PROVIDENCE HEALTH PLANS AND PROVIDENCE HEALTH ASSURANCE MEDICAL POLICY

Peroral Endoscopic Myotomy (POEM)

Effective Date: 4/1/2019

Medical Officer Date

Section: SUR Policy No: 407

Medical Policy Committee Approved Date: 12/17; 12/18; 2/19

See Policy CPT CODE section below for any prior authorization requirements

APPLIES TO:

All lines of business

BENEFIT APPLICATION

Medicaid Members

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) for coverage determinations.

For other lines of business, refer to the Policy Criteria section below:

POLICY CRITERIA

Peroral endoscopic myotomy (POEM) is considered investigational and is not covered as a treatment for any indication, including but not limited to:

- Achalasia
- Dysphagia
- Gastroesophageal reflux
- Diffuse esophageal spasm
- Distal esophageal spasm
- Jackhammer (hypercontractile) esophagus
- Gastroparesis
- Other esophageal disorders

Link to Policy Summary
PROVIDENCE HEALTH PLANS AND PROVIDENCE HEALTH ASSURANCE MEDICAL POLICY

Peroral Endoscopic Myotomy (POEM)

CPT CODES

<table>
<thead>
<tr>
<th>All Lines of Business</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unlisted Codes</strong></td>
</tr>
<tr>
<td>All unlisted codes will be reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is billed related to services addressed in this policy then it will be <strong>denied as not covered</strong>.</td>
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<td>43499</td>
</tr>
</tbody>
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DESCRIPTION

Peroral endoscopic myotomy (POEM) is a newer endoscopic technique that was originally developed to treat achalasia. POEM is a form of natural orifice transluminal endoscopic surgery (NOTES) considered to be an endoscopic equivalent to surgical myotomy. The POEM procedure allows for myotomy of the lower esophageal muscles to be performed via mucosal incision and entry into the submucosa of the esophagus, thus eliminating the need for direct incisions. In addition, “POEM allows surgeons to isolate the inner circular muscles for myotomy and offers better access to the mediastinal esophagus without disrupting the crura of the diaphragm.”

Surgical myotomy, particularly Heller myotomy performed laparoscopically (known as laparoscopic Heller myotomy [LHM]), is currently the standard interventional treatment option for patients with achalasia. Another interventional procedure commonly used to treat achalasia pneumatic dilation of the lower esophageal sphincter. The POEM procedure combines the minimal invasiveness of pneumatic dilation with the therapeutic goal of a surgical myotomy.

Although POEM was developed for achalasia, it is has recently been proposed as a potential treatment for other disorders, including spastic esophageal disorders as well as conditions like gastroesophageal reflux. In addition, the POEM procedure has been adapted to be performed in the stomach (termed gastric peroral endoscopic pyloromyotomy or G-POEM) for the treatment of gastroparesis.

G-POEM is an endoscopic equivalent of surgical pyloroplasty where the pylorus. G-POEM differs from POEM in that it is pylorus, rather than the lower esophageal sphincter, that is myotomized. Otherwise, G-POEM consists of the same steps as POEM and essentially the same postoperative care.

REVIEW OF EVIDENCE

A review of the ECRI, Hayes, Cochrane, and PubMed databases was conducted regarding the use of the POEM procedure as a treatment for any indication. Below is a summary of the available evidence identified through January 2019.
Achalasia

There have been a large number of nonrandomized studies published on the use of POEM for achalasia. Therefore, the evidence review for this indication will focus on recent systematic reviews and randomized controlled trials (RCTs) and comparative studies published after the publication of the most recent reviews. In addition, key comparative studies included in the systematic reviews have been described below.

