Peroral Endoscopic Myotomy for Treatment of Esophageal Achalasia

Policy Number: 2.01.91  
Origination: 3/2018  
Last Review: 1/2020  
Next Review: 3/2020

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will not provide coverage for Peroral Endoscopic Myotomy for Treatment of Esophageal Achalasia. This is considered investigational.

When Policy Topic is covered
n/a

When Policy Topic is not covered
Peroral endoscopic myotomy is considered investigational as a treatment for pediatric and adult esophageal achalasia.

Considerations
There are no specific CPT codes for this procedure. It would likely be reported with the unlisted procedure, esophagus code 43499.

Description of Procedure or Service

<table>
<thead>
<tr>
<th>Populations</th>
<th>Interventions</th>
<th>Comparators</th>
<th>Outcomes</th>
</tr>
</thead>
</table>
| Individuals:  
  • Who are adults with achalasia | Interventions of interest are:  
  • Peroral endoscopic myotomy | Comparators of interest are:  
  • Esophageal dilatation  
  • Heller myotomy  
  • Botulinum toxin injection | Relevant outcomes include:  
  • Symptoms  
  • Functional outcomes  
  • Health status measures  
  • Resource utilization  
  • Treatment-related morbidity |
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Summary

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. This procedure is intended to reduce the total number of incisions needed and thus the overall invasiveness of surgery.

For adults who have achalasia who receive POEM, the evidence includes systematic reviews of observational studies, a randomized controlled trial, nonrandomized comparative studies, and case series. The relevant outcomes are symptoms, functional outcomes, health status measures, resource utilization, and treatment-related morbidity. The comparative studies have primarily reported similar outcomes for POEM and for Heller myotomy 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. In the case series, treatment success at short follow-up periods was reported for a high proportion of patients treated with POEM. However, the incidence of adverse events was relatively high, with POEM-specific complications, including subcutaneous emphysema, pneumothorax, and thoracic effusion, reported across studies. Additionally, a substantial proportion of patients undergoing POEM developed gastroesophageal reflux disease and esophagitis and required treatment. Case series do not permit conclusions about the efficacy of POEM relative to established treatment, and long-term outcomes of the procedure are not well described in the literature. The evidence is insufficient to determine the effects of the technology on health outcomes.

For pediatric patients who have achalasia who receive POEM, the evidence includes several nonrandomized studies and a systematic review. The 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 pressure. No
randomized clinical trials have been reported. The evidence is insufficient to determine the effects of the technology on health outcomes.

**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. The estimated U.S. prevalence of achalasia is 10 cases per 100000, and the estimated incidence is 0.6 cases per 100000 per year.1, 2

**Treatment**

Treatment options for achalasia have included pharmacotherapy (eg, injections with botulinum toxin), pneumatic dilation, and laparoscopic Heller myotomy.1, 2 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%. Heller myotomy is the most invasive of the procedures, requiring laparoscopy and surgical dissection of the esophagogastric junction.2 One-year response rates of 86% and major mucosal tear rates requiring the subsequent intervention of 0.6% have been reported.3

Peroral endoscopic myotomy (POEM) is a novel endoscopic procedure developed in Japan.2, 4 POEM is performed with the patient under general anesthesia.5 After tunneling an endoscope down the esophagus toward the esophagogastric junction, a surgeon performs the myotomy by cutting only the inner, circular lower esophageal sphincter 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 lower esophageal sphincter muscle layers. Cutting the dysfunctional muscle fibers that prevent the lower esophageal sphincter from opening allows food to enter the stomach more easily.2, 5

Note that the acronym POEM in this review refers to *peroral endoscopic myotomy*. POEMS syndrome, which has a similar acronym, is discussed in a separate policy.

**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.

**Rationale**

This evidence review was created in September 2013 and has been updated regularly with searches of the MEDLINE database. The most recent literature update was performed through September 9, 2019.
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, two domains are examined: the relevance, and 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 (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs 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.

**Peroral Endoscopic Myotomy for Adult Patients with Achalasia**

**Clinical Context and Therapy Purpose**
The purpose of POEM in patients who have esophageal achalasia is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of POEM improve the net health outcome of patients with esophageal achalasia?

