al. POEM (per oral endoscopic myotomy): 3-year experience by a gastroenterologist at a US center: still safe and effective even in patients with advanced age, severe achalasia, and severe co-morbidities [abstract]. Gastrointest Endosc 2013;77:AB459.
86. Stavropoulos SN, Modayil R, Brathwaite C, et al. Per oral endoscopic myotomy (POEM) for achalasia: excellent long term safety, efficacy and durability in a large single center 4 year series. Am J Gastroenterol 2013;108:S619.
87. Gockel I, Gith A, Drescher D, et al. Minimally invasive surgery for achalasia in patients $>$40 years: more favorable than anticipated. Langenbecks Arch Surg 2012;397:69-74.
88. Carter JT, Nguyen D, Roll GR, et al. Predictors of long-term outcome after laparoscopic esophagomyotomy and Dor fundoplication for achalasia. Arch Surg 2011;146:1024-8.
89. Parise P, Santi S, Solito B, et al. Laparoscopic Heller myotomy plus Dor fundoplication in 137 achalasic patients: results on symptoms relief and successful outcome predictors. Updates Surg 2011;63:11-5.
90. Salvador R, Costantini M, Zaninotto G, et al. The preoperative manometric pattern predicts the outcome of surgical treatment for esophageal achalasia. J Gastrointest Surg 2010;14:1635-45.
91. Rosemurgy AS, Morton CA, Rosas M, et al. A single institution's experience with more than 500 laparoscopic Heller myotomies for achalasia. J Am Coll Surg 2010;210:637-45, 645-7.
92. Finley CJ, Kondra J, Clifton J, et al. Factors associated with postoperative symptoms after laparoscopic Heller myotomy. Ann Thorac Surg 2010;89:392-6.
93. Snyder CW, Burton RC, Brown LE, et al. Multiple preoperative endoscopic interventions are associated with worse outcomes after laparoscopic Heller myotomy for achalasia. J Gastrointest Surg 2009;13:2095-103.
94. Rebecchi F, Giaccone C, Farinella E, et al. Randomized controlled trial of laparoscopic Heller myotomy plus Dor fundoplication versus Nissen fundoplication for achalasia: long-term results. Ann Surg 2008;248:1023-30.

95. Zaninotto G, Costantini M, Rizzetto C, et al. Four hundred laparoscopic myotomies for esophageal achalasia: a single centre experience. Ann Surg 2008;248:986-93.
96. Schuchert MJ, Luketich JD, Landreneau RJ, et al. Minimally-invasive esophagomyotomy in 200 consecutive patients: factors influencing postoperative outcomes. Ann Thorac Surg 2008;85:1729-34.
97. Wright AS, Williams CW, Pellegrini CA, et al. Long-term outcomes confirm the superior efficacy of extended Heller myotomy with Toupet fundoplication for achalasia. Surg Endosc 2007;21:713-8.
98. Youssef Y, Richards WO, Sharp K, et al. Relief of dysphagia after laparoscopic Heller myotomy improves long-term quality of life. J Gastrointest Surg 2007;11:309-13.
99. Horgan S, Galvani C, Gorodner MV, et al. Robotic-assisted Heller myotomy versus laparoscopic Heller myotomy for the treatment of esophageal achalasia: multicenter study. J Gastrointest Surg 2005;9:1020-9; discussion 1029-30.
100. Rossetti G, Brusciano L, Amato G, et al. A total fundoplication is not an obstacle to esophageal emptying after heller myotomy for achalasia: results of a long-term follow up. Ann Surg 2005;241:614-21.
101. Raftopoulos Y, Landreneau RJ, Hayetian F, et al. Factors affecting quality of life after minimally invasive Heller myotomy for achalasia. J Gastrointest Surg 2004;8:233-9.
102. Zaninotto G, Costantini M, Molena D, et al. Minimally invasive surgery for achalasia. J Laparoendosc Adv Surg Tech A 2001;11:351-9.