Systematic Reviews

- Prior to 2015, four older systematic reviews on the use of POEM for achalasia were identified, but these reviews will not be described individually below. These reviews included a combination of RCTs, nonrandomized studies, case series and retrospective analyses. In general, these older reviews reported that POEM was comparable to Laparoscopic Heller myotomy (LHM) for most outcomes including the Eckardt score, as well as for adverse events including incidence of perforation, hospital length of stay and operative time. However, these reviews acknowledged that some included studies had overlapping patient populations and others had significant study heterogeneity. Overall, while the older reviews recognized the POEM procedure as being relatively safe and effective, all reviews noted the need for randomized comparative studies of LHM and POEM, as well as studies in different patient populations (treatment-naïve patients versus patients who are refractory for other treatment).

- In 2015 (updated 2018), Hayes published a review of the use of POEM for the treatment of achalasia, with an evidence search through December of 2015. The review included 13 studies (two RCTs, one case-control study, one retrospective cohort, two prospective cohort studies with historical controls, four prospective cohort studies, and three pretest/posttest studies). Overall, the review reported that the POEM procedure led to improved health outcomes (improved symptom relief including reduced frequency of dysphagia, regurgitation of chest pain; reduced esophageal sphincter [LES] pressure; and weight gain). The two included RCTS compared two different POEM techniques, and did not compare the POEM procedure to other treatments. In the studies (n=3) that compared POEM to LHM, there were no significant differences between treatments in terms of efficacy and adverse events. However, all included studies were considered to be of low quality, primarily due to methodological weaknesses and lack of follow-up longer than 12-months.

- In 2016, Marano et al. published the results from a systematic review which compared the safety and efficacy of POEM with the current preferred surgical treatment, LHM for the treatment of achalasia, including seven nonrandomized retrospective case-control studies (N=486 patients: 196 in the POEM group and 290 in LHM group). No significant differences were found between POEM and LHM with regards to Eckardt score reduction (a composite score), operative time, postoperative pain score, analgesic medication, length of hospital stay, or complication rate. However, LHM had a significantly lower incidence of post-procedure symptomatic gastroesophageal reflux compared to POEM (OR = 1.81, 95% CI: 1.11–2.95, p = 0.017).

- In 2017, Awaiz et al. published the results of a systematic review which evaluated perioperative outcomes of POEM compared to LHM for achalasia, including seven nonrandomized trials consisting
of 483 (LHM=250, POEM=233) patients.\textsuperscript{7} Perioperative outcomes including operative time, overall complication rate, length of hospital stay, postoperative pain score, and long-term GERD (one-year follow-up) were comparable for both procedures. However, there was a significantly higher short-term clinical treatment failure rate for LHM (OR, 9.82; 95% CI, 2.06-46.80; p<0.01). The review concluded that although POEM compares favorably to LHM for achalasia treatment in short-term perioperative outcomes, long-term postoperative follow-up data for POEM beyond one year are needed.

- In 2018, ECRI published an evidence review evaluating the safety and efficacy of POEM for the treatment of achalasia.\textsuperscript{8} Having systematically searched the literature through January 2018 according to pre-defined criteria, ECRI included 5 systematic reviews and meta-analyses, 1 RCT, 3 non-randomized cohort studies and 5 case series for review. Outcomes of interest were symptom resolution at one year follow-up, symptom resolution compared to patients receiving laparoscopic Heller myotomy (LHM), recurring symptoms following surgery, and adverse events.

All included studies reported positive results for the primary outcome of symptom resolution (Eckardt score <3). Three cohort studies (n = 242) and one meta-analysis, evaluating 23 studies (n = 2,373), reported symptom resolution one-year follow-up in >98% of patients treated with POEM. Compared to LHM, two meta-analyses (77 studies; n = 8,278) and three nonrandomized studies (n = 244) reported comparable or superior symptom resolution among patients receiving POEM, similar or fewer complications, shorter operative times, similar or longer hospital stays, but a greater risk of GERD onset. One systematic review (36 studies, n = 2,373) reported GERD symptoms in 9% of patients at a median eight-month follow-up after POEM. Across three cohort studies (n = 1,874) and one systematic review (n = 1,122), serious adverse events were reported in 1% to 6% of patients. Only one RCT and five case series reported on procedure success, symptoms, complications, and GERD medication use in patients treated with POEM at three-year follow-up.