The following PICOs were used to select literature to inform this review.

**Patients**
The relevant population of interest are patients 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 lower esophageal sphincter (LES) muscles through a submucosal tunnel created in the proximal esophageal mucosa.
Patients receive general anesthesia during the POEM procedure, which is conducted in tertiary care facilities.

**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 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.

LHM 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 4 or greater represent treatment failure.

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.

**Systematic Reviews**
Multiple systematic reviews and meta-analyses have been published to evaluate POEM as a treatment for achalasia. Several systematic reviews include overlapping
studies but these reviews have variable objectives; assessing data on POEM alone, LHM alone and, POEM compared to LHM. The reviews primarily include observational studies.

Li et al (2019) published a systematic review evaluating the long-term efficacy and safety POEM treatment for achalasia.7 Ten studies, published between 2015 and 2017, included 373 patients (range, 6-123) with a mean follow-up time of 30 months. Of the 372 patients who underwent POEM, 34.8% had a prior treatment history including LHM. Clinical success measures included an Eckardt score was defined as ≤ 3. The rate of late occurring gastroesophageal reflux was 10.2%. The review was limited by the sample size, predominance of studies from a single country (eight from China and two from the U.S.) and the lack of statistical analysis.

Schlottmann et al (2018) conducted a systematic review and meta-analysis of 53 studies using LHM (5834 patients) and 21 studies using POEM (1958 patients) for the treatment of esophageal achalasia.8 The probability for improvement in dysphagia at 24 months was 90% for patients receiving LHM and 93% for patients receiving POEM (p=0.01). However, patients receiving POEM were significantly more likely to develop GERD (odds ratio, 1.7; 95% confidence interval [CI], 1.3 to 2.1).

Crespin et al (2017) evaluated outcomes for 1299 patients from 19 case series.9 Improvements in Eckardt scores were statistically significant in all studies. The most frequently reported complications were mucosal perforation, pneumothorax, pneumoperitoneum, and subcutaneous emphysema. Akintoye et al (2016) evaluated outcomes for 2373 patients from 36 case series.10 Clinical success rates were achieved in 98% of patients (95% CI, 97% to 100%) and mean Eckardt scores decreased from baseline at 1, 6, and 12 months. Patel et al (2016) evaluated outcomes for 1122 patients from 22 case series.11 Eckardt scores dropped from 6.8 at baseline to 1.2 postoperatively. There were improvements in LES pressure and symptoms.

Two systematic reviews have focused on included studies comparing POEM with an alternative surgical treatment.12,13 BCBSA only reported results from the review by Marano et al (2016) because it included the period covered in the other review and assessed more patients and studies.12 Marano et al (2016) evaluated outcomes for 486 patients (196 receiving POEM, 290 receiving LHM) from 11 studies.14 None of the studies was randomized. Reviewers rated all studies as having a moderate risk of bias. No information on differences in disease severity between treatment groups was provided. There were no significant differences in the reduction of Eckardt scores, postoperative pain scores, or requirements for analgesics between procedures. Hospital lengths of stay were shorter for POEM. The meta-analysis by Zhang et al (2016) included not only 4 observational studies that compared POEM to LHM (all of which are described in this review), but the authors found that the efficacy and safety of the 2 procedures were comparable.12
Talukdar et al (2014) published a systematic review and meta-analysis assessing POEM and LHM as treatments for achalasia. Of the 29 studies, nineteen evaluated change in Eckardt’s score after POEM, which showed a significant reduction with an overall effect size of -7.95 (p<0.001). Sixteen studies evaluated the change in resting LES after POEM; there was a significant improvement in the resting LES pressure with an overall effect size of -7.28 (p<0.001). Five studies compared POEM and LHM. There were no statistically significant differences between POEM and LHM in reduction in Eckardt’s score (overall effect size [Z]=-1.77; p=0.078), post-operative pain scores (Z=-0.691; p=0.489) and analgesic requirements (Z=-0.755; p=0.450), length of hospital stay (Z=-1.41; p=0.156), adverse events (Z=1.227; p=0.220), and symptomatic gastroesophageal reflux/reflux esophagitis (Z=-1.41; p=0.156); however, POEM had significantly lower operative time compared with LHM (Z=-2.220; p=0.026). The review was limited by the lack of randomization, potential overlapping populations in separate reports, heterogeneity of the included studies, and the lack of long-term follow-up.

