Medical Policy

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(See policy history boxes for previous effective dates)

Title: Peroral Endoscopic Myotomy for Treatment of Esophageal Achalasia or Gastroparesis

Description/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 two 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%. Laparoscopic 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]

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.

Regulatory Status

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

Medical Policy Statement

Peroral endoscopic myotomy (POEM) as a treatment for pediatric and adult esophageal achalasia or gastroparesis is experimental/investigational. It has not been scientifically demonstrated to be as safe and effective as conventional treatment.

Inclusionary and Exclusionary Guidelines

N/A

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

N/A

Other codes (investigational, not medically necessary, etc.):

43499 43497

Rationale

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are 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 to 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, two domains are examined: the relevance, the quality and credibility. To be relevant, studies must represent one 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 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 effect. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

PERORAL ENDOSCOPIC MYOTOMY FOR ADULT PATIENT 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**s were used to select literature to inform this review.

Populations
The relevant population of interest are 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 dilatation, and laparoscopic Heller myotomy (LHM), and botulinum toxin injection.

Esophageal dilation is performed in a graded approach, starting with a small balloon (typically 30mm), then progressing to larger balloons (35-40mm) two to four 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 five small incisions to insert the camera and surgical instruments. Reported success rates are high (>90%), with a five-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 one year.

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

Symptom relief may be measured by Eckardt score, which is comprised of four major symptoms of achalasia: dysphagia, regurgitation, retrosternal pain, weight loss. Each symptom receives a score from 0 (none) to 3 (severe), for a maximum score of 12. Total scores of four or greater represent treatment failure.[9]

A treatment-related morbidity of concern is the development of gastroesophageal reflux disease (GERD). GERD 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 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

Multiple systematic reviews and meta-analyses have been published to evaluate POEM as a treatment for achalasia. They are heterogenous in whether they assessed data on POEM alone or compared POEM to LHM, which outcomes they assessed, which studies they included, and in the statistical methods they 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. [10-14] 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] They calculated pooled success rates for POEM, LHM, and 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 than 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 Observational Studies of POEM vs. LHM Included in SR & M-A

Study	Dirks et al (2021)	Facciorusso et al (2021)	Martins et al (2020)	Aiolfi et al (2020)
Hungness et al (2013)	●		●	●
Teitelbaum et al (2013)			●	●
Ujiki et al (2013)	●		●	●
Bhayani et al (2014)	●		●	●
Kumagai et al (2015)	●		●	●

Kumbhari et al (2015)	●			●
Chan et al (2016)			●	●
Sanaka et al (2016)	●		●	
Schneider et al (2016)	●		●	
Kashab et al (2017)	●		●	
Leeds et al (2017)	●			●
de Pascale et al (2017)	●		●	
Peng et al (2017)	●		●	
Ward et al (2017)	●		●	
Hanna et al (2018)	●			●
Ramirez et al (2018)	●			●
Caldaro et al (2015)	●			
Fumagalli et al (2016)	●			
Greenleaf et al (2018)	●			
Kim et al (2019)	●			
Meng et al (2017)	●			
Miller et al (2017)	●			
Ponds et al (2019)	●	●		
Sanaka et al (2019)	●			
Wang et al (2016)	●			
Werner et al (2019)	●	●		
Wirsching et al (2019)	●			
Zheng et al (2019)	●			
Podboy et al (2020)	●			
Tan et al (2016)	●			
Boeckxstaens et al (2011)		●		
Borges et al (2014)		●		
Kostic et al (2007)		●		
Hamdy et al (2015)		●		

POEM: Peroral Endoscopic Myotomy; LHM: Laparoscopic Heller Myotomy; SR: systematic review; M-A: meta-analysis