ECRI concluded that a large body of evidence exists, which indicates that POEM is a safe and effective for treating achalasia. Given achalasia’s chronic nature, however, ECRI noted that “an evidence gap remains,”\textsuperscript{8} and called for additional studies to assess outcomes at follow-up beyond three years.

- In 2019, Evensen and colleagues published a systematic review evaluating the efficacy of POEM in treatment-naïve achalasia patients.\textsuperscript{9} Independent reviewers systematically identified eligible studies, assessed quality, and extracted data. Outcomes of interest were symptom score and objective testing (i.e. high resolution manometry (HRM) or timed barium esophagogram (TBE)).

Having searched the literature through November 2017, investigators ultimately included 7 studies (6 retrospective cohort studies; 1 prospective cohort study) for review. Sample sizes ranged from 32 to 100 patients and follow-up ranged from 3 to 51 months. All studies reported a short-term clinical success rate of >90% (defined as an Eckardt score ≤3). HRM was applied pre- and post-surgery in all of the included studies, each reporting significant decreases in lower-esophageal pressure. Only two studies included their TBE protocol with barium height analysis.
Strengths of this study include the systematic review of literature following a pre-defined protocol and evaluation of methodological quality by two independent reviewers. Limitations of the study are centered on the quality of the studies included for review. Each study suffered from small sample sizes, low follow-up rates, the limited application of objective tests, retrospective study designs, and the low-middle income treatment setting (i.e. China) for 6 out of the 7 reviewed studies. Given these limitations, investigators concluded that “a definite conclusion of the effect of POEM in treatment-naïve patients can at present hardly be drawn.”

Randomized Controlled Trials (RCTs)

No RCTs were found that compare the use of POEM to any other treatment for achalasia.

Nonrandomized Comparative Studies

- In 2013, Ujiki et al. published the results of a non-randomized study comparing short-term outcomes of achalasia patients, including 18 patients who underwent POEM, and 21 patients who underwent LHM. Thirteen patients from each group had undergone previous treatment of some sort. The authors reported that both POEM and LHM resulted in statistically significant changes in Eckardt score from baseline at approximately 3- and 12-months (p<0.001 for both groups). However, the differences between treatment groups was nonsignificant, with mean Eckardt scores of 0.7 ± 0.5 at 116 days follow-up among patients undergoing POEM, compared with an Eckardt score of 1.0 ± 0.4 at 164 days follow-up among LHM patients. Limitations of this study include lack of randomization, small sample size, and short-term follow-up.

- In 2014, Bhayani et al. published the results of a non-randomized study comparing short-term outcomes of achalasia patients, including 64 consecutive patients who underwent LHM (42% Toupet and 58% Dor fundoplications) and 37 consecutive patients who underwent POEM. Previous interventions were reported POEM group, but not the LHM group. The statistical significance of the difference in change from baseline for each treatment group was not reported. One-month Eckardt scores were significantly better for POEM than for LHM (1.8 vs 0.8, respectively; p < 0.0001). However, at 6-month follow-up, there was no significant difference between the groups (1.2 versus 1.7 in the POEM versus LHM groups, respectively). It should be noted that only 73% of POEM patients and 61% of LHM patients were available for the 6-month follow-up assessment.

- In 2015, Teitelbaum et al. published the results of a non-randomized study comparing post-operative outcomes of achalasia patients, including 20 patients undergoing LHM and 36 undergoing POEM. Almost equal numbers of patients in each treatment group had previous interventions. The authors reported that both POEM and LHM resulted in statistically significant changes in Eckardt score from baseline at approximately 3- and 12-months. However, at 12 months follow-up, Eckardt scores among POEM-treated and LHM-treated patients were comparable (0.7 and 1.0, respectively) but p-values were not reported. Of note, 58% of POEM patients and 55% of LHM patients were available for follow-up.