**Section Summary: Systematic Reviews**

Conclusions on comparative efficacy cannot be determined from the systematic reviews of case series because of the lack of comparators. The systematic reviews evaluating comparative studies only assessed nonrandomized studies and did not appear to have taken into account differences in patient characteristics.

**Randomized Controlled Trials**

Ponds et al (2019) published a randomized clinical trial comparing POEM and pneumatic dilation for treatment-naïve patients with achalasia. Between 2012 and 2015, patients from 6 sites in 5 countries were randomized to receive either POEM or pneumatic dilation (Tables 1 and 2). Overall treatment success was defined as an Eckardt score ≤ 3 and the absence of severe complications or retreatment. 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.

**Table 1. Summary of Key RCT Characteristics**

<table>
<thead>
<tr>
<th>Study</th>
<th>Countries</th>
<th>Sites</th>
<th>Dates</th>
<th>Participants²</th>
<th>Interventions¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ponds (2019)</td>
<td>Netherlands, Germany, Italy, Hong Kong</td>
<td>6</td>
<td>2012-2015</td>
<td>Treatment naïve adults with newly diagnosed achalasia and</td>
<td>POEM (N=64) Pneumatic dilation Initial with 30 mm balloon</td>
</tr>
</tbody>
</table>
Subsequent with 35 mm balloon if Eckardt score ≥3 at 3 weeks (N=66)

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

<table>
<thead>
<tr>
<th>Study</th>
<th>Eckardt score ≥3</th>
<th>PPI use</th>
<th>Endoscopic Reflux Esophagitis</th>
<th>Retreatment</th>
<th>Treatment-related SAE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ponds (2019)</td>
<td>126</td>
<td>92</td>
<td>92</td>
<td>126</td>
<td>126</td>
</tr>
<tr>
<td>POEM</td>
<td>63 No.(%) SD 3(5) 2.7</td>
<td>58 Median(IQR) SD 24(41) 6.5</td>
<td>54 No.(%) SD 22(41) 6.5</td>
<td>63 No.(%) SD 3(5) 2.7</td>
<td>63 No.(%) SD 0</td>
</tr>
<tr>
<td>Pneumatic dilation</td>
<td>63 No (%) SD 21(33) 5.9</td>
<td>34 Median(IQR) SD 7(21) 7</td>
<td>29 No.(%) SD 2(7) 4.7</td>
<td>63 No.(%) SD 19(30) 5.7</td>
<td>63 No.(%) SD 1(1.6) 1.6</td>
</tr>
</tbody>
</table>

IQR: interquartile range; PPI: proton pump inhibitor; RCT: randomized controlled trial; SAE: severe adverse even; SD: standard deviation.

The purpose of the limitations tables (Tables 3 and 4) is to display notable limitations identified in each study. This information is synthesized as a summary of the body of evidence following each table and provides the conclusions on the sufficiency of the evidence supporting the position statement.

Table 3. Relevance Limitations

<table>
<thead>
<tr>
<th>Study</th>
<th>Population(^a)</th>
<th>Intervention(^b)</th>
<th>Comparator(^c)</th>
<th>Outcomes(^d)</th>
<th>Follow-Up(^e)</th>
</tr>
</thead>
</table>
The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.