Tables 2 and 3 summarize characteristics and results of the included systematic reviews published ≥ 2020 that address the comparison of POEM to LHM using data from comparative observational studies. The included comparative observational studies are heterogenous in their patient populations, proportions of patients with any previous treatments (i.e., none

versus prior pneumatic dilation or botulinum toxin, or prior pneumatic dilation and botulinum toxin), and proportions of each achalasia subtype I-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 pneumatic dilation.[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 pneumatic dilation. POEM was associated with improved dysphasia remission and Eckardt scores, but higher risk of GERD compared to LHM. Results of the comparison to pneumatic dilation 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)	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)	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)	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)	2012-2018	10	Esophageal achalasia	645 (23 to 101)	Observational	NR

SR: systematic review; M-A: Meta-Analysis; N: sample size; NR: Not reported

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)					
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)					
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 years: RR, 1.76 (1.37 to 2.25)			
Martins et al (2020)[,]					
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)					
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; MD: Mean Difference; N: sample size; N/A: Not applicable; NR: Not reported; OR=Odds Ratio; POEM: Peroral Endoscopic Myotomy; RD: Risk Difference; RR=Risk Ratio; WMD: weighted mean difference;

Peroral Endoscopic Myotomy Versus Pneumatic Dilation

Zhong et al (2020) conducted a meta-analysis of 7 observational studies comparing POEM (n=298) to pneumatic dilation (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; thus, 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 (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 pneumatic dilation (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 pneumatic dilation.[18] Overall, 19 studies of 4407 patients were included. Of those, none directly compared POEM and pneumatic dilation.

Therefore, data from the POEM and pneumatic dilation arms of studies that compared them each, respectively, to LHM, were indirectly compared in the network meta-analysis. Compared to pneumatic dilation, 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 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 randomized clinical trial comparing POEM and pneumatic dilation 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 pneumatic dilation (Tables 4 and 5). The primary outcome was overall treatment success at 2 years, defined as an Eckardt score < 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 pneumatic dilation. Two serious adverse events (including one perforation) occurred after pneumatic dilation; no serious adverse events occurred after POEM. The study was limited by the lack of blinding, lack of 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%) of 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 pneumatic dilation, 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 proton-pump inhibitors 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)	Netherlands, Germany, Italy, Hong Kong	6	2012-2015	Treatment naïve adults with newly diagnosed achalasia and Eckardt score ≥3	POEM (n=64)	PD Initial with 30 mm balloon Subsequent with 35 mm balloon if Eckardt score ≥3 at 3 weeks (n=66)
Werner et al (2019)	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)	Brazil	1	2017-2018	Adults diagnosed with achalasia	POEM (n=20)	LHM plus partial fundoplication(n=20)
Saleh et al (2023)	Netherlands, Belgium, Italy	3	2014-2020	Adults with symptomatic achalasia and Eckardt score ≥3 following LHM	POEM (n=45)	PD (n=45)

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

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

Study	Treatment success, n (%)	PPI use	Endoscopic Reflux Esophagitis	Retreatment	Treatment-related SAE
Ponds et al (2019)	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)	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)	40		40		40
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)	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 Risk Ratio (95% confidence interval[CI])
[b] Unadjusted Absolute Difference (95% CI)
[c] Odds Ratio (95% CI)
IQR: interquartile range; PPI: proton pump inhibitor; RCT: randomized controlled trial; SAE: severe adverse even; SD: standard deviation.

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

Table 6. Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Ponds et al (2019)			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)	4. Non-US		2. LHM plus Dor's fundoplication		
Mourna et al (2022)	4. Non-US		2. LHM plus partial fundoplication	4. Eckardt score not validated symptom assessment	
Saleh et al (2023)	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 limitations 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 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)		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)		1. Not blinded outcome assessment				
Mourna et al (2022)		1. Not blinded outcome assessment				
Saleh et al (2023)		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 limitations 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=0.472) or at time of discharge (1.6±2.420 vs. 2.09±2.157, p=0.0657). The POEM group required significantly fewer less narcotics while hospitalized than the LHM group (35.8mg vs. 101.8mg, p<0.001), and fewer POEM patients needed a prescription for a narcotic analgesic at discharge (6.81% vs. 92.4%, p<0.001). Also, the average length of stay was 31.2 hours for POEM and 55.79 for LHM (p<0.001). 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 pneumatic dilation (n=10) in patients ages 65 years and older.[42] All were treated successfully, with decreases in Eckhardt scores. At a mean follow-up of 21.8 months for POEM and 35 months for pneumatic dilation patients, one POEM case failed, and two pneumatic dilation 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 groups 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 (odds ratio, 11.32; p=0.06). 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=0.01). However, an important limitation of this study is that LHM patients had a 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 **PICOs** were used to select literature to inform this review.