- In 2016, Sanaka et al. published the results of a non-randomized retrospective chart review comparing the efficacy of POEM to LHM and pneumatic dilation (PD), including 200 achalasia patients. The study included patients who had undergone previous treatments and evaluated the outcomes of POEM and LHM. The authors reported that both POEM and LHM were effective in improving Eckardt scores, with statistically significant improvements noted at 3 and 12 months. However, the study was limited by its retrospective nature and the variable follow-up times among patients.

In addition to the above studies, there are other nonrandomized comparative studies published in recent years. These studies have provided valuable insights into the outcomes of POEM compared to other treatments, but the overall conclusions are inconsistent and the effectiveness of POEM remains uncertain due to the limitations of the available evidence.
patients (36 underwent POEM, 22 underwent PD and 142 underwent LHM). \(^{13}\) Compared to LHM, POEM patients were reported as being older (55.4 ± 16.8 years vs 46.5 ± 15.7 years, \(p = 0.013\)) and had higher BMI (29.1 ± 5.9 kg/m\(^2\) vs 26 ± 5.1 kg/m\(^2\), \(p = 0.012\)). In addition, a higher number of patients that had undergone POEM or PD had undergone prior treatments compared to LHM group (72.2% vs 68.2% vs 44.3% respectively, \(p = 0.003\)). At two months post-treatment, there was significant improvement in basal LES pressure in both LHM (\(p < 0.001\)) and POEM groups (\(p < 0.001\)). However, between treatment groups, there were no significant differences in outcomes. Limitations of this study include its retrospective design and short-term follow-up. The authors concluded “larger, prospective studies with homogeneous patient populations and longer follow-up are required to compare the efficacy of these treatment modalities in achalasia.”

- In 2017, Peng et al. published the results of a non-randomized retrospective study comparing long-term outcomes of achalasia patients, including 13 patients who underwent POEM and 13 patients who underwent LHM, with a minimum postoperative follow-up of three years. \(^{14}\) After over 3 years’ follow-up, 12 patients who underwent POEM and 15 patients who underwent LHM were available for analysis. Among POEM patients, Eckardt scores decreased from 7.5±1.3 at baseline to 2.6±1.5 (\(p=0.00\)) at follow-up, and for LHM patients scores were significantly reduced from 7.3±1.6 to 2.8±1.3 (\(p=0.00\)). Final Eckardt scores were not significantly different between treatment groups (2.6±1.5 for POEM versus 2.8±1.3 for LHM). Treatment success rates were also nonsignificant between the groups (83.3% for POEM versus 80.0% for LHM). The authors concluded that longer-term data are still needed to analyze whether the effectiveness of POEM is maintained over time and multicenter randomized trial comparing POEM with LHM should be conducted.

- Since the ECRI review described above, five other clinical trials \(^{15-19}\) and a non-systematic narrative review \(^{20}\) evaluating POEM for the treatment of achalasia have been published. While three clinical trials reported improvements in mean symptom resolution (measured by Eckardt scores) at up to 24-months, these studies were limited by small sample sizes (n=51-132), inadequate follow-up, and the lack of comparator groups receiving treatment alternative to POEM. The one study to date reporting outcomes at 5 year follow-up has a particularly small sample size (n=29). \(^{19}\) A larger study, reporting results for 237 patients at median follow-up of four years, was limited by the lack of reported \(p\)-values, poor patient compliance with diagnostic tests, incomplete access to prior medical records and the study’s low-middle income treatment setting (i.e. China). \(^{18}\) Investigators from all studies called for additional, larger trials with longer follow-up to definitively determine POEM’s safety and efficacy.