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
Li et al (2017) published a single-center study assessing POEM for the treatment of achalasia. Between 2010 and 2012, 564 consecutive patients were included with a median follow-up of 49 months. Mean Eckardt score decreased from 8 to 2 (p<0.05) and the median lower esophageal sphincter pressure decreased from...
29.7 mm Hg to 11.9 mm Hg (p<0.05). Fifteen failures occurred within 3 months, 23 between 3 months and 3 years, and 10 after 3 years. Major perioperative adverse events (AEs) occurred in 36 (6.4%) patients, including delayed mucosal barrier failure (n=3), delayed bleeding (n=3), hydrothorax (n=6), and pneumothorax (n=21). Ninety-three (16.5%) patients experienced mucosal injuries, and 48 patients required nasogastric tube placement at the end of the procedure. Other minor AEs included estimated blood loss >200mL (n=3), subcutaneous emphysema (n=1), and pneumoperitoneum (n=1). The study was limited by a high loss to follow-up and poor patient compliance at diagnostic tests. Also, late initiation of CO2 insufflation may have made the AE rate unrealistically high.

Docimo et al (2016) published a retrospective study comparing POEM and LHM for individuals with achalasia.18 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 narcotics while hospitalized than the LHM group (35.8 mg vs 101.8 mg, 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.

Sanaka et al (2016) compared outcomes at their own institution for 36 patients undergoing POEM, 142 undergoing LHM, and 36 undergoing pneumatic dilation.19 At baseline, patients undergoing the three procedures had different characteristics. POEM patients were older, had a higher body mass index, and had more prior treatments. After treatment, patients undergoing all three procedures had significant improvements as measured by high-resolution esophageal manometry and timed barium esophagram. Eckardt symptom scores were only available for POEM patients. Long-term outcomes were not reported.

Wang et al (2016) retrospectively reviewed outcomes for POEM (n=21) and pneumatic dilation (n=10) in patients ages 65 years and older.20 All were treated successfully, with decreases in Eckardt scores. At a mean follow-up of 21.8 months for POEM and 35 months for pneumatic dilation patients, 1 POEM case failed, and 2 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 and 25 patients who underwent LHM.21 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=0.01). However, LHM patients had a more severe disease by several different measures. 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).

In a retrospective study of a prospective U.S. university database, Bhayani et al (2014) compared outcomes in 37 patients who underwent POEM and 64 patients who underwent LHM for achalasia. Full-thickness esophageal injury occurred in four POEM patients, and eight esophageal and three gastric perforations occurred in LHM patients. Mean hospitalization was 1.1 days in the POEM group and 2.2 days in the LHM group (p<0.001). Eckardt scores were statistically lower postoperatively in the POEM group than in the LHM group (p<0.001) at 1 month, but not at 6 months (64% of patients assessed), Eckardt scores did not differ statistically between groups (p=0.1). Postoperative decreases in LES pressures were similar between groups. At 6 months, resting LES pressure was higher in the POEM group (16 mm Hg) than in the LHM group (7 mm Hg; p=0.006). (LES pressure >15 mm Hg predicts recurrent dysphagia.22)

In a nonrandomized trial with historical controls, Hungness et al (2013) reported on perioperative outcomes in patients with achalasia treated with POEM (n=18) or LHM (n=55) at a single U.S. center. Surgical times were shorter for POEM (113 minutes) than for LHM (125 minutes; p<0.05). Additionally, estimated blood loss was lower in patients treated with POEM (≤10 mL in all POEM cases vs 50 mL for LHM, p<0.001). Myotomy lengths, complication rates, and lengths of stay were also similar between groups. Pain scores were similar postanesthesia and postoperatively on the first day, but were higher at two hours for POEM patients (3.5 vs 2.0, p=0.03). Narcotic use was similar between groups, although fewer patients treated with POEM received ketorolac, a nonsteroidal anti-inflammatory. POEM patients’ median Eckardt scores decreased (1 postoperative vs 7 preoperative, p<0.001), and 16 (89%) patients had treatment success (score ≤3) at a median of 6 months follow-up.

Ujiki et al (2013) compared outcomes for 18 patients undergoing POEM with 21 patients undergoing LHM. Postoperative Eckardt scores were similar (POEM=0.7 vs LHM=1.0). Several outcomes related to recovery from surgery favored POEM (postoperative pain, analgesic use, return to activities of daily living).

Section Summary: Nonrandomized Comparative Studies
The nonrandomized studies comparing POEM with other procedures are retrospective and involved patients who might not have been comparable in terms of age and severity of the disease. Although outcomes were generally similar between POEM and the comparator treatments (LHM, pneumatic dilation), potential confounding and selection bias makes outcome comparisons uncertain. The comparative studies did not report long-term outcomes.

