2.01.91	Peroral Endoscopic Myotomy for Treatment of Esophageal Achalasia and Gastroparesis		
Original Policy Date:	January 30, 2015	**Effective Date:**	January 1, 2025
Section:	2.0 Medicine	**Page:**	Page 1 of 33

Policy Statement

I. Peroral endoscopic myotomy is considered **investigational** as a treatment for pediatric and adult esophageal achalasia.

II. Gastric peroral endoscopic myotomy is considered **investigational** as a treatment for gastroparesis.

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

Coding
See the Codes table for details.

Description

Esophageal achalasia is characterized by reduced numbers of neurons in the esophageal myenteric plexuses and reduced peristaltic activity, making it difficult for patients to swallow food and possibly leading to complications such as regurgitation, coughing, choking, aspiration pneumonia, esophagitis, ulceration, and weight loss. Peroral endoscopic myotomy (POEM) is a novel endoscopic procedure that uses the oral cavity as a natural orifice entry point to perform myotomy of the lower esophageal sphincter (LES). This procedure is intended to reduce the total number of incisions needed and thus the overall invasiveness of surgery. Gastric peroral endoscopic myotomy (G-POEM) is a similar procedure with the exception that it myotomizes the pylorus rather than LES.

Related Policies

- Magnetic Esophageal Sphincter Augmentation to Treat Gastroesophageal Reflux Disease
- Transesophageal Endoscopic Therapies for Gastroesophageal Reflux Disease

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

Peroral endoscopic myotomy uses available laparoscopic instrumentation and, as a surgical procedure, is not subject to regulation by the U.S. Food and Drug Administration.

Rationale

Background

Esophageal Achalasia

Esophageal achalasia is characterized by reduced numbers of neurons in the esophageal myenteric plexuses and reduced peristaltic activity, making it difficult for patients to swallow food and possibly leading to complications such as regurgitation, coughing, choking, aspiration pneumonia, esophagitis, ulceration, and weight loss. Achalasia is estimated to affect 18 out of every 100,000 individuals in the U.S., and the incidence of 10.5 per 100,000 person-years, with increased rates reported with more advanced age.[1,]

Treatment

Treatment options for achalasia have included pharmacotherapy (e.g., injections with botulinum toxin), pneumatic dilation, and laparoscopic Heller myotomy.[2,3,] Although the latter 2 are considered the standard treatments because of higher success rates and relatively long-term efficacy compared with pharmacotherapy, both are associated with a perforation risk of about 1%. Heller myotomy is the most invasive of the procedures, requiring laparoscopy and surgical dissection of the esophagogastric junction.[3,] One-year response rates of 86% and major mucosal tear rates requiring subsequent intervention of 0.6% have been reported.[4,]

Peroral endoscopic myotomy (POEM) is a novel endoscopic procedure developed in Japan.[3,5,] This procedure is performed with the patient under general anesthesia.[6,] After tunneling an endoscope down the esophagus toward the esophageal-gastric junction, a surgeon performs the myotomy by cutting only the inner, circular lower esophageal sphincter (LES) muscles through a submucosal tunnel created in the proximal esophageal mucosa. POEM differs from laparoscopic surgery, which involves the complete division of both circular and longitudinal LES muscle layers. Cutting the dysfunctional muscle fibers that prevent the LES from opening allows food to enter the stomach more easily.[3,6,]

Note that the acronym POEM in this review refers to *peroral endoscopic myotomy*. POEMS syndrome, which has a similar acronym, is discussed in Blue Shield of California Medical Policy: Hematopoietic Cell Transplantation for Plasma Cell Dyscrasias, Including Multiple Myeloma and POEMS Syndrome.

Gastroparesis

Gastroparesis is characterized by symptoms of nausea, vomiting, bloating, early satiety, and pain, which is caused by delayed gastric emptying without mechanical obstruction.[7,]The estimated U.S. prevalence of difficult to ascertain due to the weak correlation of symptoms with gastric emptying which results in a high rate of underdiagnosis. A systematic review of the literature determined that the prevalence of confirmed gastroparesis, characterized by symptoms and delayed gastric emptying, varies widely in the general population, with estimates ranging from 14 to 268 cases per 100,000 adults. Furthermore, the incidence of this condition spans from 1.9 to 6.3 per 100,000 person-years.[8,]

Treatment

Treatment options for gastroparesis have included dietary modification (smaller meal sizes, avoidance of carbonated beverages, smoking or high doses of alcohol, and in some cases enteral nutrition via jejunostomy), optimization of hydration and glycemic control, pharmacotherapy (e.g.,

antiemetics or Metoclopramide, or off-label medications for symptom control such as domperidone, erythromycin, tegaserod or centrally acting antidepressants), gastric electrical stimulation, venting gastrostomy, feeding jejunostomy, intra-pyloric botulinum injection, partial gastrectomy, and pyloroplasty.[7,] Gastric peroral endoscopic myotomy (G-POEM), which endoscopically performs the equivalent of pyloroplasty, is being investigated for the treatment of gastroparesis. G-POEM myotomizes the pylorus rather than the circular LES but otherwise consists of the same techniques described above.

Literature Review

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and ability to function, including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.
To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

Peroral Endoscopic Myotomy for Adult Individuals with Achalasia

Clinical Context and Therapy Purpose

The purpose of peroral endoscopic myotomy (POEM) in individuals who have esophageal achalasia is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with esophageal achalasia. Esophageal achalasia is characterized by reduced numbers of neurons in the esophageal myenteric plexuses and reduced peristaltic activity, making it difficult for individuals to swallow food and possibly leading to complications such as regurgitation, coughing, choking, aspiration pneumonia, esophagitis, ulceration, and weight loss.

Interventions

The therapy being considered is POEM. The POEM procedure involves tunneling an endoscope down the esophagus toward the esophageal-gastric junction. A surgeon performs the myotomy by cutting only the inner, circular lower esophageal sphincter (LES) muscles through a submucosal tunnel created in the proximal esophageal mucosa.

Comparators
Comparators of interest include esophageal dilation, laparoscopic Heller myotomy (LHM), and botulinum toxin injection.

Esophageal dilation is performed in a graded approach, starting with a small balloon (typically 30 mm), then progressing to larger balloons (35 to 40 mm) 2 to 4 weeks later. The balloons are placed at the level of the gastroesophageal junction and inflated slowly, in order to tear the muscle fibers in a controlled manner. Esophageal perforations are a potential complication. Long-term studies have estimated that approximately one-third of patients may need a repeat procedure.
Laparoscopic Heller myotomy is a minimally invasive procedure in which the thick muscle of the lower esophagus and the upper stomach is cut to open the tight LES. The procedure involves 5 small incisions to insert the camera and surgical instruments. Reported success rates are high (>90%), with a 5-year follow-up study showing an 8% rate of symptom recurrence.

Endoscopic botulinum toxin is injected with a sclerotherapy needle approximately 1 cm above the esophagogastric junction. The complication rate is low and approximately 80% of patients experience immediate symptom relief. The effect diminishes over time, with more than 60% of patients reporting recurrent symptoms at 1 year.

Outcomes
The general outcomes of interest are symptom relief and treatment-related morbidity.
Symptom relief may be measured by the Eckardt score, which is comprised of 4 major symptoms of achalasia: dysphagia, regurgitation, retrosternal pain, and weight loss. Each symptom receives a score from 0 (none) to 3 (severe), for a maximum score of 12. Total scores of 4 or greater represent treatment failure.[9,]

Treatment-related morbidity of concern is the development of gastroesophageal reflux disease (GERD). Gastroesophageal reflux disease risk is high with this procedure because POEM involves ablating the LES without adding any type of anti-reflux mechanism. Additional complications include thoracic effusion, subcutaneous emphysema, and esophagitis.

Symptom relief may be experienced shortly following the procedure. Assessment of durability of relief requires a follow-up of months to years.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence
Systematic Reviews
Multiple systematic reviews and meta-analyses have been published to evaluate POEM as a treatment for achalasia. These reviews are heterogenous in whether they assessed data on POEM alone or compared POEM to other interventions , which outcomes they assessed, which studies they included, and in the statistical methods used. The majority addressed the comparison of POEM to LHM.

Results of systematic reviews that primarily relied on data from noncomparative case series studies are not comprehensively summarized herein.[10,11,12,13,14,] This is because conclusions on comparative

effects cannot be determined from their findings. Some systematic reviews of noncomparative case series did not calculate comparative treatment effects. Others that did had important limitations in their statistical methods, including use of unadjusted indirect comparison approaches, which are subject to a variety of confounding factors that may bias the effect estimate. For example, Andolfi et al (2019) published a meta-analysis of success rates based on manometric subtypes.[14] The authors calculated pooled success rates for POEM, LHM, and pneumatic dilation (PD) in type I, II, and III achalasia, respectively, based primarily on data from noncomparative case series studies. Pooled success rates for POEM in types I, II, and III were 94% (95% confidence interval [CI], 89% to 98%), 97% (95% CI, 93% to 99%), and 93% (95% CI, 88% to 97%), respectively, which were significantly higher compared to LHM for type I (odds ratio [OR], 2.97; 95% CI, 1.09 to 8.03) and type III (OR, 3.50; 95% CI, 1.39 to 8.77), but not type II. However, the use of an unadjusted indirect comparison approach in this analysis precludes drawing conclusions based on these findings.

Peroral Endoscopic Myotomy Versus Laparoscopic Heller Myotomy or Pneumatic Dilation

Below are summarized the most recent systematic reviews (published on or after 2020) that address the comparison of POEM to LHM or PD using data from comparative observational studies and RCTs. Table 1 provides a crosswalk of the comparative studies included in these systematic reviews.

Table 1. Comparison of Studies of POEM versus LHM or PD Included in Meta-Analysis

Study	Dirks et al (2021)[15]	Facciorusso et al (2021)[16]	Martins et al (2020)[17]	Aiolfi et al (2020)[18]
Hungness et al (2013)[6]	●		●	●
Teitelbaum et al (2013)[19]			●	●
Ujiki et al (2013)[20]	●		●	●
Bhayani et al (2014)[21]	●		●	●
Kumagai et al (2015)[22]	●		●	●
Kumbhari et al (2015)[23]	●			●
Chan et al (2016)[24]			●	●
Sanaka et al (2016)[25]	●		●	
Schneider et al (2016)[26]	●		●	
Kashab et al (2017)[27]	●		●	
Leeds et al (2017)[28]	●			●
de Pascale et al (2017)[29]	●		●	
Peng et al (2017)[30]	●		●	
Ward et al (2017)[31]	●		●	
Hanna et al (2018)[32]	●			●
Ramirez et al (2018)[33]	●			●
Caldaro et al (2015)[34]	●			
Fumagalli et al (2016)[35]	●			
Greenleaf et al (2018)[36]	●			
Kim et al (2019)[37]	●			
Meng et al (2017)[38]	●			
Miller et al (2017)[39]	●			
Ponds et al (2019)[40]	●	●		
Sanaka et al (2019)[41]	●			
Wang et al (2016)[42]	●			
Werner et al (2019)[43]	●	●		
Wirsching et al (2019)[44]	●			
Zheng et al (2019)[45]	●			
Podboy et al (2020)[46]	●			
Tan et al (2016)[47]	●			
Boeckxstaens et al (2011)[48]		●		
Borges et al (2014)[49]		●		
Kostic et al (2007)[50]		●		
Hamdy et al (2015)[51]		●		

LHM: laparoscopic Heller myotomy; M-A: meta-analysis; PD: pneumatic dilation; POEM: peroral endoscopic myotomy; SR: systematic review.

Tables 2 and 3 summarize characteristics and results of the included systematic reviews published on or after 2020 that address the comparison of POEM to LHM or PD using data from comparative studies. The included comparative studies are heterogenous in their patient populations, proportions of patients with any previous treatments, and proportions of each achalasia subtype I through III, follow-up duration, and definition of treatment success. These differences limit interpretation of their findings.