Prepared by:
ASGE PIVI COMMITTEE
Vinay Chandrasekhara, MD, Chair
David Desilets, MD, PhD
Gary W. Falk, MD, MS
Haruhiro Inoue, MD, PhD
John R. Romanelli, MD
Thomas J. Savides, MD
Stavros N. Stavropoulos, MD
Lee L. Swanstrom, MD

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SUPPLEMENTAL TABLE 1. Representative studies of thoracoscopic surgical myotomy for achalasia

Study	Study design,	No. (thor/lap)	Surgical approach	Follow-up, mo	Outcome measures	Results
Raftopoulos et al, 2004[71]	Retro SI	14/88	Lap	25	QOL/Sx	Equivalent to lap, 88% good to excellent.
Lee et al, 2004[72]	Retro SI	14	VATS	56	Sx score	94% good to excellent.
Kesler et al, 2004[73]	Retro SI	38/19 (open)	VATS vs open	17	LOS, Sx	11% morbidity, 10% conversion, 91% good dysphagia relief compared with open, less blood loss, shorter LOS, less pain.
Codispoti et al, 2003[74]	Retro SI	25	VATS	64	Sx	46% asymptomatic, 4% reintervention, 24% GER Sx
Ramacciato et al, 2002[75]	Retro SI	16/17	THM/LHM + fundo (n = 7) w/o fundo (n = 10)	9	LOS, operating time, Sx, barium, manometry	Mean operating time LHM vs THM (150 vs 222 min, $P = .0001$). LOS after LHM vs THM (2.0 ± 1.0 vs 5.1 ± 2.2 days, $P = .0001$). Persistent or recurrent dysphagia 5.8% in the LHM group vs 37.5% in the THM group, $P = .04$. Heartburn in 1 patient after LHM (5.8%) vs symptoms in 5 patients (31.2%) after THM, $P = .07$. Regurgitation in 5.8% after LHM vs 25% after THM, $P = .149$. Lower esophageal sphincter basal pressure decreased from 32.1 ± 5.9 to 10.5 ± 1.7 after LHM vs 30.1 ± 5.07 to 15.3 ± 2.1 after THM, $P = .0001$.
Urbach et al, 2001[37]	Markov model		THM, LHM, open, balloon	NA	QALY	THM lowest QALY of all strategies.
Bloomston et al, 2000[76]	Retro SI	11/67	VATS	18	Sx	91% improved, 27% GER, 27% complications.
Cade, 2000[77]	Retro, SI	18/18	VATS vs lap	24	Sx	82% "successful" vs 95% lap.
Maher et al, 2001[78]	Retro SI	45/4	VATS vs lap/fundo	24	Sx	3 conversions, 80% good or excellent dysphagia relief, 4 failures (8%).
Patti et al, 1999[79]	Retro MI	35/133	VATS vs lap/Dor	48	Sx, or time, LOS, GER Sx	Thoracoscopic: 85% good or excellent relief; 60% GER; 72-h inpatient stay. Lap + fundoplication: 93% good or excellent relief; 17% GER; 48-h inpatient stay. 8 patients required second operation for persistent dysphagia; 2 patients required esophagectomy.
Stewart et al, 1999[5]	Retro MI	24/63		42		THM: mean operating time, 4.3 h (range 2.9-5.6 h); 3 perforations, 5 conversions to open procedure (21%); mean postoperative LOS, 6.1 days (range 1-17 days); 31% with no or minimal dysphagia after a median of 42 mo; none or minimal heartburn (67%), regurgitation (86%). LHM: Mean operating time, 3.0 h (range 1.5-.5 h) ($P = .01$), 2 perforations, 1 conversion to open procedure (2%, $P = .005$); mean postoperative LOS, 4.0 days (range 1-12 days, $P = 0.03$); 90% with no or minimal dysphagia ($P < .01$) after a median of 17 mo; none or minimal heartburn (89%, $P < .05$); regurgitation, (94%, $P = .3$)
Cuschieri, 1993[80]	Retro SI	23/12	THM for noncardiac chest pain	6	Sx	18 had chest pain relief, 5 had none (78% success).

thor, Thoracotomy; *lap*, laparoscopy; *Retro SI*, retrospective case series from a single institution; *QOL*, quality of life; *Sx*, symptoms; *VATS*, video-assisted thoracoscopic surgery; *LOS*, length of stay; *MI*, multiple institutions; *GER*, gastroesophageal reflux; *fundo*, fundoplication; *w/o*, without; *LHM*, laparoscopic Heller myotomy; *THM*, thoracoscopic Heller myotomy; *Open*, open thoracotomy; *NA*, not available; *QALY*, quality-adjusted life year; *comp*.