Case Series
Several case series have evaluated the use of POEM and series with 50 or more cases are included for review.
Hungness et al (2016) conducted a retrospective chart review of 115 patients who had undergone POEM in a single high-volume center and had at least 1 year of follow-up. Treatment success was defined as an Eckardt score of 3 or less without reintervention. GERD was defined by an abnormal pH or reflux esophagitis greater than Los Angeles grade A. After a mean follow-up of 2.4 years (range, 1.0-4.3 years), the overall success rate was 92%. GERD was reported in 40% of the patients.

Ramchandani et al (2016) reported on outcomes for 200 consecutive patients at an institution in India. Outcomes at 1 year were available for 102 patients. Clinical success, defined as an Eckardt score of 3 or less, was achieved in 92% on a per-protocol analysis and 83% on intention-to-treat analysis, which included additional patients with technical failure and patients lost to follow-up. The mean Eckardt score was 1.18 after POEM.

Inoue et al (2015) reported outcomes on 500 consecutive patients at a Japanese institution. Outcomes were available for a variable proportion of patients at different intervals after the procedure: 302 (60.4%) at 2 months, 102 (27.6%) of 370 at 1 to 2 years, and 61 (58.1%) of 105 at more than 3 years. The median Eckardt score at all time points was one. LES pressure ranged from 13.4 to 11.7 mm Hg. Between 16.8% and 21.3% of subjects reported symptoms of GERD. The overall complication rate was 3.2%.

Teitelbaum et al (2014) also evaluated 1-year outcomes after POEM. Forty-one patients treated at an academic medical center and more than one-year post-POEM were included. Most patients (37 [90%]) had no previous endoscopic treatment (botulinum toxin injection or pneumatic dilation). Ninety-two percent of 39 patients available for symptom assessment had treatment success (Eckardt score <4). In 21 patients evaluated, mean LES pressure was 11 mm Hg.

Ling et al (2014) reported on the quality of life outcomes in 2 patient cohorts (probably overlapping) who underwent POEM for achalasia at a single-center in China. Quality of life was assessed at pretreatment and at 1-year follow-up using the 36-Item Short-Form Health Survey; Physical Component Summary and Mental Component Summary raw scores were transformed to a 0 (poor health) to 100 (good health) scale. In a group of 21 patients who had failed previous pneumatic dilation, mean Physical Component Summary scores improved from 30 to 65, and mean Mental Component Summary scores improved from 43 to 67 (p<0.001 for both comparisons). Incidences of intraoperative subcutaneous emphysema and pneumothorax were 14% and 5%, respectively; postoperative esophagitis developed in 19%. In 87 previously untreated patients, mean Physical Component Summary scores improved from 33 to 69 (p<0.001), and mean Mental Component Summary scores improved from 44 to 67 (p=0.003). Incidence rates of intraoperative subcutaneous emphysema and pneumothorax were 12% and 1%, respectively; postoperative esophagitis developed in 6%.

In a prospective case series, Von Renteln et al (2013) reported on 70 patients who underwent POEM at 5 centers in Europe and North America. Mean follow-up
was 10 months (range, 3-12 months). Follow-up evaluations at 6 months and 1 year showed sustained treatment success of 89% and 82%, respectively. Mean pretreatment Eckardt scores were 6.9 compared with 1.3 at 6 months and 1.7 at 1 year (p<0.001 for both comparisons vs pretreatment score). In multivariate analysis, neither age, previous treatment (botulinum toxin injection, dilatation), myotomy length, preprocedure LES pressure, pretreatment Eckardt score, sex, procedure duration, nor full-thickness dissection during POEM were significant predictors of treatment failure at one year. At 3 months after POEM, esophagitis was observed in 42% of cases. However, the severity of esophagitis was minor (grade A or B), and all patients could be managed adequately with proton pump inhibitor therapy. At 3 months, 22% of patients required occasional and 12% required daily proton pump inhibitor therapy. The 1-year follow-up evaluation showed overall rates of GERD of 37% and proton pump inhibitor use of 29%. Other complication rates of POEM ranged from 1% to 4%.