Dirks et al (2021) conducted a systematic review and meta-analysis that evaluated the efficacy and safety of POEM in comparison to LHM and PD.[15,] The review included 28 studies (2 RCTs [Ponds et al (2019)[40,] and Werner et al (2019)[43,]]; 26 observational studies). Most comparative studies on POEM included LHM (n=21), with a minority involving POEM versus PD (n=8). One study included all 3 interventions. Since POEM is a relatively new intervention, studies evaluating POEM often had shorter follow-up. Two studies included children, with 1 each comparing POEM to PD and LHM. The majority of included studies had a baseline achalasia subtype that was either predominantly type 2 and/or type 1; only 1 study had predominantly type 3 achalasia. The vast majority of included studies had <100 total patients. Results revealed POEM to have similar efficacy to LHM. However, POEM treated dysphagia better than PD in a RCT and observational studies and POEM needed reintervention less than PD in a RCT (risk ratio [RR] 0.19; 95% CI, 0.08 to 0.47) and LHM in an observational study (RR 0.33; 95% CI, 0.16 to 0.68). POEM had similar safety outcomes to LHM and PD. The authors concluded that POEM has similar outcomes to LHM and greater efficacy than PD; Facciorusso et al (2021) completed a systematic review and network meta-analysis of first-line therapeutic interventions for achalasia.[16,] The review included 6 RCTs in adults with achalasia that compared the efficacy of PD (n=260), LHM (n=309) and POEM (n=176). Four trials compared LHM with PD, 1 compared POEM to PD, and 1 compared POEM with LHM. Overall, low-quality evidence, based primarily on direct evidence, supported the use of POEM over PD for treatment success at 1 year while there was no significant difference observed between LHM and POEM. Severe esophagitis occurred at an incidence of 5.3%, 3.7%, and 1.5% for POEM, LHM, and PD, respectively. Procedure-related serious adverse events after POEM, LHM, and PD were 1.4%, 6.7%, and 4.2%, respectively. The authors concluded that POEM and LHM have comparable efficacy and may increase treatment success as compared to PD, with low confidence in estimates.

Martins et al (2020) conducted a systematic review and meta-analysis of the largest number of comparative observational studies and patients treated with POEM (n=359) or LHM (n=534).[17,] Study quality was assessed using the Modified New Castle Ottawa Scale and all included studies were considered to be adequate for analysis. POEM demonstrated small improvements in Eckardt scores and reduced length of stay, comparable operative time, but more major adverse events. Most of the major adverse events were described as being related to unrecognized intraoperative mucosal perforation. An important limitation of this meta-analysis is that it did not take into account between-group differences in pre-operative Eckardt score levels at baseline.

Aiolfi et al (2020) conducted a systematic review and Bayesian random-effects network meta-analysis that compared POEM to LHM and PD.[18,] Overall, 19 studies of 4407 patients were included. Of those, 10 studies of 645 patients directly compared POEM and LHM and none directly compared POEM and PD. POEM was associated with improved dysphasia remission and Eckardt scores, but higher risk of GERD compared to LHM. Results of the comparison to PD are discussed below Table 3. Important limitations of this network meta-analysis include its inclusion of arm-based indirect comparisons and the inherent bias of its reliance on observational studies.

Table 2. Meta-Analysis Characteristics

Systematic Review	Dates	Included Comparative Studies	Participants	N (Range)	Design	Duration
Dirks et al (2021)[15,]	2010-2019	28	Adult and pediatric patients with achalasia	2339 (15 to 241)	26 observational; 2 RCTs	Follow-up: ≥2 months to 5.4 years; most studies had <2 year follow-up
Facciorusso et al (2021)[16,]	Through Dec 2019	6	Adults with achalasia	745 (50 to 221)	RCTs	Minimum follow-up of 1 year; range: 1 to 5 years
Martins et al (2020)[17,]	2012-2017	12	All adult patients (≥18 years of age) with 1 of 3 subtypes of achalasia, with or without prior history of therapy for achalasia	893 (31 to 178)	Observational	9 to 260 weeks
Aiolfi et al (2020)[18,]	2012-2018	10	Esophageal achalasia	645 (23 to 101)	Observational	NR

M-A: meta-analysis; NR: not reported; RCT: randomized controlled trial; SR: systematic review.

Table 3. Meta-Analysis Results

Systematic Review	Dysphasia	Eckardt Score/Treatment Success	GERD	Length of Hospital Stay	Overall major / severe adverse events
Dirks et al (2021)[15,]					
POEM vs. LHM; Pooled effect (95% CI)		RCT (success by Eckhardt score): 83% vs. 82%; RR, 1.02 (0.9 to 1.15)	RCT (severe reflux esophagitis): 4.6% vs. 6.4%; RR, 0.73 (0.20 to 2.58)	RCT (mean): 2.9 vs.3.2; MD, -0.3 (-0.67 to 0.07)	RCT (treatment-related serious adverse events): 3% vs. 7%; RR, 0.32 (0.9 to 1.17)
POEM vs. PD Pooled effect (95% CI)		RCT (success by Eckhardt score): 92% vs. 54%; RR, 1.71 (1.34 to 2.17)	RCT (severe reflux esophagitis): 6% vs. 0%; RR, 3.82 (0.20 to 71.48)		RCT (treatment-related serious adverse events): 0% vs. 1.6%; RR, 0.19 (0.08 to 0.47)
Facciorusso et al (2021)[16,]					
POEM vs. LHM RR (95% CI)		Treatment success at 1 year: no significant difference observed Treatment success at 2 years: RR, 1.02 (0.90 to 1.15)			
POEM vs. PD RR (95% CI)		Treatment success at 1 year: RR, 1.29 (0.99 to 1.69) Treatment success at 2			

Systematic Review	Dysphasia	Eckardt Score/Treatment Success	GERD	Length of Hospital Stay	Overall major / severe adverse events
		years: RR, 1.76 (1.37 to 2.25)			
Martins et al (2020)[17,]					
Total N	N/A	249	354	451	Total N
Pooled effect (95% CI)	NR	MD, -0.257 (-0.512 to -0.002)	RD, 0.00 (-0.09 to 0.09) I^2: 0%	MD, -0.6 (-1.11 to -0.09) I^2=70%	"Major events (CD III a and IIIb) were more common in the POEM group"; analysis NR
Aiolfi et al (2020)[18,]					
Total N	NR	NR	NR	N/A	N/A
Pooled effect (95% CI)	Remission RR, 1.21 (1.04 to 1.47) I^2=0.0%	MD, -0.6 (-1.4 to -0.2) I^2=17.5%	RR, 1.75 (1.35 to 2.03) I^2=6.3%	NR	NR

CD: Clavien-Dindo; CI: confidence interval; GERD: gastroesophageal reflux disease; LHM: laparoscopic Heller myotomy; M-A: meta-analysis; MD: mean difference; N/A: not applicable; NR: not reported; PD: pneumatic dilation; POEM: peroral endoscopic myotomy; RCT: randomized controlled trial; RD: risk difference; RR: risk ratio; SR: systematic review.

Peroral Endoscopic Myotomy Versus Pneumatic Dilation

Zhong et al (2020) conducted a meta-analysis of 7 observational studies comparing POEM (n=298) to PD (n=321).[52,] Achalasia type varied, with 33% type I, 55% type II, and 12% type III. The mean age of the patients in the included studies ranged from 14 to 69 years , including 2 pediatric studies and 2 studies of older adults. Follow-up ranged from 2 to 49.23 months. POEM improved the clinical success rate (24-month RR, 1.35; 95% CI, 1.10 to 1.65; I^2=70%) and change in Eckardt scores (mean difference [MD], 1.19, 95% CI 0.78 to 1.60, I^2=70%); however, the risk of GERD and other complications was higher for POEM compared with PD (RR, 4.17, 95% CI, 1.52 to 11.45, and RR, 3.78; 95% CI, 1.41 to 10.16, respectively). Important limitations of this meta-analysis include the inherent bias of reliance on observational studies and the high between-study clinical and statistical heterogeneity.

Aiolfi et al (2020) conducted a systematic review and Bayesian random-effects network meta-analysis that compared POEM to LHM and PD.[18,] Overall, 19 studies of 4407 patients were included. Of those, none directly compared POEM and PD. Therefore, data from the POEM and PD arms of studies that compared them each, respectively, to LHM, were indirectly compared in the network meta-analysis. Compared to PD, POEM was associated with improved dysphasia remission (RR, 1.40; 95% CI, 1.14 to 1.79) and Eckardt scores (MD, -1.2; 95% CI, -2.3 to -0.2), but a higher risk of GERD (RR, 1.36; 95% CI, 1.18 to 1.68). Important limitations of this network meta-analysis include its inclusion of arm-based indirect comparisons and the inherent bias of its reliance on observational studies.

Randomized Controlled Trials

Although included in the 2 most recent meta-analyses, the RCTs by Ponds et al (2019)[40,] and Werner et al (2019)[43,] remain the landmark studies involving POEM. These are described below along with 2 more recent trials which have yet to be included in a review or meta-analysis.[53,54,]

Ponds et al (2019) published a RCT comparing POEM and PD for treatment-naïve patients with achalasia.[40,] Between 2012 and 2015, patients from 6 sites in 5 countries were randomized to receive either POEM or PD (Tables 4 and 5). The primary outcome was overall treatment success at 2 years, defined as an Eckardt score $\leq$3 and the absence of severe complications or retreatment. Based on previously reported success rates, the power calculation for the primary outcome was based on a difference of at least 20%. Treatment success at 2 years was significantly higher in the POEM group. However, POEM had higher rates of reflux esophagitis than PD. Two serious adverse events (including 1 perforation) occurred after PD; no serious adverse events occurred after POEM. The study

was limited by lack of blinding, lack of an intention-to-treat analysis, and by the follow-up time starting at treatment initiation rather than at randomization.

Results at 5 years from the RCT by Ponds et al (2019) were published by Kuipers et al (2022).[55,] A total of 62 patients in the POEM group and 63 in the PD group were available for analysis. Treatment success (Eckardt score ≤ 3) at 5 years follow-up favored the POEM group with 50 (81%) having success when compared to 25 (40%) of those treated with pneumatic dilation (absolute difference, 41%; 95% CI, 25% to 57%; p<.0001). The median time to treatment failure was 60 months in the POEM group compared with 24 months in the PD group. Retreatment occurred in 8 (13%) \patients in the POEM group compared with 7 (11%) in the PD group. Recurrence of symptoms (defined as having an Eckhardt score >3) occurred in 11 (18%) of POEM patients and 25 (40%) of PD patients. The rate of adverse events was 0% in the POEM group and 2% in the PD group. Amongst patients still in clinical remission at 5 years, proton pump inhibitor (PPI) use was significantly more common in patients treated with POEM (46%) than participants treated with PD (13%; P=.0082). In this same subset of patients, the mean GERD questionnaire scores in the POEM group (7; range, 6 to 9) were also significantly higher (P=.0081) than in the PD group (6; range, 6 to 7) at 5 years follow-up.

Werner et al (2019) published a randomized, noninferiority trial that compared POEM to LHM plus Dor's fundoplication in patients with idiopathic achalasia.[43,] The primary outcome was clinical success at 2 years, defined as an Eckardt score ≤3, without the use of additional treatments. A noninferiority margin of -12.5 percentage points was prespecified as "clinically acceptable" for the primary end point, based on input from the interventional gastroenterologists and surgeons involved in the trial. Analyses were primarily performed in a modified intention-to-treat population of 221 patients, which excluded 20 (8%) patients who withdrew consent, had exclusion criteria discovered post-randomization, or did not undergo treatment. Among the modified intention-to-treat population, the mean age was 48.6 years, 64.2% had no previous therapy, 26.2% had a previous endoscopic PD, and their mean Eckardt symptom score was 6.8. POEM was noninferior to LHM plus Dor's fundoplication for clinical success at 2 years, but rates of reflux esophagitis were higher for POEM. This resulted in more patients in the POEM group receiving daily low-dose PPIs at 24 months. Although a higher rate of serious adverse events was reported in the LHM group, the difference was not statistically significant. This was likely owing to insufficient statistical power for measuring differences in rare outcomes. The most common serious adverse event in the LHM group was mucosal perforation (n=3; 2.7%). The RCT was limited by the lack of blinding of outcome assessment.