**Comparative Study Summary:**

Overall, identified comparative studies recruited mixed patients populations, including treatment-naïve patients as well as patients with one or more previous treatments (including botox, pneumatic dilation and/or LHM), with a significant percentage of patients (approx. 25-45%) lost to follow-up. No comparative studies were identified that reported on outcomes beyond 12-months. Randomized trials with consistent patient populations and longer follow-up and are needed to establish comparative effectiveness between POEM and standard treatments such as LHM, and whether beneficial results are sustained over long periods of time.
Gastroparesis

A review of the evidence found no RCTs or systemic reviews evaluating POEM for the treatment of gastroparesis. Despite reporting symptom relief, non-randomized clinical trials studies to date suffer from small sample sizes (n=7 to 47), heterogeneous patient cohorts, a lack of comparator groups and inadequate follow-up (≤18 months).²¹⁻³⁰

Other Indications for POEM

Systematic Reviews

- In 2017, Khan and colleagues published results from their systematic review and meta-analysis evaluation POEM for the treatment of spastic esophageal disorders (SEDs) – including spastic achalasia (type III), diffuse esophageal spasm (DES), and nutcracker/jackhammer esophagus (JH).³¹ Searching the literature through January 2016, independent reviewers systematically identified eligible studies, assessed quality, and extracted data. Outcomes of interest were weighted pooled rates for clinical success (defined as Eckardt scores ≤ 3), severity of dysphagia based on a health-related quality of life questionnaire, and adverse events (AEs). Clinical success rates and AEs were calculated using fixed- or random-effects models based on heterogeneity. Eight observational studies, with sample sizes varying from 3 months to 3 years, were ultimately included for review.

The patient cohort across all eight studies (n=179) included 116 patients with type III achalasia, 37 patients with JH, and 18 patients with DES. Using the National Institutes of Health quality assessment tool, investigators assessed 2 studies of the 8 studies to be “good quality” and 6 to be “fair quality.” Cumulative clinical success of POEM for the treatment of all SEDs was 87% (78, 93%; 95% CI), I² = 37%. Adverse events of POEM in all SEDs was calculated to be 14% (9, 20%; 95%CI), I² = 0%, with no difference in safety among individual SEDs.

All studies included for review suffered from small sample sizes, lack of long-term follow-up, and non-randomized observational study designs. Validity is further undermined by investigators’ inability to evaluate differences in clinical outcomes based on patient demographics. Investigators concluded that larger, prospective studies are required before POEM complements or replaces Heller myotomy in the treatment of SEDs.

Nonrandomized Studies

- In 2018, Khashab and colleagues conducted a multi-center retrospective study evaluating POEM for the treatment of non-achalasia esophageal motility disorders.³² In total, 50 patients (56% female; mean age 61.7 years) underwent POEM at 11 centers for esophagogastric junction outflow obstruction (EGJOO), diffuse esophageal spasm (DES) and jackhammer esophagus (JE). Follow-up ranged from 6 to 9 months. Outcomes of interest were rates or technical success, clinical response (Eckardt scores ≤ 3) and adverse events. Mean Eckardt score decreased from 6.2 to 1.0 in EGJOO (p < 0.001) and from 6.9 to 1.9 in DES/JE (p < 0.001). A total of 9 (18%) adverse events occurred, rated as mild in 55.6% and moderate in 44.4%. Limitations include the
study’s small sample size, retrospective design, and inadequate follow-up. Investigators concluded that randomized trials were needed to confirm the safety and efficacy of POEM for non-achalasia esophageal motility disorders.

CLINICAL PRACTICE GUIDELINES

American Gastroenterological Association (AGA)

In 2017, the AGA published a clinical practice update, evaluating POEM for the treatment of achalasia.\textsuperscript{33} Having conducted a comprehensive literature review, investigators recommended POEM be “considered as a treatment option of comparable efficacy to [laparoscopic Heller myotomy], albeit with no long-term outcomes data and minimal controlled outcomes data currently available.”\textsuperscript{33} Investigators also noted that POEM patients are at high-risk for developing reflux esophagitis and may require medical management post-procedure to manage symptoms.