A study by Ren et al (2012) highlighted POEM-specific complications. In this series of 119 cases, 23% of patients developed subcutaneous emphysema intraoperatively and another 56%, postoperatively. Three of these patients required subcutaneous needle decompression. Additionally, 3% of patients developed a pneumothorax intraoperatively and another 25% postoperatively. Postoperatively, the incidence of thoracic effusion was 49%; the incidence of mild inflammation or segmental atelectasis of the lungs was 50%. All complications were resolved with conservative treatment.

At least 2 other small case series (both 2013) have evaluated the efficacy and feasibility of POEM for patients with failed LHM/achalasia recurrence; success rates have been reported in over 90% of cases up to 10 months after rescue POEM. Studies also have compared different POEM techniques; comparable outcomes have been reported between patients undergoing full-thickness and circular myotomy.

Section Summary: Case Series
Case series have shown improvements in symptoms of achalasia after POEM. These reports also point to defined short- and long-term complications and adverse events. Such studies do not permit comparison with other established treatments.

Section Summary: POEM for Adult Patients with Achalasia
Studies on POEM for adults with achalasia included systematic reviews, nonrandomized studies, case series, and one RCT. Conclusions on comparative efficacy cannot be determined from the systematic reviews because many case series, which lack comparators, were included in the reviews. The systematic reviews evaluating comparative studies only assessed nonrandomized studies and did not appear to have accounted for differences in patient characteristics. Findings from the one RCT identified showed POEM had a similar treatment success rate based on the Eckardt score and fewer adverse events compared with pneumatic dilation. However, POEM had significantly higher rates of endoscopically
confirmed reflux esophagitis. 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, pneumatic dilation), potential confounding and selection bias makes outcomes comparisons uncertain. The comparative studies did not report long-term outcomes. Case series have shown improvements in symptoms of achalasia after POEM. These reports also point to defined short-term and long-term complications and adverse events. Such studies do not permit comparison with other established treatments.

**Peroral Endoscopic Myotomy for Pediatric Patients with Achalasia**

**Clinical Context and Therapy Purpose**
The purpose of POEM in patients who have esophageal achalasia is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the use of POEM improve the net health outcome of pediatric patients with esophageal achalasia?

The following PICOs were used to select literature to inform this review.

**Patients**
The relevant population of interest are pediatric patients 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.

Patients receive general anesthesia during the POEM procedure, which is conducted in tertiary care facilities.

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

Esophageal dilatation 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.10

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**
Lee et al (2019) published a systematic review and meta-analysis evaluating POEM for the treatment of pediatric achalasia.35. 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**
Nabi et al (2019) published a retrospective study assessing POEM for the treatment of children with achalasia.36. 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.37, Twenty-one children (aged 11 months – 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 2.7 kg 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 Patients with Achalasia**

One systematic review and meta-analysis available evaluating POEM for the treatment of pediatric achalasia was 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 all of the included studies had sample sizes <30. Two comparative studies were available evaluating POEM for the treatment of pediatric achalasia. Both studies reported high rates of success for POEM and alleviation of achalasia symptoms.

**Summary of Evidence**

For adults who have achalasia who receive POEM, the evidence includes systematic reviews of observational studies, an RCT, nonrandomized comparative studies, and case series. The relevant outcomes are symptoms, functional outcomes, health status measures, resource utilization, and treatment-related morbidity. The comparative 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. In the case series, treatment success at short follow-up periods was reported for a high proportion of patients treated with POEM. However, the incidence of adverse events was relatively high, with POEM-specific complications, including subcutaneous emphysema, pneumothorax, and thoracic effusion, reported across studies. Additionally, a substantial proportion of patients undergoing POEM developed gastroesophageal reflux disease and esophagitis and required treatment. Case series do not permit conclusions about the efficacy of POEM relative to established treatment, and long-term outcomes of the procedure are not well described in the literature. The evidence is insufficient to determine the effects of the technology on health outcomes.
For pediatric patients who have achalasia who receive POEM, the evidence includes several nonrandomized studies and a systematic review. The 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 LES pressure. No randomized clinical trials have been reported. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

American Gastroenterological Association Institute
The American Gastroenterological Association Institute (2017) published a clinical practice update on the use of peroral endoscopic myotomy (POEM) for the treatment of achalasia. 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 (eg, proton pump inhibitor therapy and/or surveillance endoscopy) prior to undergoing POEM.