Mourna et al (2022) published an RCT that compared POEM to LHM and partial fundoplication in adult patients with achalasia at a single center.[53,] The primary outcome was reflux esophagitis assessed at baseline, 1 month, 6 months, and 1 year post-treatment. Both groups significantly improved from baseline Eckhardt scores at all time points follow-up, but no significant between-group differences were observed. In the combined LHM and partial fundoplication group, treatment success, defined as ≤ 3-point reduction in Eckardt score, was confirmed in all patients at each time point follow-up; the POEM group had 100% success at 1 month which fell to 90% and 95% at 6 and 12 months follow-up, respectively. The rates of esophagitis were significantly higher in the POEM group at 1, 6, and 12 months follow-up. No differences in the rate of adverse events were detected between groups.

Saleh et al (2023) published an RCT that compared POEM to pneumatic dilation in adult patients with persistent achalasia symptoms after LHM.[54,] The primary outcome was clinical success at 1 year, defined as an Eckardt score ≤3, without the use of additional treatments. Two patients in the POEM group were lost to follow-up after randomization or treatment, but analyses of the primary and secondary outcomes were intention-to-treat analyses, and *a priori* power calculations required only 43 participants in each study arm. The median age was 52.5 years with a range of 36% to 40% male participation. At enrollment, both groups had a mean Eckardt score of 6 (interquartile range of 4 to 8). Patients randomized to POEM were significantly more likely to have treatment success at 1-year follow-up than those in the PD group; however, the rate of endoscopic reflux esophagitis was higher

amongst participants treated with POEM than PD. The rate of serious adverse events attributed to the intervention was equivalent between groups, but POEM was associated with a greater number of adverse events (31.1%) than PD (20%). Events included candida esophagitis (n=1), Heliobacter pylori infection (n=3), periprocedural mucosal bleeding (n=2), gastric perforations (n=2), foot impaction (n=1), and several other non-upper-gastrointestinal related adverse events (n=5). The RCT was limited by the lack of blinding of outcome assessment and having outcome data through 1-year follow-up.

Table 4. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Ponds et al (2019)[40,]	Netherlands, Germany, Italy, Hong Kong	6	2012-2015	Treatment naïve adults with newly diagnosed achalasia and Eckardt score ≥3	POEM (n=64)	PD (n=66) Initial with 30 mm balloon Subsequent with 35 mm balloon if Eckardt score ≥3 at 3 weeks
Werner et al (2019)[43,]	Belgium, Czech Republic, Germany, Italy, Netherlands, Sweden	8	2012-2015	Adults with symptomatic achalasia and Eckardt score ≥3	POEM (n=120)	LHM plus Dor's fundoplication (n=121)
Mourna et al (2022)[53,]	Brazil	1	2017-2018	Adults diagnosed with achalasia	POEM (n=20)	LHM plus partial fundoplication(n=20)
Saleh et al (2023)[54,]	Netherlands, Belgium, Italy	3	2014-2020	Adults with symptomatic achalasia and Eckardt score ≥3 following LHM	POEM (n=45)	PD (n=45) Initial with 30 mm balloon and subsequent treatment w 35 mm balloon. Patients with recurrent symptoms between 3 and 12 moths were offered additional treatments with 35mm or 40mm balloons.

LHM: laparoscopic Heller's myotomy; PD: pneumatic dilation; POEM: peroral endoscopic myotomy; RCT: randomized controlled trial.

Table 5. Summary of Key RCTs: 2-Year Results

Study	Treatment success, n (%)	PPI use	Endoscopic Reflux Esophagitis	Retreatment	Treatment-related SAE
Ponds et al (2019)[40,]	126	92	92	126	126
POEM	58 (92%)	58 Median(IQR) SD 24(41) 6.5	54 No.(%) SD 22(41) 6.5	63 No.(%) SD 5 (8) 3.4	63 No.(%) SD 0
PD	34 (54%)	34 Median (IQR) SD 7(21) 7	29 n (%) SD 2(7) 4.7	63 n (%) SD 26 (41) 10.5	63 n (%) SD 1(1.6) 1.7
Comparative treatment effect (95% CI)	RR, 1.71 (1.34 to 2.17)[a]	AD, 20 (1 to 38)[a]	AD, 34 (12 to 49)[a]	AD, 33 (17 to 47)[a]	AD, 1.6 (-5 to 10)[a]
Werner et al (2019)[43,]	221	221	165		221
POEM	93 (83.0)	n (%) 41 (38.7)	n (%) 38 (44)	NR	n (%) 3 (2.7)
LHM	89 (81.7)	n (%) 21 (19.4)	n (%) 23 (29)	NR	n (%) 8 (7.3)
Comparative treatment effect (95% CI)	RR, 1.4 (-8.7 to 11.4)[a]	NR	OR, 2.00 (1.03 to 3.85)	NR	RR, 4.6 (-1.1 to 10.4)[a]
Mourna et al (2022)[53,]	40		40		40

Study	Treatment success, n (%)	PPI use	Endoscopic Reflux Esophagitis	Retreatment	Treatment-related SAE
POEM	6 months: 90% 12 months: 95%	NR	6 months: 10 (63%) 12 months: 11 (65%)	NR	Any AE: 3 (15%)
LHM	6 months: 100% 12 months: 100%	NR	6 months: 1 (6%) 12 months: 2 (11.%)	NR	Any AE: 1 (5%)
Comparative treatment effect (95% CI)	6 months: p=.487 12 months: p=1	NR	6 months: p<.001 12 months: p=.002	NR	p=.605
Saleh et al (2023)[54,]	90	90	90	90	90
POEM	28 (62.2%)	29 (69%)	12 (34.3%)	2 (4.44%)	1 (2.22%)
PD	12 (26.7%)	26 (57.8%)	6 (15%)	14 (42.9%)	1 (2.22%)
Comparative treatment effect (95% CI)	RR: 2.33 (1.37 to 3.99)	NS	NS	NR	NR

[a] Unadjusted

AD: absolute difference; AE: adverse event; CI: confidence interval; IQR: interquartile range; LHM: laparoscopic Heller's myotomy; NR: not reported; NS: not significant; OR: odds ratio; PD: pneumatic dilation; POEM: peroral endoscopic myotomy; PPI: proton pump inhibitor; RCT: randomized controlled trial; RR: risk ratio; SAE: severe adverse even; SD: standard deviation.

Tables 6 and 7 summarize the important limitations of the RCTs discussed above.

Table 6. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Ponds et al (2019)[40,]			2. PD protocol limited to 1 to 2 dilations as compared to clinical practice 2. Optimal comparator would be LHM	4. Eckardt score not validated symptom assessment	
Werner et al (2019)[43,]	4. Non-US		2. LHM plus Dor's fundoplication		
Mourna et al (2022)[53,]	4. Non-US		2. LHM plus partial fundoplication	4. Eckardt score not validated symptom assessment	
Saleh et al (2023)[54,]	4. Non-US			4. Eckardt score not validated symptom assessment	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.

[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

LHM: laparoscopic Heller's myotomy; PD: pneumatic dilation.

Table 7. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Follow-Up[d]	Power[e]	Statistical[f]
Ponds et al (2019)[40,]		1. Blinding not possible due to different technical approaches to each procedure	6. Per protocol analysis	6. Not intent to treat analysis 6. Follow-up insufficient to define long-term effects		3. Inadequate statistical analysis and reporting
Werner et al (2019)[43,]		1. Not blinded outcome assessment				
Mourna et al (2022)[53,]		1. Not blinded outcome assessment				
Saleh et al (2023)[54,]		1. Blinding not possible due to different technical approaches for each procedure				

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Follow-Up key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4.Comparative treatment effects not calculated.

Nonrandomized Comparative Studies

Numerous nonrandomized comparative studies have compared POEM and LHM in adults with achalasia. The majority of these studies are included in the systematic reviews described above and will not be comprehensively summarized herein. Those that were not included in previous systematic reviews or that have notable characteristics (i.e., focus on important subpopulations, have long-term follow-up) are summarized below.

Docimo et al (2016) published a retrospective study comparing POEM and LHM for individuals with achalasia that was not included in any above-described systematic review.[56,] Patients who underwent POEM (n=44) or LHM (n=122) between 2006 and 2015 were included. There was no difference in average pain scores for POEM and LHM after the first 24 hours (2.7±2.067 vs. 3.29±1.980, p=.472) or at time of discharge (1.6±2.420 vs. 2.09±2.157, p=.0657). The POEM group required significantly fewer narcotics while hospitalized than the LHM group (35.8 mg vs. 101.8 mg, p<.001), and fewer POEM patients needed a prescription for a narcotic analgesic at discharge (6.81% vs. 92.4%, p<.001). Also, the average length of stay was 31.2 hours for POEM and 55.79 for LHM (p<.001). The study was limited by its retrospective nature and its lack of randomization and blinding.
Wang et al (2016) retrospectively reviewed outcomes for POEM (n=21) and PD (n=10) in patients ages 65 years and older.[42,] All were treated successfully, with decreases in Eckardt scores. At a mean follow-up of 21.8 months for POEM and 35 months for PD patients, 1 POEM case failed, and 2 PD procedures failed.

In a retrospective study of patients with type III achalasia, Kumbhari et al (2015) compared outcomes for 49 patients who underwent POEM across 8 centers between 2011 and 2013, and a historical control group of 25 patients who underwent LHM between 2000 and 2013.[23,] Defining clinical response as a reduction in Eckardt score of no more than 1, clinical response was more frequent in the POEM group (98.0%) than the LHM group (80.8%; p=.01). On multivariable analysis, there was no statistically significant difference in the odds of failure between procedures, although the point estimate of the odds favored POEM (OR, 11.32; p=.06). Procedure times were shorter with POEM. There was no difference in length of stay. The overall rate of adverse events was lower in the POEM group (6% vs. 27%, p=.01). However, an important limitation of this study is that LHM patients had more severe disease at baseline by several different measures (i.e., higher Eckardt symptom stage, prior endoscopic interventions). Also, the LHM and POEM groups differed in the achalasia diagnostic criteria used, with the LHM group lacking use of the current gold standard of high-resolution esophageal manometry to diagnose type III because it was not yet available at that time.

Haseeb et al (2023) published a retrospective study using National Readmission Database data from 2016 to 2019 to compare short-term outcomes after POEM (n=1911) to LHM (n=9710) and PD (n=2453) in adults with achalasia.[57,] The rate of readmissions was highest in patients treated with PD (12.6%), followed by POEM (4.3%) and LHM (3.9%). PD had significantly greater adjusted odds of readmission compared to POEM (OR, 2.42; 95% CI, 1.56 to 3.75), but no difference was identified between POEM and LHM (OR, 0.91; 95% CI, 0.62 to 1.33). No significant differences were detected in the rate of mortality, length of stay, or periprocedural adverse events between POEM and LHM. Compared to PD, POEM had a lower rate of mortality (0% vs 1.1%; p=.012), sepsis (1% vs. 2.3%; p=.016), blood transfusions (0.7% vs 2.3%; p<.001), and length of stay (3.4 days vs 6.29 days; p<.001).

Shally et al (2023) conducted a retrospective cohort study of POEM compared to LHM in adult patients with achalasia at a single center from 2014 to 2021.[58,] A total of 33 POEM and 25 LHM patients were included and were well-balanced on pre-operative characteristics. Treatment success was defined as having an Eckardt score of ≤3 at follow-up and was achieved by 88% of patients in the POEM group and 76% of patients in LHM group (p=.302). Patients in the POEM group had a significantly shorter median operative time (106 minutes) compared to those in the LHM group (145 minutes; p=.003); additionally, individuals treated with POEM had lengths of stay less than one day in 48.5% of patients compared to 0% in the LHM group (P<.001). Both groups observed improvements in dysphagia, heartburn, regurgitation, Eckardt score, GERD health-related quality of life, and anti-reflux medication use. Between-group differences were observed in the improvement of dysphagia scores with POEM patients having a superior resolution of dysphagia (2.3 vs 1.12; p=.003).