American College of Gastroenterology (ACG)

The ACG’s 2013 clinical guideline on the diagnosis and management of achalasia\textsuperscript{34} discusses POEM as an emerging therapy and concluded that the available evidence from prospective cohort studies indicates POEM has promise as an alternative to the laparoscopic approach. However, the panel noted that randomized prospective comparison trials with standard approaches are needed, and POEM should only be performed in the context of clinical trials with the understanding that effective alternatives are available.

The ACG did not mention the POEM procedure as a potential treatment in any of their other guidelines, including guidance on the management of GERD, gastroparesis or Barrett’s Esophagus.

Society of the American Gastrointestinal and Endoscopic Surgeons (SAGES)

SAGES’ most recent guidelines for the surgical treatment of achalasia\textsuperscript{35} was published in May 2011 and includes evidence gleaned from a literature search done in October 2009. The statement describes POEM as a technique in its infancy and concluded that more experience is needed before recommendations can be provided.

The SAGES did not mention the use of POEM as a treatment for GERD in their practice guidelines or position statements.

American Society for Gastrointestinal Endoscopy (ASGE)

In 2014, the ASGE published guidelines on the role of endoscopy in the evaluation and management of dysphagia.\textsuperscript{36} These guidelines state that POEM is becoming more widely used in expert centers; however, long-term data and randomized trials comparing POEM to conventional modalities are needed before it can be adopted into clinical practice.
The ASGE made no recommendations specifically regarding the use of POEM in managing achalasia. In addition, ASGE does not mention the POEM procedure as a potential treatment in any of their other guidelines, including guidance on the management of GERD, gastroparesis, Barrett’s Esophagus or other disorders of the esophagus.

CENTERS FOR MEDICARE & MEDICAID

As of December 2018, no Centers for Medicare & Medicaid (CMS) coverage guidance was identified which addresses peroral endoscopic myotomy (POEM) as a treatment for any esophageal disorder or gastroparesis.

POLICY SUMMARY

There is insufficient evidence that the use of peroral endoscopic myotomy (POEM) as a treatment for any esophageal disorder or gastroparesis has long-term efficacy when compared to surgical myotomy or other endoscopic techniques. The evidence base is limited to nonrandomized studies of heterogeneous populations with short-term follow-up. No randomized controlled trials (RCTs) have been published that compared POEM with standard surgical or endoscopic techniques for any indication, including comparing POEM to laparoscopic Heller myotomy or pneumatic dilation to treat achalasia. Although non-randomized, studies comparing POEM to laparoscopic Heller myotomy to treat achalasia show promise, only one small study was identified that followed patients for greater than 12 months. In addition, no evidence-based clinical practice guidelines recommend POEM as a treatment of any esophageal disorder or gastroparesis.

INSTRUCTIONS FOR USE

Providence Health Plan (PHP) and Providence Health Assurance (PHA) Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. PHP and PHA Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. PHP and PHA reserve the right to determine the application of Medical Policies and make revisions to its Medical Policies at any time. Providers will be given at least 60-days’ notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and PHP and PHA Medical Policy will be resolved in favor of the coverage agreement.
REGULATORY STATUS

Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

REFERENCES

1. Hayes Inc. Peroral Endoscopic Myotomy for Treatment of Esophageal Achalasia. 2015 (updated 2018). https://www.hayesinc.com/subscribers/displaySubscriberArticle.do?articleId=35726&searchStore=%24search_type%3DAll%24id%3D%24keywords%3DPeroral%2CEndoscopic%2CMyotomy%24status%3DAll%24page%3D1%24from_date%3D%24to_date%3D%24report_type_options%3D%24technology_type_options%3D%24organ_system_options%3D%24specialty_options%3D%24order%3DAssearchRelevance\, Accessed 01/16/2019.


Page 10 of 12
SUR407