Populations

The relevant population of interest are 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 patients 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 dilatation, and 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 (35-40 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 five 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 four major symptoms of achalasia: dysphagia, regurgitation, retrosternal pain, weight loss. Each symptom receives a score from 0 (none) to 3 (severe), for a maximum score of 12. Total scores of four or greater represent treatment failure.[12]

A treatment-related morbidity of concern is the development of GERD. GERD 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.

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 gastoesophageal reflux 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 (mean difference 6.88, 95% CI 6.28–7.48, p<0.001) and a reduction in LES pressure of 20.73 mmHg (mean difference 20.73, 95% CI 15.76–25.70, p<0.001). Improvement or resolution of short- and long-term achalasia symptoms was experienced in 93% of patients. The study was limited by several of the including 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 Comparative 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 Aes, including retroperitoneal CO2 (n=7), capnoperitoneum (n=3), and mucosal injury (n=1). Clinical success at 1, 2, 3, and 4 years 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 GER in about half the patients, and the small number of patients who completed three 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 11months –18 years) diagnosed with achalasia and treated between 2014 and 2016 were included. Mean follow-up time was 13.2 months. No severe Aes 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<0.001). At 6 months, an average weight gain of 2.7kg was observed. Four patients had gastroesophageal reflux and two had concomitant gastroesophageal reflux and reflux esophagitis at three months follow-up. No limitations to the study were reported.

Section Summary: POEM 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 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 **PICOs** were used to select literature to inform this review.

Populations
The relevant population of interest are 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 gastric POEM (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 only the inner, circular LES 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.

Antiemetic 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.

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 Including in Meta-Analysis

Study	Kamal et al (2022)	Canakis et al (2023)
Labond et al (2022)		

Canakis et al (2023)	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), all results at 1 year f/u					
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), 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)	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)	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

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)	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)	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)	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)	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)					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)			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: G-POEM for Patients with 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.

SUMMARY OF EVIDENCE
For adults who have achalasia who receive peroral endoscopic myotomy (POEM) , the evidence includes systematic reviews of primarily observational studies, 4 randomized controlled trials (RCTs) , and nonrandomized comparative studies. Relevant outcomes are symptoms, functional outcomes, health status measures, resource utilization, and treatment-related morbidity. Compared with pneumatic dilation (PD) or laparoscopic Heller myotomy (LHM), findings from RCTs demonstrated that POEM had a similar or greater treatment success rate based on the Eckardt score and similar or fewer overall adverse event rates. However, POEM had significantly higher rates of endoscopically confirmed reflux esophagitis and more daily proton-pump inhibitor use at 24 months. 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 comparative observational studies have primarily reported similar outcomes for POEM and for LHM in symptom relief, as assessed by the Eckardt score. Some studies have shown a shorter length of stay and less postoperative pain with POEM. However, potential imbalances in patient characteristics in these nonrandomized studies might have biased the treatment comparisons. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For pediatric individuals who have achalasia who receive POEM, the evidence includes several nonrandomized studies and 3 systematic reviews. Relevant outcomes are symptoms, functional outcomes, health status measures, resource utilization, and treatment-related morbidity. The studies reported treatment success for POEM based on decreases in Eckardt scores and lower esophageal sphincter (LES) pressure. No RCTs have been reported. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For adults who have gastroparesis who receive gastric POEM (G-POEM), the evidence includes 2 meta-analyses, 2 RCTs, and several nonrandomized studies. Relevant outcomes are symptoms, functional outcomes, health status measures, resource utilization, and treatment-related morbidity. The studies generally reported treatment success for G-POEM based on a decrease in Gastroparesis Cardinal Symptom Index (GCSI) score and ranged from 61 % at 1 year to 75% at 3 years in the meta-analyses. 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. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