Section Summary: Peroral Endoscopic Myotomy for Adult Individuals with Achalasia

Studies on POEM for adults with achalasia included systematic reviews, nonrandomized studies, and 4 RCTs. Conclusions on comparative efficacy cannot be determined from the systematic reviews because they did not appear to have accounted for differences in patient characteristics in the nonrandomized studies. Findings from RCTs demonstrated that POEM had a similar or greater treatment success rate based on the Eckardt score and similar or fewer adverse events compared with PD or LHM. However, POEM had significantly higher rates of endoscopically confirmed reflux esophagitis. An important conduct limitation of the RCTs is that blinded assessment of outcomes was not used. Given that the primary outcome was based on subjective patient report of symptoms, this is a potential source of bias. Additionally, a potential relevance limitation is that the RCTs did not include any US sites. The nonrandomized studies comparing POEM with other procedures were retrospective and involved patients who might not be comparable in terms of age and severity of the disease. Although outcomes were generally similar between POEM and the comparator treatments (LHM, PD), potential confounding and selection bias makes outcome comparisons uncertain. Long-term follow-up was available for 1 RCT which showed a greater rate of clinical success at 5 years for POEM patients compared to PD, but the POEM group also showed higher rates of PPI usage and GERD questionnaire scores.

Peroral Endoscopic Myotomy for Pediatric Individuals with Achalasia

Clinical Context and Therapy Purpose

The purpose of POEM in pediatric individuals who have esophageal achalasia is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is pediatric individuals with esophageal achalasia. Esophageal achalasia is characterized by reduced numbers of neurons in the esophageal myenteric plexuses and reduced peristaltic activity, making it difficult for individuals to swallow food and possibly leading to complications such as regurgitation, coughing, choking, aspiration pneumonia, esophagitis, ulceration, and weight loss.

Interventions

The therapy being considered is POEM. The POEM procedure involves tunneling an endoscope down the esophagus toward the esophageal-gastric junction. A surgeon performs the myotomy by cutting only the inner, circular LES muscles through a submucosal tunnel created in the proximal esophageal mucosa.

Comparators

Comparators of interest include esophageal dilation, LHM, and botulinum toxin injection.

Esophageal dilation is performed in a graded approach, starting with a small balloon (typically 30 mm), then progressing to larger balloons (35 to 40 mm) 2 to 4 weeks later. The balloons are placed at the level of the gastroesophageal junction and inflated slowly, in order to tear the muscle fibers in a controlled manner. Esophageal perforations are a potential complication. Long-term studies have estimated that approximately one-third of patients may need a repeat procedure.

Heller laparoscopic myotomy is a minimally invasive procedure in which the thick muscle of the lower esophagus and the upper stomach is cut to open the tight LES. The procedure involves 5 small incisions to insert the camera and surgical instruments. Reported success rates are high (>90%), with a 5-year follow-up study showing an 8% rate of symptom recurrence.

Endoscopic botulinum toxin is injected with a sclerotherapy needle approximately 1 cm above the esophagogastric junction. The complication rate is low and approximately 80% of patients experience immediate symptom relief. The effect diminishes over time, with more than 60% of patients reporting recurrent symptoms at 1 year.

Outcomes

The general outcomes of interest are symptom relief and treatment-related morbidity.

Symptom relief may be measured by the Eckardt score, which is comprised of 4 major symptoms of achalasia: dysphagia, regurgitation, retrosternal pain, and weight loss. Each symptom receives a score from 0 (none) to 3 (severe), for a maximum score of 12. Total scores of 4 or greater represent treatment failure.[12,]

A treatment-related morbidity of concern is the development of GERD. Gastroesophageal reflux disease risk is high with this procedure because POEM involves ablating the LES without adding any type of anti-reflux mechanism. Additional complications include thoracic effusion, subcutaneous emphysema, and esophagitis.

Symptom relief may be experienced shortly following the procedure. Duration of relief is measured after months to years of follow-up.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

Nabi et al (2023) published a meta-analysis pooling outcomes of POEM in pediatric achalasia. The review included 14 studies from 2010 to 2021 (N=419; 234 boys). [59,] The mean age of patients ranged from 10.9 to 15.2 years with symptom duration of 6.3 to 30.1 months. Technical success occurred in 415 individuals with a pooled rate of 97.1% (95% CI, 94.5% to 98.5%; I^2, 0%). A pooled clinical success rate in the intention-to-treat-analysis population was 88% (95% CI, 84.4% to 90.9%). The MD from baseline in Eckhardt scores was available from 9 studies and was significantly different from baseline (MD, 6.71; 95% CI, 6.14 to 7.28; I^2, 81%); however, this estimate had substantial heterogeneity. The overall pooled rate of any adverse event was 12.9% (95% CI, 7.4 to 21.7%, I^2, 64.5%) and for major adverse events, the rate was 4.2% (95% CI, 2.4% to 7.4). The authors concluded that POEM was a safe and effective modality for treating children with achalasia, but noted that prospective studies with longer-term follow-up and objective evaluation of gastroesophageal reflux are necessary.

Zhong et al (2021) published an updated systematic review and meta-analysis evaluating clinical outcomes of POEM for the treatment of achalasia in children.[60,] The review included 11 studies published between January 2009 to June 2020 (N=389; 222 boys). The mean age of the patients ranged from 5.5 to 15.2 years with symptom duration ranging from 1.7 to 26.4 months. The pooled technical success (completion of the POEM procedure successfully) was achieved in 385 children (97.4%; 95% CI, 94.7% to 98.7%) and the pooled clinical success (decrease in Eckhardt score to ≤3 during follow-up) was achieved in 343 children (92.4%; 95% CI, 89% to 94.8%). The Eckhardt score was significantly reduced by 6.76 points following POEM (95% CI, 6.18 to 7.34; p<.00001). Regarding adverse events, the pooled major adverse event rate was 12.8% (95% CI, 4.5% to 31.5%) with a pooled GERD rate of 17.8% (95% CI, 14.2% to 22%). The authors concluded that POEM was effective and safe for treating children with achalasia; however, all included studies in the analysis were observational in nature.

Lee et al (2019) published a systematic review and meta-analysis evaluating POEM for the treatment of pediatric achalasia.[61,] Twelve studies, published between 2013 and 2018, with a total of 146 patients (53.68% female), were included in the analysis. There was a reduction in the Eckardt score of 6.88 points (95% CI 6.28 to 7.48, p<.001) and a reduction in LES pressure of 20.73 mmHg (95% CI 15.76 to 25.70, p<.001). Improvement or resolution of short- and long-term achalasia symptoms was experienced in 93% of patients. The study was limited by several of the included studies being case series (5/12) with no control groups or comparators, all of the studies having a sample size of <30, and by most studies only reporting follow-up of ≤2 years.

Nonrandomized Studies

Bi et al (2023) published a retrospective cohort study of POEM for the treatment of pediatric achalasia and compared pediatric patients to a 1:1 matched adult cohort on gender, operating physician, surgery date, and baseline Chicago and Ling classification between 2012 and 2020.[62,] A total of 48 pediatric patients were included with a median age of 16 years (range 7 to 18 years of age). Most patients (75%) lacked prior treatment for achalasia. Fourteen patients were lost to follow-up, and a total of 34 pediatric patients were available for long-term follow-up with a mean of 5.7 years (range, 2.6 to 10.6 years). The clinical success rate, defined as a post-POEM Eckhardt score of <3, was

97%. Pediatric patients had significant improvements between pre- and post-POEM for Eckhardt score (8 vs 1.1, p<.001), Urbach score (24.7 vs 12.8, p<.001), dysphagia, regurgitation, chest pain, and weight loss (p<.001). In addition, the number of absences from school decreases from a median of 3.3 months versus 0.1 months post-POEM (p<.001). Adverse events reported in the pediatric group following POEM at 5 years included symptomatic reflux (17.6%), reflux esophagitis (5.9%), and clinical reflux (11.8%); all adverse events were controlled with medical therapy. Compared to a matched adult cohort (n=34), pediatric patients had identical rates of complications post-treatment (14.6%), similar rates of clinical success, changes in Eckardt and Urbach scores, clinical reflux evaluations, and procedure times.

Petrosyan et al (2022) conducted a retrospective study of all patients who underwent POEM for pediatric achalasia from 2015 to 2021 at a single center.[63,] A total of 37 children (mean age, 11.6 years) were treated; 43.2% had a pre-POEM intervention for achalasia. Participants were followed for a median of 15 months (range 5.5 to 74 months) following POEM. Baseline Eckhardt scores were 6.73 (standard deviation ±1.5), and following POEM, scores decreased to a mean of 0.6 ± 0.9. One patient failed POEM (2.7%). The reintervention rate was 16.2% (5 patients required PD and 1 patient required LHM). Intraoperative complications occurred in 16 (43.2%) patients; however, these complications did not require reoperation during index admission. Intraoperative complications included mucosectomy distal to submucosal tunnel entry (13.5%), pneumothoraxes (24.3%), pneumomediastinum (5.4%), pneumoperitoneum (27%). Post-operative complications were recurrent dysphagia (13.5%) and GERD (8.1%).

Nabi et al (2019) published a retrospective study assessing POEM for the treatment of children with achalasia.[64,] Forty-four patients ≤18 years old and weighing ≥10kg who were diagnosed with achalasia between 2013 and 2018 were included. POEM was successfully performed in 43 patients (technical success 97.72%). Eleven (25.6%) children experienced intra-operative adverse events, including retroperitoneal carbon dioxide (n=7), capnoperitoneum (n=3), and mucosal injury (n=1). Clinical success at 1, 2, 3, and 4 years of follow-up was 92.8%, 94.4%, 92.3%, and 83.3%, respectively. The study was limited by its retrospective design, the lack of confirmation of GERD in about half the patients, and the small number of patients who completed 3 or more years of follow-up.

Miao et al (2017) published a retrospective, single-center study of POEM for the treatment of pediatric achalasia.[65,] Twenty-one children (aged 11 months to 18 years) diagnosed with achalasia and treated between 2014 and 2016 were included. Mean follow-up time was 13.2 months. No severe adverse events were reported, and for all patients, difficulty in feeding or swallowing was significantly alleviated or resolved. By 1 month after POEM, all Eckardt scores were <3 and by 6 months were 0.75 on average (average pre-operative score: 7.18; p<.001). At 6 months, an average weight gain of 2.7 kg was observed. Four patients had gastroesophageal reflux and 2 had concomitant gastroesophageal reflux and reflux esophagitis at 3 months follow-up. No limitations to the study were reported.

Section Summary: Peroral Endoscopic Myotomy for Pediatric Individuals with Achalasia

Three systematic reviews and meta-analyses evaluating POEM for the treatment of pediatric achalasia were identified. A significant decrease was observed in both Eckardt scores and LES pressure, as well as improvement in symptoms; however, no RCTs were included and the majority of included studies had sample sizes <30. Four comparative observational studies were available evaluating POEM for the treatment of pediatric achalasia. All four studies reported high rates of success for POEM and alleviation of achalasia symptoms. One study retrospectively compared POEM in pediatric patients to a matched adult cohort and found similar rates of clinical success, clinical reflux symptoms, and adverse events.

Gastric Peroral Endoscopic Myotomy for Adult Individuals with Gastroparesis

Clinical Context and Therapy Purpose

The purpose of gastric peroral endoscopic myotomy (G-POEM) in individuals who have gastroparesis is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is individuals with gastroparesis. Gastroparesis is characterized by nausea, vomiting, bloating, early satiety, with or without abdominal pain which is caused by delayed gastric emptying without any mechanical obstruction.

Interventions
The therapy being considered is G-POEM. The G-POEM procedure involves tunneling an endoscope down the esophagus toward the esophageal-gastric junction. A surgeon performs the myotomy by cutting the pylorus muscles through a submucosal tunnel created in the proximal esophageal mucosa.

Comparators
Comparators of interest include sham control, medical management with metoclopramide or antiemetics, gastric electrical stimulation, and botulinum toxin injection.

Anti-emetic drugs can provide symptom relief to individuals for whom dietary modifications are insufficient to alleviate symptoms. Metoclopramide is a prokinetic medication that has been approved by the US Food and Drug Administration (FDA) for the treatment of gastroparesis; it is usually taken 15 minutes before a meal 5 times per day and is approved for 12 weeks of treatment due to the potential for adverse effects (anxiety, restlessness, hyperprolactinemia, and QT prolongation).