American Society of Gastrointestinal and Endoscopic Surgeons
The American Society of Gastrointestinal and Endoscopic Surgeons (2014) issued evidence-based, consensus guidelines on the use of endoscopy in the evaluation and management of dysphagia, including esophageal achalasia. The Society recommended that:

"...Endoscopic and surgical treatment options for achalasia should be discussed with the patient. In patients who opt for endoscopic management and are good surgical candidates, pneumatic dilation with large-caliber balloon dilators for the endoscopic treatment of achalasia was recommended.....Long-term data and randomized trials comparing peroral endoscopic myotomy to conventional modalities of management are necessary before it can be adopted into clinical practice, but the procedure is becoming more widely used in expert centers."

American College of Gastroenterology
The American College of Gastroenterology (2013) issued clinical guidelines on the diagnosis and management of achalasia. POEM was discussed as an emerging therapy and stated to have promise as an alternative to the laparoscopic approach. The guidelines further stated that randomized prospective comparison
trials are needed, and the procedure should be performed in the context of clinical trials.

**Society of American Gastrointestinal and Endoscopic Surgeons**
The Society of American Gastrointestinal and Endoscopic Surgeons (2012) issued evidence-based, consensus guidelines on the surgical management of esophageal achalasia. The guidelines stated that the POEM technique "is in its infancy and further experience is needed before providing recommendations."^41.

**International Society for Diseases of the Esophagus**
The International Society for Diseases of the Esophagus (2018) published guidelines on the diagnosis and management of achalasia. They 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 5 summarizes POEM recommendations.

### Table 5. Recommendations for the Treatment of Achalasia

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

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

**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 6.

Table 6. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ongoing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT03228758</td>
<td>Efficacy of Anterior Versus Posterior Myotomy Approach in Peroral Endoscopic Myotomy (POEM) for the Treatment of Achalasia - a Single Operator Analysis</td>
<td>290</td>
<td>Nov 2019</td>
</tr>
<tr>
<td>NCT01402518</td>
<td>Observational Study of the Peroral Endoscopic Myotomy (POEM) Procedure</td>
<td>100</td>
<td>Nov 2019</td>
</tr>
<tr>
<td>NCT01601678</td>
<td>Endoscopic Versus Laparoscopic Myotomy for Treatment of Idiopathic Achalasia: A Randomized, Controlled Trial</td>
<td>240</td>
<td>Dec 2020</td>
</tr>
<tr>
<td>NCT01832779</td>
<td>Prospective Evaluation of the Clinical Utility of Peroral Endoscopic Myotomy (POEM)</td>
<td>600</td>
<td>Dec 2022</td>
</tr>
<tr>
<td>NCT01793922</td>
<td>A Prospective Randomized Multi-center Study Comparing Endoscopic Pneumodilation and Per Oral Endoscopic Myotomy (POEM) as Treatment of Idiopathic Achalasia</td>
<td>150</td>
<td>Jan 2023</td>
</tr>
<tr>
<td><strong>Unpublished</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02138643</td>
<td>Laparoscopy Heller Myotomy With Fundoplication Associated Versus Peroral Endoscopic Myotomy (POEM)</td>
<td>30</td>
<td>Dec 2017 (last update posted April)</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

REFERENCES


ICD-10 Codes
K22.0  Achalasia of cardia

Additional Policy Key Words
N/A

Policy Implementation/Update Information
3/1/18  New Policy, considered investigational.
9/1/18  No policy statement changes.
3/1/19  No policy statement changes.
9/1/19  No policy statement changes.
1/1/20  PICO added for pediatric achalasia and policy statement edited for consistency; intent of statement unchanged.

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