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 that 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." (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 (AGA)

In 2017, the American Gastroenterological Association Institute published a clinical practice update on the use of peroral endoscopic myotomy (POEM) for the treatment of achalasia.[57] Based on 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:
  - Have undergo esophagogastroduodenoscopy to confirm no mechanical gastric outlet obstruction
  - Had a solid phase gastric emptying scan (GES) confirming delayed gastric emptying, preferably with retention >20% at 4 hours
  - 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 and Endoscopic Surgeons

In 2020, 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, post procedure 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 United States, 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 5 summarizes POEM recommendations.

Table 8. 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; BCBSM: not applicable; 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)

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 6.

Table 9. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01793922	A prospective randomized multi-center study comparing endoscopic pneumodilation and peroral endoscopic myotomy (POEM) as treatment of idiopathic achalasia	150	Jan 2025
NCT04349670	Safety and efficacy of GPOEM in the treatment of gastroparesis	30	Jun 2025
NCT05830994	Randomized Sham-controlled Trial Investigating Efficacy of Gastric Peroral Endoscopic Myotomy in Treatment of Diabetic Gastroparesis	20	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			
BCBSM01402518	Observational Study of the Per-oral Endoscopic Motomy (POEM) Procedure	100	Nov 2019
NCT03228758	Efficacy of Anterior Versus Posterior Myotomy Approach in Peroral Endoscopic Myotomy (POEM) for the Treatment of Achalasia – a Single Operator Analysis	290	Nov 2019
NCT01601678	Endoscopic vs. laparoscopic myotomy for treatment of idiopathic achalasia: a randomized, controlled trial	240	Dec 2019
NCT01832779	Prospective Evaluation of the Clinical Utility of Peroral Endoscopic Myotomy (POEM)	600	Dec 2022
NCT02138643	Laparoscopy Heller Myotomy with Fundoplication Associated vs. Peroral Endoscopic Myotomy (POEM)	30	Dec 2017 (ongoing)

NCT: national clinical trial

Government Regulations
National/Local:

There is no national coverage determination or local (Michigan) coverage determination on this topic.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically.

Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Gastric Electrical Stimulation

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through January 2025, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
9/1/16	6/21/16	7/12/16	Joint policy established
9/1/17	6/20/17	6/20/17	Updated background and rationale sections, added the following references 6-8, 10, 11, 16 and 17. No change in policy status.
9/1/18	6/19/18	6/19/18	Updated rationale, added reference #28. No change in policy status.
9/1/19	6/18/19		Policy updated with literature review through September 4, 2018; reference 9, 19, 30, and 34 added. Policy statement unchanged.
9/1/20	6/16/20		Updated rationale section, added references # 7, 15-18, 35-37 and 43-46. Added “Pediatric and Adult” and “gastroparesis” to MPS.
9/1/21	6/15/21		Updated rationale section, added references #12, 13, 38. No change in policy status.
5/1/22	2/15/22		Added code 43497
5/1/23	2/21/23		Rationale updated, several references added. No change in policy status. (ds)
5/1/24	2/20/24		Routine policy maintenance, meeting with provider regarding G-POEM, no change in policy status. Vendor managed: N/A (ds)
5/1/25	2/18/25		Rationale updated, several references added. No change in policy status. Vendor managed: N/A (ds)

Next Review Date: 2nd Qtr. 2026

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: PERORAL ENDOSCOPIC MYOTOMY FOR TREATMENT OF ESOPHAGEAL ACHALASIA OR GASTROPARESIS

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Not covered.
BCNA (Medicare Advantage)	See government section.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.