Gastric electrical stimulation is a non-pharmacologic approach to relieve some symptoms of gastroparesis, chiefly vomiting and the need for nutritional support. Individuals with gastroparesis who do not respond to medical management may consider gastric electrical stimulation as an FDA-approved therapy under a humanitarian device exemption. The device needs implantation of a pair of leads which is done via laparotomy or laparoscopically in the muscularis propria proximal to the pylorus which is then connected to a pulse generator. Risks include infection of the device, risk of lead migration, perforation, and battery replacement, which may necessitate additional procedures. Botulinum toxin is administered endoscopically as an intrapyloric injection under direct visualization using a sclerotherapy needle, delivering 20-25 U botulinum neurotoxin/mL into each of the four quadrants. Patients are usually discharged on the same day with dietary advancement as tolerated, and an endoscopic ultrasonography-guided approach can enhance precision in targeting the pyloric sphincter.

Outcomes
The general outcomes of interest are symptom relief and treatment-related morbidity.

Symptom relief may be measured by the Gastroparesis Cardinal Symptom Index (GCSI), which is comprised of 3 major symptoms of gastroparesis: postprandial fullness/early satiety (4 items), nausea/vomiting (3 items), and bloating (2 items). Each item receives a score from 0 (none) to 5 (severe), for a maximum score of 45. An average GCSI score of ≥ 3 is defined as severe gastroparesis.[66,]

Treatment-related morbidity of concern is infection, ulcers near the pylorus, bleeding or tears in the gastric mucosa.

Symptom relief may be experienced shortly following the procedure. Assessment of durability of relief requires a follow-up of months to years.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse effects, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Systematic Reviews

Two systematic reviews and meta-analyses evaluating G-POEM for the treatment of gastroparesis were identified.[67,68,] Both reviews included only observational studies of G-POEM for gastroparesis in adult patients. Outcome data was reported up to 1-year post-treatment in the study by Kamal et al (2022) and up to 3 years post-treatment in the study by Canakis et al (2023). Clinical success was found to be 60.7% (95% CI, 49.1% to 71.2%) at 1 year with high heterogeneity pooling data from 8 studies. Pooled clinical success rates at 3 years follow-up across 4 studies was 75% (95% CI, 68.2% to 80.5%) with low heterogeneity. Following G-POEM, mean GCSI scores decreased by -1.44 (95% CI, -1.91 to -0.97) at 1 year post-treatment in 7 studies and by -3.3 (95% CI, -1.8 to -4.7) in 4 studies at 3-years follow-up; both estimates had very high heterogeneity between studies. One study reported a pooled rate of adverse events at 1-year follow-up of 8.2% and the other meta-analysis reported strata of events (bleeding, perforation, pain or other) which ranged from 0.7% to 4.1% at 3-years following G-POEM.

Table 8. Comparison of Studies of G-POEM Included in Meta-Analysis

Study	Kamal et al (2022)[67,]	Canakis et al (2023)[68,]
Labond et al (2022)[69,]		●
Hernandez-Mondragon et al (2022)[70,]		●
Vosoughi et al (2021)[71,]	●	
Gregor et al (2021)[72,]	●	
Conchillo et al (2020)[73,]	●	
Abdelfatah et al (2021)[74,]	●	●
Hustak et al (2020)[75,]	●	
Tan et al (2021)[76,]	●	
Attaar et al (2021)[77,]	●	
Ragi et al (2020)[78,]	●	
Shen et al (2020)[79,]		●
Vosoughi et al (2020)[80,]	●	
Xu et al (2018)[81,]	●	
Davis et al (2017)[82,]		●

M-A: meta-analysis; G-POEM: gastric peroral endoscopic myotomy; SR: systematic review.

Table 9. Meta-Analysis Characteristics

Systematic Review	Dates	Included Studies	Participants	N (Range)	Design	Duration
Kamal et al (2023)[67,]	Through June 2021	10	Adults with gastroparesis treated with G-POEM	482 (9 to 97)	7 retrospective 3 prospective	Minimum follow-up of 1 year
Canakis et al (2023)[68,]	Through March 2023	5	Adults with gastroparesis treated with G-POEM	560 (23 to 374)	3 retrospective 2 prospective	Minimum follow-up of 3 years

G-POEM: gastric peroral endoscopic myotomy; M-A: meta-analysis; SR: systematic review.

Table 10. Meta-Analysis Results

Systematic Review	Clinical Success	Technical Success	Pre and Post G-POEM GCSI	Length of Hospital Stay (days)	Adverse Events
Kamal et al (2023)[83,], all results at 1 year f/u					

Systematic Review	Clinical Success	Technical Success	Pre and Post G-POEM GCSI	Length of Hospital Stay (days)	Adverse Events
N studies	8		7		8
Pooled effect (95% CI)	60.7% (49.1% to 71.2%) I^2: 74%		SMD: -1.44 (-1.91 to -0.97) I^2: 97%		8.2% (5.9% to 11.4%), I^2: 0%
Canakis et al (2023)[68], all results at 3 years f/u					
N studies	4	5	4	4	3 to 4 per event
Pooled effect (95% CI)	75% (68.2% to 80.5%) I^2: 20%	98.6% (91% to 99.8%) I^2: 70%	SMD: -3.3 (-1.8 to -4.7) I^2: 94%	SMD 3.06 (2.6 to 3.5%) I^2: 91%	Perforation: 0.7% (0.2% to 2.4%), I^2: 0% Bleeding: 4.1% (2.7% to 6.3%), I^2: 0% Pain: 0.9% (0.3% to 3.1%), I^2: 0% Other (clip dislodgement, pre-pyloric ulcer, or mucosal tear): 3.4% (2.1% to 5.5%), I^2: 0%

CI: confidence interval; GCSI: gastroparesis cardinal symptom index; G-POEM: gastric peroral endoscopic myotomy; M-A: meta-analysis; SMD: standardized mean difference; SR: systematic review.

Randomized Controlled Trials

Gonzalez et al (2024) conducted a French multi-center RCT (N=40 patients) comparing the clinical efficacy of G-POEM versus pyloric botulinum toxin injection for refractory gastroparesis.[84,] [Patients were medically managed for >6 months and confirmed by gastric emptying scintigraphy (GES), with follow-up of 1 year. The primary end point was the 3-month clinical efficacy, defined as a >1-point decrease in the mean GCSI score. Secondary end points were: 1-year efficacy, GES evolution, adverse events, and quality of life. POEM showed a trend towards higher 3-month clinical success than botulinum toxin, along with non-significantly higher 1-year clinical success on intention-to-treat analysis.(Table 12) The GCSI decreased in both groups at 3 months and 1 year. Only three minor adverse events occurred in the POEM group. The GES improvement rate was 72% in the POEM group versus 50% in the botulinum toxin group (non-significant).

Martinek et al (2022) published a randomized, multi-center trial that compared G-POEM to sham treatment in patients with gastroparesis.[85,] From November 2017 to February 2021 a total of 41 participants were recruited who were randomized 1:1 to either G-POEM (n=21) or sham control (n=20) (Table 11); 1 individual in the sham control group withdrew consent and 1 participant in the G-POEM group could not have the procedure completed due to submucosal fibrosis and were not included in the per-protocol analysis. The median age of patients in the G-POEM arm was 43 years (range, 30 to 51 years) and was 51 years (range, 45 to 56 years) in the sham control group. Participants in the G-POEM group had a higher baseline GCSI score of 3.5 compared to 3.2 in the sham control group. Treatment success (≥50% reduction in GCSI score) at 6 months post-intervention occurred in 15 (71%) of the G-POEM patients in the intention to treat (ITT) analysis and 14 (70%) in the per-protocol analysis compared with 21% or 22% in the sham control group. Twelve patients crossed over to G-POEM and 9 (75%) had treatment success 6 months after crossing over. At 6 months follow-up the median reduction in GCSI score favored G-POEM over sham control (Table 12); in the patients that crossed over from sham control to G-POEM, an additional median reduction in GCSI of 0.3 (95% CI, 0.1 to 1.6) was observed 6 months from the time of crossing over. The authors found that gastric retention decreased significantly after G-POEM compared to sham control and that after crossing over from sham to G-POEM, a similar effect was observed in the cross-over patients. A sub-group analysis showed a greater level of treatment effect in patients with a diabetic etiology of gastroparesis over post-surgical or idiopathic etiologies.

Table 11. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Gonzalez et al (2024)[84,]	France	2	2017-2020	Adults with refractory gastroparesis, medically managed for >6 months and confirmed by gastric emptying scintigraphy	G-POEM (n=20)	Botulinum toxin injection (n=20)
Martinek et al (2022)[85,]	Czech Republic	2	2017-2021	Adults with severe gastroparesis with a Gastroparesis Cardinal Symptom Index score of >2.3 and who were refractory for >6 months	G-POEM (n=21)	Sham (n=20)

G-POEM: gastric peroral endoscopic myotomy; RCT: randomized controlled trial.

Table 12. Summary of Key RCTs Results

65% versus 40%, respectively (95%CI −0.16 to 0.48; P = 0.10

Study	Clinical efficacy at 3 months, n (%)	GCSI mean change at 3 months, mean (SD)	Clinical efficacy at 1 year, n (%)	GCSI mean change at 12 months, mean (SD)
Gonzalez et al (2024)[84,]	40	40	40	40
G-POEM	ITT: 13 (65%)	1.5 (1.2)	ITT: 12 (60%)	1.2 (1.1)
Botulinum toxin injection	ITT: 8 (40%)	1.2 (1.2)	ITT: 8 (40%)	0.9 (1.1)
Comparative treatment effect (95% CI)	(95% CI -0.16 to 0.48; p=0.10)	p=0.32 (NR)	(95% CI -0.30 to 0.40; p=0.20)	p= 0.62 (NR)
	Treatment success, n (%)	**Median GCSI, (95% CI)**	**Median Quality of Life Index, change from BL at 3 mos**	**Treatment-related SAE**
Martinek et al (2022)[85,]	41	41	41	41
G-POEM	ITT: 15 (71%) PP: 14 (70%)	BL: 3.5 (3.2 to 3.7) 3 mos: 1.4 (0.9 to 1.9) 6 mos: 1.1 (0.5 to 1.5)	1.1 (0.1 to 1.6)	7*
Sham	ITT: 4 (22%) PP: 4 (21%)	BL: 3.2 (2.8 to 3.4) 3 mos: 2.5 (1.9 to 3.1) 6 mos: 2.5 (1.9 to 3.2)	0.4 (-0.1 to 0.8)	3
Comparative treatment effect (95% CI)	OR: 9.0 (95% CI: 2 to 40.2)	2.4 (2.0 to 2.8) vs 0.7 (0 to 1.2) at 6 mos		

* 5 events occurred in the initial group and then 2 occurred after patients in the sham group crossed over; 3 events were related to the G-POEM procedure. BL: baseline; CI: confidence interval; G-POEM: gastroparesis peroral endoscopic myotomy; GCSI: gastroparesis cardinal symptom index; ITT: intention to treat; NR: not reported; OR: odds ratio; PP: per protocol; RCT: randomized controlled trial; SAE: severe adverse event.

Tables 13 and 14 summarize the important limitations of the RCTs discussed above.

Table 13. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Gonzalez et al (2024)[84,]	4. Non-US		2. Does not include sham procedure	1. Quality-of-life assessment was limited due to absence of interpretable data	
Martinek et al (2022)[85,]	4. Non-US		1. Sham procedure is not clearly defined, and no assessment of the adequacy of blinding		1. Follow-up is limited to 6 months where patients in the control group were eligible to cross-over

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 14. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Follow-Up[d]	Power[e]	Statistical[f]
Gonzalez et al (2024)[84,]					3. Sample size was insufficient to have enough power to demonstrate any potential difference between study groups	3. Inadequate statistical analysis and reporting 4. Comparative treatment effects not calculated for all study outcomes
Martinek et al (2022)Martinek et al (2022)[85,]			6. Per protocol analysis for some outcomes	6. Follow-up insufficient to define long-term effects	5. Trial terminated for success prior to recruiting # of participants specified in protocol	3. Inadequate statistical analysis and reporting

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Follow-Up key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4.Comparative treatment effects not calculated.

Nonrandomized Studies

Numerous nonrandomized single-arm studies have been published many of which are included in the 2 meta-analyses discussed above.[69,-82,] This section will focus on the largest of these studies which also provides long-term efficacy outcomes through 4 years follow-up.

Hernandez-Mondragon et al (2022) retrospectively analyzed data from a prospective cohort of adult refractory gastroparesis patients (N=374) collected at a single center from 2017 to 2021.[70,] Patients were followed for 4 years and evaluated at baseline and then following G-POEM at 1 month, 6 months and every 6 months thereafter through 48 months. The technical success of the procedure was 100% with an average hospital length of stay of 2 days. Prior to treatment with G-POEM, the mean GCSI score was 3.84±0.53 which was significantly reduced to 2.1±0.7 (p<.001) at 4 years follow-up (n=102). The clinical success rate was 77.5% at 4 years follow-up. Adverse events occurred in 8.6% of patients and were all managed conservatively or treated endoscopically. Twelve patients (3.2%) had a treatment failure with G-POEM and 72 (19.2%) had a recurrence of gastroparesis symptoms. Patients were stratified by the etiology of their gastroparesis for the purposes of subgroup analyses: 141 patients (37.7%) had diabetic gastroparesis, 115 (30.7%) had idiopathic gastroparesis, 102 (27.3%) had postsurgical gastroparesis, and 16 (4.3%) had another etiology. Between group comparisons based on etiology showed variations in the rate of recurrence (with diabetic etiology having a lower rate) as well as in the rate of final clinical success (with diabetic etiology showing a significantly greater rate of success than idiopathic, postsurgical, or other etiologies of gastroparesis [p<.01]).

Section Summary: Gastric Peroral Endoscopic Myotomy for Gastroparesis

Two systematic reviews and meta-analyses evaluating G-POEM for the treatment of gastroparesis were identified. Pooled rates of clinical success were 60.7% at 1 year and 75% at 3 years following G-POEM with significant reductions in GCSI scores at 1 and 3 years post-treatment. All studies included in these reviews were observational. One RCT demonstrated a notably higher success rate and improvement in gastric retention for G-POEM compared to a sham control group, with the most significant benefit observed in patients with diabetic gastroparesis. Another RCT indicated a trend towards superior 3-month clinical outcomes for POEM over botulinum toxin injection, although the 1-year clinical success rate on intention-to-treat analysis was not significantly higher.

Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American College of Gastroenterology

In 2020, the American College of Gastroenterology (ACG) issued evidence-based clinical guidelines on the diagnosis and management of achalasia.[86,] The quality of the evidence and the strength of recommendations were rated based on the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework. The evidence review includes the 2 randomized controlled trials (RCTs) of peroral endoscopic myotomy (POEM) compared to laparoscopic Heller myotomy (LHM) or pneumatic dilation (PD). Based on their evaluation, the ACG made the following recommendations:

- "In patients with achalasia who are candidates for definite therapy, PD, LHM, and POEM are comparable effective therapies for type I or type II achalasia and POEM would be a better treatment option in those with type III achalasia.

- "We suggest that POEM or PD result in comparable symptomatic improvement in patients with types I or II achalasia." (GRADE quality=Low, Recommendation strength=Conditional)
- "We recommend that POEM and LHM result in comparable symptomatic improvement in patients with achalasia." (GRADE quality=Moderate; Recommendation strength=Strong)
- "We recommend tailored POEM or LHM for type III achalasia as a more efficacious alternative disruptive therapy at the lower esophageal sphincter compared to PD." (GRADE quality=Moderate; Recommendation strength=Strong)
- "We suggest that in patients with achalasia, POEM compared with LHM with fundoplication or PD is associated with a higher incidence of GERD [gastroesophageal reflux disease]." (GRADE quality=Moderate; Recommendation strength=Strong)
- "We suggest that POEM is a safe option in patients with achalasia who have previously undergone PD or LHM." (GRADE quality=Low; Recommendation strength=Strong)

American Gastroenterological Association Institute

In 2017, the American Gastroenterological Association (AGA) Institute published a clinical practice update on the use of POEM for the treatment of achalasia.[83,] Based on the expert review, the Institute made the following recommendations:

- POEM should be performed by experienced physicians in high-volume centers (competence achieved after an estimated 20 to 40 procedures)
- If expertise is available, POEM should be considered primary therapy for type III achalasia
- If expertise is available, POEM should be considered comparable to Heller myotomy for any achalasia syndromes
- Patients receiving POEM should be considered high-risk to develop reflux esophagitis and be advised of management considerations (e.g., proton pump inhibitor therapy and/or surveillance endoscopy) prior to undergoing POEM.

In 2023, the AGA Institute issued a clinical practice update commentary regarding gastric peroral endoscopic myotomy for gastroparesis.[87,] Based on an expert review the following recommendations were provided:

- Gastric POEM (G-POEM), also called peroral endoscopic pyloromyotomy, should be considered for patients with medically refractory gastroparesis
  - 1) Have undergo esophagogastroduodenoscopy to confirm no mechanical gastric outlet obstruction
  - 2) had a solid phase gastric emptying scan (GES) confirming delayed gastric emptying, preferably with retention >20% at 4 hours
  - 3) have moderate to severe symptoms including nausea and vomiting as the dominant symptoms on the gastroparesis cardinal symptom index
    - Patients who have failed gastric electrical stimulator therapy, pyloric stenting and botulinum toxin injection should be offered G-POEM but failure of these alternatives therapies should not be a prerequisite.
- G-POEM should not be offered to the following patients:
  - Patients with opioid dependence should be weaned off opioids whenever possible and have their gastric emptying re-evaluated.
  - Most patients with postinfectious gastroparesis should not be offered G-POEM
- G-POEM should only be performed by interventional endoscopists with expertise or training in third-space endoscopy
- Patients should remain on a liquid diet for at least 24 hours before G-POEM to minimize residual gastric contents
- A high-definition gastroscope, with a waterjet, affixed with a clear distal cap, should be used to perform G-POEM. And a modern electrosurgical generator capable of modulating power based on tissue resistance and circuit impedance is necessary for G-POEM.

American Society of Gastrointestinal Endoscopy

In 2020, the American Society of Gastrointestinal Endoscopy (ASGE) issued an evidence-based guideline on the management of achalasia.[88,] The methodologic quality of systematic reviews was assessed using the Methodological Quality of Systematic Reviews-2 (AMSTAR-2) tool and the certainty of the body of evidence was rated as very low to high based on the GRADE framework. ASGE rated the strength of individual recommendations based on the aggregate evidence quality and an assessment of the anticipated benefits and harms. ASGE used the phrase "we suggest" to indicate weaker recommendations and "we recommend" to indicate stronger recommendations. This guideline did not include either of the 2 available RCTs of POEM. Based on their evaluation, ASGE issued the following recommendations:

- "We suggest POEM as the preferred treatment for management of patients with type III achalasia." (Very low quality evidence)
- "In patients with failed initial myotomy (POEM or laparoscopic Heller myotomy), we suggest PD or redo myotomy using either the same or an alternative myotomy technique (POEM or laparoscopic Heller myotomy)." (Very low quality evidence)
- "We suggest that patients undergoing POEM are counseled regarding the increased risk of postprocedure reflux compared with PD and laparoscopic Heller myotomy. Based on patient preferences and physician expertise, postprocedure management options include objective testing for esophageal acid exposure, long-term acid suppressive therapy, and surveillance upper endoscopy." (Low quality evidence)
- We suggest that POEM and laparoscopic Heller myotomy are comparable treatment options for management of patients with achalasia types I and II, and the treatment option should be based on shared decision-making between the patient and provider." (Low quality evidence)

These 2020 ASGE guidelines were endorsed by the American Neurogastroenterology and Motility Society and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES).

International Society for Diseases of the Esophagus

In 2018, the International Society for Diseases of the Esophagus published guidelines on the diagnosis and management of achalasia.[89,] The Society convened 51 experts from 11 countries, including several from the U.S., to systematically review evidence, assess recommendations using the GRADE system, and vote to integrate the recommendations into the guidelines (>80% approval required for inclusion). Table 15 summarizes POEM recommendations.

Table 15. Recommendations for the Treatment of Achalasia

Recommendation	LOR	GOR
POEM is an effective therapy for achalasia both in short- and medium-term follow-up with results comparable to Heller myotomy.	Conditional	Very low
POEM is an effective therapy for achalasia both in short- and medium-term follow-up with results comparable to PD.	Conditional	Low
Pretreatment information on GERD, nonsurgical options (PD), and surgical options with lower GERD risk (Heller myotomy) should be provided to the patient.	Good practice	NA
POEM is feasible and effective for symptom relief in patients previously treated with endoscopic therapies.	Conditional	Very low
POEM may be considered an option for treating recurrent symptoms after laparoscopic Heller myotomy.	Conditional	Low
Appropriate training (in vivo/in vitro animal model) and proctorship should be considered prior to a clinical program of POEM.	Good practice	NA

GERD: gastroesophageal reflux disease; GOR: grade of recommendation; LOR: level of recommendation; NA: not applicable; PD: pneumatic dilation; POEM: peroral endoscopic myotomy.

Society of American Gastrointestinal and Endoscopic Surgeons

In 2020, SAGES endorsed the guideline on the management of achalasia issued by ASGE (2020) as described above.[88,]

In 2021, SAGES issued its own evidence-based guidelines for the use of POEM for the treatment of achalasia.[90,] The expert panel agreed on 4 recommendations for adults and children with achalasia. These include:

- The panel suggests that adult and pediatric patients with type I and II achalasia may be treated with either POEM or LHM based on surgeon and patient's shared decision making (conditional recommendation; very low certainty evidence).
- The panel suggests POEM over LHM for type III adult or pediatric achalasia. (expert opinion)
- The panel recommends POEM over PD in patients with achalasia (strong recommendation, moderate certainty evidence)
- For the subgroup of patients who are particularly concerned about the continued use of proton pump inhibitors post-operatively, the panel suggests that either POEM or PD can be used based on joint patient and surgeon decision-making (conditional recommendation, very low certainty evidence)

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently ongoing and unpublished trials that might influence this review are listed in Table 16.

Table 16. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01793922	A Prospective Randomized Multi-center Study Comparing Endoscopic Pneumodilation and Per Oral Endoscopic Myotomy (POEM) as Treatment of Idiopathic Achalasia	150	Jan 2025
NCT04434781	Gastric Per-Oral Endoscopic Myotomy (G-POEM) for the Treatment of Gastroparesis: A Database Repository	75	Aug 2024
NCT05830994	Randomized Sham-controlled Trial Investigating Efficacy of Gastric Peroral Endoscopic Myotomy in Treatment of Diabetic Gastroparesis	20	Jun 2025
NCT04869670	A Pilot and Feasibility Trial of G-POEM for Gastroparesis to Assess Safety, Physiological Mechanisms and Efficacy	30	Jun 2025
NCT02518542	Per Oral Endoscopic Myotomy (POEM) and Prolonged Dilatation (PRD) as Additional Endoscopic Treatment Options for Achalasia and Other Esophageal Motility Disorders	400	Jun 2027
Unpublished			
NCT01601678	Endoscopic Versus Laparoscopic Myotomy for Treatment of Idiopathic Achalasia: A Randomized, Controlled Trial	240	May 2023 (last update posted June 2023)
NCT01832779	Prospective Evaluation of the Clinical Utility of Peroral Endoscopic Myotomy (POEM)	143	May 2024 (last update posted May 2024)
NCT03228758	Efficacy of Anterior Versus Posterior Myotomy Approach in Peroral Endoscopic Myotomy (POEM) for the Treatment of Achalasia - a Single Operator Analysis	89	May 2019 (last update posted May 2020)

NCT: national clinical trial.

References

1. Gaber CE, Eluri S, Cotton CC, et al. Epidemiologic and Economic Burden of Achalasia in the United States. Clin Gastroenterol Hepatol. Feb 2022; 20(2): 342-352.e5. PMID 33652152
2. Cheatham JG, Wong RK. Current approach to the treatment of achalasia. Curr Gastroenterol Rep. Jun 2011; 13(3): 219-25. PMID 21424734
3. Pandolfino JE, Kahrilas PJ. Presentation, diagnosis, and management of achalasia. Clin Gastroenterol Hepatol. Aug 2013; 11(8): 887-97. PMID 23395699
4. Yaghoobi M, Mayrand S, Martel M, et al. Laparoscopic Heller's myotomy versus pneumatic dilation in the treatment of idiopathic achalasia: a meta-analysis of randomized, controlled trials. Gastrointest Endosc. Sep 2013; 78(3): 468-75. PMID 23684149
5. Inoue H, Minami H, Kobayashi Y, et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia. Endoscopy. Apr 2010; 42(4): 265-71. PMID 20354937
6. Hungness ES, Teitelbaum EN, Santos BF, et al. Comparison of perioperative outcomes between peroral esophageal myotomy (POEM) and laparoscopic Heller myotomy. J Gastrointest Surg. Feb 2013; 17(2): 228-35. PMID 23054897
7. Reddivari AKR, Mehta P. Gastroparesis. [Updated 2022 Sep 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK551528/
8. Dilmaghani S, Zheng T, Camilleri M. Epidemiology and Healthcare Utilization in Patients With Gastroparesis: A Systematic Review. Clin Gastroenterol Hepatol. Aug 2023; 21(9): 2239-2251.e2. PMID 35870768
9. Eckardt AJ, Eckardt VF. Treatment and surveillance strategies in achalasia: an update. Nat Rev Gastroenterol Hepatol. Jun 2011; 8(6): 311-9. PMID 21522116
10. Li H, Peng W, Huang S, et al. The 2 years' long-term efficacy and safety of peroral endoscopic myotomy for the treatment of achalasia: a systematic review. J Cardiothorac Surg. Jan 03 2019; 14(1): 1. PMID 30606216
11. Crespin OM, Liu LWC, Parmar A, et al. Safety and efficacy of POEM for treatment of achalasia: a systematic review of the literature. Surg Endosc. May 2017; 31(5): 2187-2201. PMID 27633440
12. Akintoye E, Kumar N, Obaitan I, et al. Peroral endoscopic myotomy: a meta-analysis. Endoscopy. Dec 2016; 48(12): 1059-1068. PMID 27617421
13. Patel K, Abbassi-Ghadi N, Markar S, et al. Peroral endoscopic myotomy for the treatment of esophageal achalasia: systematic review and pooled analysis. Dis Esophagus. Oct 2016; 29(7): 807-819. PMID 26175119
14. Andolfi C, Fisichella PM. Meta-analysis of clinical outcome after treatment for achalasia based on manometric subtypes. Br J Surg. Mar 2019; 106(4): 332-341. PMID 30690706
15. Dirks RC, Kohn GP, Slater B, et al. Is peroral endoscopic myotomy (POEM) more effective than pneumatic dilation and Heller myotomy? A systematic review and meta-analysis. Surg Endosc. May 2021; 35(5): 1949-1962. PMID 33655443
16. Facciorusso A, Singh S, Abbas Fehmi SM, et al. Comparative efficacy of first-line therapeutic interventions for achalasia: a systematic review and network meta-analysis. Surg Endosc. Aug 2021; 35(8): 4305-4314. PMID 32856150
17. Martins RK, Ribeiro IB, DE Moura DTH, et al. PERORAL (POEM) OR SURGICAL MYOTOMY FOR THE TREATMENT OF ACHALASIA: A SYSTEMATIC REVIEW AND META-ANALYSIS. Arq Gastroenterol. 2020; 57(1): 79-86. PMID 32294740
18. Aiolfi A, Bona D, Riva CG, et al. Systematic Review and Bayesian Network Meta-Analysis Comparing Laparoscopic Heller Myotomy, Pneumatic Dilatation, and Peroral Endoscopic Myotomy for Esophageal Achalasia. J Laparoendosc Adv Surg Tech A. Feb 2020; 30(2): 147-155. PMID 31364910
19. Teitelbaum EN, Soper NJ, Santos BF, et al. Symptomatic and physiologic outcomes one year after peroral esophageal myotomy (POEM) for treatment of achalasia. Surg Endosc. Dec 2014; 28(12): 3359-65. PMID 24939164

20. Ujiki MB, Yetasook AK, Zapf M, et al. Peroral endoscopic myotomy: A short-term comparison with the standard laparoscopic approach. Surgery. Oct 2013; 154(4): 893-7; discussion 897-900. PMID 24074429
21. 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. Jun 2014; 259(6): 1098-103. PMID 24169175
22. Kumagai K, Tsai JA, Thorell A, et al. Per-oral endoscopic myotomy for achalasia. Are results comparable to laparoscopic Heller myotomy?. Scand J Gastroenterol. May 2015; 50(5): 505-12. PMID 25712228
23. Kumbhari V, Tieu AH, Onimaru M, et al. Peroral endoscopic myotomy (POEM) vs laparoscopic Heller myotomy (LHM) for the treatment of Type III achalasia in 75 patients: a multicenter comparative study. Endosc Int Open. Jun 2015; 3(3): E195-201. PMID 26171430
24. Chan SM, Wu JC, Teoh AY, et al. Comparison of early outcomes and quality of life after laparoscopic Heller's cardiomyotomy to peroral endoscopic myotomy for treatment of achalasia. Dig Endosc. Jan 2016; 28(1): 27-32. PMID 26108140
25. Sanaka MR, Hayat U, Thota PN, et al. Efficacy of peroral endoscopic myotomy vs other achalasia treatments in improving esophageal function. World J Gastroenterol. May 28 2016; 22(20): 4918-25. PMID 27239118
26. Schneider AM, Louie BE, Warren HF, et al. A Matched Comparison of Per Oral Endoscopic Myotomy to Laparoscopic Heller Myotomy in the Treatment of Achalasia. J Gastrointest Surg. Nov 2016; 20(11): 1789-1796. PMID 27514392
27. Khashab MA, Kumbhari V, Tieu AH, et al. Peroral endoscopic myotomy achieves similar clinical response but incurs lesser charges compared to robotic heller myotomy. Saudi J Gastroenterol. 2017; 23(2): 91-96. PMID 28361839
28. Leeds SG, Burdick JS, Ogola GO, et al. Comparison of outcomes of laparoscopic Heller myotomy versus per-oral endoscopic myotomy for management of achalasia. Proc (Bayl Univ Med Cent). Oct 2017; 30(4): 419-423. PMID 28966450
29. de Pascale S, Repici A, Puccetti F, et al. Peroral endoscopic myotomy versus surgical myotomy for primary achalasia: single-center, retrospective analysis of 74 patients. Dis Esophagus. Aug 01 2017; 30(8): 1-7. PMID 28575245
30. Peng L, Tian S, Du C, et al. Outcome of Peroral Endoscopic Myotomy (POEM) for Treating Achalasia Compared With Laparoscopic Heller Myotomy (LHM). Surg Laparosc Endosc Percutan Tech. Feb 2017; 27(1): 60-64. PMID 28145968
31. Ward MA, Gitelis M, Patel L, et al. Outcomes in patients with over 1-year follow-up after peroral endoscopic myotomy (POEM). Surg Endosc. Apr 2017; 31(4): 1550-1557. PMID 27858209
32. Hanna AN, Datta J, Ginzberg S, et al. Laparoscopic Heller Myotomy vs Per Oral Endoscopic Myotomy: Patient-Reported Outcomes at a Single Institution. J Am Coll Surg. Apr 2018; 226(4): 465-472.e1. PMID 29410262
33. Ramirez M, Zubieta C, Ciotola F, et al. Per oral endoscopic myotomy vs. laparoscopic Heller myotomy, does gastric extension length matter?. Surg Endosc. Jan 2018; 32(1): 282-288. PMID 28660419
34. Caldaro T, Familiari P, Romeo EF, et al. Treatment of esophageal achalasia in children: Today and tomorrow. J Pediatr Surg. May 2015; 50(5): 726-30. PMID 25783358
35. Fumagalli U, Rosati R, De Pascale S, et al. Repeated Surgical or Endoscopic Myotomy for Recurrent Dysphagia in Patients After Previous Myotomy for Achalasia. J Gastrointest Surg. Mar 2016; 20(3): 494-9. PMID 26589525
36. Greenleaf EK, Winder JS, Hollenbeak CS, et al. Cost-effectiveness of per oral endoscopic myotomy relative to laparoscopic Heller myotomy for the treatment of achalasia. Surg Endosc. Jan 2018; 32(1): 39-45. PMID 29218664
37. Kim GH, Jung KW, Jung HY, et al. Superior clinical outcomes of peroral endoscopic myotomy compared with balloon dilation in all achalasia subtypes. J Gastroenterol Hepatol. Apr 2019; 34(4): 659-665. PMID 30695124
38. Meng F, Li P, Wang Y, et al. Peroral endoscopic myotomy compared with pneumatic dilation for newly diagnosed achalasia. Surg Endosc. Nov 2017; 31(11): 4665-4672. PMID 28411346

39. Miller HJ, Neupane R, Fayezizadeh M, et al. POEM is a cost-effective procedure: cost-utility analysis of endoscopic and surgical treatment options in the management of achalasia. Surg Endosc. Apr 2017; 31(4): 1636-1642. PMID 27534662
40. Ponds FA, Fockens P, Lei A, et al. Effect of Peroral Endoscopic Myotomy vs Pneumatic Dilation on Symptom Severity and Treatment Outcomes Among Treatment-Naive Patients With Achalasia: A Randomized Clinical Trial. JAMA. Jul 09 2019; 322(2): 134-144. PMID 31287522
41. Sanaka MR, Thota PN, Parikh MP, et al. Peroral endoscopic myotomy leads to higher rates of abnormal esophageal acid exposure than laparoscopic Heller myotomy in achalasia. Surg Endosc. Jul 2019; 33(7): 2284-2292. PMID 30341655
42. Wang X, Tan Y, Lv L, et al. Peroral endoscopic myotomy versus pneumatic dilation for achalasia in patients aged ≥ 65 years. Rev Esp Enferm Dig. Oct 2016; 108(10): 637-641. PMID 27649684
43. Werner YB, Hakanson B, Martinek J, et al. Endoscopic or Surgical Myotomy in Patients with Idiopathic Achalasia. N Engl J Med. Dec 05 2019; 381(23): 2219-2229. PMID 31800987
44. Wirsching A, Boshier PR, Klevebro F, et al. Comparison of costs and short-term clinical outcomes of per-oral endoscopic myotomy and laparoscopic Heller myotomy. Am J Surg. Oct 2019; 218(4): 706-711. PMID 31353034
45. Zheng Z, Zhao C, Su S, et al. Peroral endoscopic myotomy versus pneumatic dilation - result from a retrospective study with 1-year follow-up. Z Gastroenterol. Mar 2019; 57(3): 304-311. PMID 30861554
46. Podboy AJ, Hwang JH, Rivas H, et al. Long-term outcomes of per-oral endoscopic myotomy compared to laparoscopic Heller myotomy for achalasia: a single-center experience. Surg Endosc. Feb 2021; 35(2): 792-801. PMID 32157405
47. Tan Y, Zhu H, Li C, et al. Comparison of peroral endoscopic myotomy and endoscopic balloon dilation for primary treatment of pediatric achalasia. J Pediatr Surg. Oct 2016; 51(10): 1613-8. PMID 27339081
48. Boeckxstaens GE, Annese V, des Varannes SB, et al. Pneumatic dilation versus laparoscopic Heller's myotomy for idiopathic achalasia. N Engl J Med. May 12 2011; 364(19): 1807-16. PMID 21561346
49. Borges AA, Lemme EM, Abrahao LJ, et al. Pneumatic dilation versus laparoscopic Heller myotomy for the treatment of achalasia: variables related to a good response. Dis Esophagus. Jan 2014; 27(1): 18-23. PMID 23551592
50. 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. Mar 2007; 31(3): 470-8. PMID 17308851
51. Hamdy E, El Nakeeb A, El Hanfy E, et al. Comparative Study Between Laparoscopic Heller Myotomy Versus Pneumatic Dilatation for Treatment of Early Achalasia: A Prospective Randomized Study. J Laparoendosc Adv Surg Tech A. Jun 2015; 25(6): 460-4. PMID 25951417
52. Zhong C, Tan S, Huang S, et al. Peroral endoscopic myotomy versus pneumatic dilation for achalasia: a systematic review and meta-analysis. Eur J Gastroenterol Hepatol. Nov 2020; 32(11): 1413-1421. PMID 32516175
53. de Moura ETH, Jukemura J, Ribeiro IB, et al. Peroral endoscopic myotomy vs laparoscopic myotomy and partial fundoplication for esophageal achalasia: A single-center randomized controlled trial. World J Gastroenterol. Sep 07 2022; 28(33): 4875-4889. PMID 36156932
54. Saleh CMG, Familiari P, Bastiaansen BAJ, et al. The Efficacy of Peroral Endoscopic Myotomy vs Pneumatic Dilation as Treatment for Patients With Achalasia Suffering From Persistent or Recurrent Symptoms After Laparoscopic Heller Myotomy: A Randomized Clinical Trial. Gastroenterology. Jun 2023; 164(7): 1108-1118.e3. PMID 36907524
55. Kuipers T, Ponds FA, Fockens P, et al. Peroral endoscopic myotomy versus pneumatic dilation in treatment-naive patients with achalasia: 5-year follow-up of a randomised controlled trial. Lancet Gastroenterol Hepatol. Dec 2022; 7(12): 1103-1111. PMID 36206786

56. Docimo S, Mathew A, Shope AJ, et al. Reduced postoperative pain scores and narcotic use favor per-oral endoscopic myotomy over laparoscopic Heller myotomy. Surg Endosc. Feb 2017; 31(2): 795-800. PMID 27338580
57. Haseeb M, Khan Z, Kamal MU, et al. Short-term outcomes after peroral endoscopic myotomy, Heller myotomy, and pneumatic dilation in patients with achalasia: a nationwide analysis. Gastrointest Endosc. May 2023; 97(5): 871-879.e2. PMID 36639060
58. Shally L, Saeed K, Berglund D, et al. Clinical and financial outcomes of per-oral endoscopic myotomy compared to laparoscopic heller myotomy for treatment of achalasia. Surg Endosc. Jul 2023; 37(7): 5526-5537. PMID 36220985
59. Nabi Z, Talukdar R, Chavan R, et al. Outcomes of Per-Oral Endoscopic Myotomy in Children: A Systematic Review and Meta-analysis. Dysphagia. Dec 2022; 37(6): 1468-1481. PMID 35092485
60. Zhong C, Tan S, Huang S, et al. Clinical outcomes of peroral endoscopic myotomy for achalasia in children: a systematic review and meta-analysis. Dis Esophagus. Apr 07 2021; 34(4). PMID 33316041
61. Lee Y, Brar K, Doumouras AG, et al. Peroral endoscopic myotomy (POEM) for the treatment of pediatric achalasia: a systematic review and meta-analysis. Surg Endosc. Jun 2019; 33(6): 1710-1720. PMID 30767141
62. Bi YW, Lei X, Ru N, et al. Per-oral endoscopic myotomy is safe and effective for pediatric patients with achalasia: A long-term follow-up study. World J Gastroenterol. Jun 14 2023; 29(22): 3497-3507. PMID 37389239
63. Petrosyan M, Mostammand S, Shah AA, et al. Per Oral Endoscopic Myotomy (POEM) for pediatric achalasia: Institutional experience and outcomes. J Pediatr Surg. Nov 2022; 57(11): 728-735. PMID 35361482
64. Nabi Z, Ramchandani M, Chavan R, et al. Outcome of peroral endoscopic myotomy in children with achalasia. Surg Endosc. Nov 2019; 33(11): 3656-3664. PMID 30671667
65. Miao S, Wu J, Lu J, et al. Peroral Endoscopic Myotomy in Children With Achalasia: A Relatively Long-term Single-center Study. J Pediatr Gastroenterol Nutr. Feb 2018; 66(2): 257-262. PMID 28691974
66. Revicki DA, Rentz AM, Dubois D, et al. Gastroparesis Cardinal Symptom Index (GCSI): development and validation of a patient reported assessment of severity of gastroparesis symptoms. Qual Life Res. May 2004; 13(4): 833-44. PMID 15129893
67. Kamal F, Khan MA, Lee-Smith W, et al. Systematic review with meta-analysis: one-year outcomes of gastric peroral endoscopic myotomy for refractory gastroparesis. Aliment Pharmacol Ther. Jan 2022; 55(2): 168-177. PMID 34854102
68. Canakis, A., et al., Long-term outcomes (3 years) after gastric peroral endoscopic myotomy for refractory gastroparesis: a systematic review and meta-analysis. iGIE, 2023. 2(3): p. 344-349.e3.
69. Labonde A, Lades G, Debourdeau A, et al. Gastric peroral endoscopic myotomy in refractory gastroparesis: long-term outcomes and predictive score to improve patient selection. Gastrointest Endosc. Sep 2022; 96(3): 500-508.e2. PMID 35413333
70. Hernández Mondragón OV, Contreras LFG, Velasco GB, et al. Gastric peroral endoscopic myotomy outcomes after 4 years of follow-up in a large cohort of patients with refractory gastroparesis (with video). Gastrointest Endosc. Sep 2022; 96(3): 487-499. PMID 35378136
71. Vosoughi K, Ichkhanian Y, Benias P, et al. Gastric per-oral endoscopic myotomy (G-POEM) for refractory gastroparesis: results from an international prospective trial. Gut. Jan 2022; 71(1): 25-33. PMID 33741641
72. Gregor L, Wo J, DeWitt J, et al. Gastric peroral endoscopic myotomy for the treatment of refractory gastroparesis: a prospective single-center experience with mid-term follow-up (with video). Gastrointest Endosc. Jul 2021; 94(1): 35-44. PMID 33373646
73. Conchillo JM, Straathof JWA, Mujagic Z, et al. Gastric peroral endoscopic pyloromyotomy for decompensated gastroparesis: comprehensive motility analysis in relation to treatment outcomes. Endosc Int Open. Feb 2021; 9(2): E137-E144. PMID 33532550

74. Abdelfatah MM, Noll A, Kapil N, et al. Long-term Outcome of Gastric Per-Oral Endoscopic Pyloromyotomy in Treatment of Gastroparesis. Clin Gastroenterol Hepatol. Apr 2021; 19(4): 816-824. PMID 32450364
75. Husťak R, Vacková Z, Krajciova J, et al. Per-oral endoscopic pyloromyotomy (g-poem) for the treatment of gastroparesis - a pilot single-centre study with mid-term follow-up. Rozhl Chir. 2020; 99(3): 116-123. PMID 32349495
76. Tan J, Shrestha SM, Wei M, et al. Feasibility, safety, and long-term efficacy of gastric peroral endoscopic myotomy (G-POEM) for postsurgical gastroparesis: a single-center and retrospective study of a prospective database. Surg Endosc. Jul 2021; 35(7): 3459-3470. PMID 32880749
77. Attaar M, Su B, Wong HJ, et al. Comparing cost and outcomes between peroral endoscopic myotomy and laparoscopic heller myotomy. Am J Surg. Jul 2021; 222(1): 208-213. PMID 33162014
78. Ragi O, Jacques J, Branche J, et al. One-year results of gastric peroral endoscopic myotomy for refractory gastroparesis: a French multicenter study. Endoscopy. May 2021; 53(5): 480-490. PMID 32575130
79. Shen S, Luo H, Vachaparambil C, et al. Gastric peroral endoscopic pyloromyotomy versus gastric electrical stimulation in the treatment of refractory gastroparesis: a propensity score-matched analysis of long term outcomes. Endoscopy. May 2020; 52(5): 349-358. PMID 32084672
80. Vosoughi K, Ichkhanian Y, Jacques J, et al. Role of endoscopic functional luminal imaging probe in predicting the outcome of gastric peroral endoscopic pyloromyotomy (with video). Gastrointest Endosc. Jun 2020; 91(6): 1289-1299. PMID 32035074
81. Xu J, Chen T, Elkholy S, et al. Gastric Peroral Endoscopic Myotomy (G-POEM) as a Treatment for Refractory Gastroparesis: Long-Term Outcomes. Can J Gastroenterol Hepatol. 2018; 2018: 6409698. PMID 30425974
82. Davis BR, Sarosiek I, Bashashati M, et al. The Long-Term Efficacy and Safety of Pyloroplasty Combined with Gastric Electrical Stimulation Therapy in Gastroparesis. J Gastrointest Surg. Feb 2017; 21(2): 222-227. PMID 27896652
83. Kahrilas PJ, Katzka D, Richter JE. Clinical Practice Update: The Use of Per-Oral Endoscopic Myotomy in Achalasia: Expert Review and Best Practice Advice From the AGA Institute. Gastroenterology. Nov 2017; 153(5): 1205-1211. PMID 28989059
84. Gonzalez JM, Mion F, Pioche M, et al. Gastric peroral endoscopic myotomy versus botulinum toxin injection for the treatment of refractory gastroparesis: results of a double-blind randomized controlled study. Endoscopy. May 2024; 56(5): 345-352. PMID 38141620
85. Martinek J, Hustak R, Mares J, et al. Endoscopic pyloromyotomy for the treatment of severe and refractory gastroparesis: a pilot, randomised, sham-controlled trial. Gut. Nov 2022; 71(11): 2170-2178. PMID 35470243
86. Vaezi MF, Pandolfino JE, Yadlapati RH, et al. ACG Clinical Guidelines: Diagnosis and Management of Achalasia. Am J Gastroenterol. Sep 2020; 115(9): 1393-1411. PMID 32773454
87. Khashab MA, Wang AY, Cai Q. AGA Clinical Practice Update on Gastric Peroral Endoscopic Myotomy for Gastroparesis: Commentary. Gastroenterology. Jun 2023; 164(7): 1329-1335.e1. PMID 37086247
88. Khashab MA, Vela MF, Thosani N, et al. ASGE guideline on the management of achalasia. Gastrointest Endosc. Feb 2020; 91(2): 213-227.e6. PMID 31839408
89. Zaninotto G, Bennett C, Boeckxstaens G, et al. The 2018 ISDE achalasia guidelines. Dis Esophagus. Sep 01 2018; 31(9). PMID 30169645
90. Kohn GP, Dirks RC, Ansari MT, et al. SAGES guidelines for the use of peroral endoscopic myotomy (POEM) for the treatment of achalasia. Surg Endosc. May 2021; 35(5): 1931-1948. PMID 33564964

Documentation for Clinical Review

- No records required

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	43497	Lower esophageal myotomy, transoral (i.e., peroral endoscopic myotomy [POEM])
	43499	Unlisted procedure, esophagus
	43999	Unlisted procedure, stomach
HCPCS	None	

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
01/30/2015	BCBSA Medical Policy adoption
03/01/2016	Policy revision without position change
12/01/2016	Policy revision without position change
10/01/2017	Policy revision without position change
01/01/2018	Policy revision without position change
01/01/2019	Policy revision without position change
02/01/2020	Annual review. No change to policy statement. Literature review updated.
02/01/2024	Policy reactivated. Previously archived from 09/01/2020 to 01/31/2024. Policy title changed from Peroral Endoscopic Myotomy for Treatment of Esophageal Achalasia to current one. Coding update.
01/01/2025	Annual review. No change to policy statement. Policy guidelines and literature review updated.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent

therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT (No changes)	
BEFORE	**AFTER**
Peroral Endoscopic Myotomy for Treatment of Esophageal Achalasia and Gastroparesis 2.01.91 **Policy Statement:** I. Peroral endoscopic myotomy is considered **investigational** as a treatment for pediatric and adult esophageal achalasia. II. Gastric peroral endoscopic myotomy is considered **investigational** as a treatment for gastroparesis.	**Peroral Endoscopic Myotomy for Treatment of Esophageal Achalasia and Gastroparesis 2.01.91** **Policy Statement:** I. Peroral endoscopic myotomy is considered **investigational** as a treatment for pediatric and adult esophageal achalasia. II. Gastric peroral endoscopic myotomy is considered **investigational** as a treatment for gastroparesis.