Peroral Endoscopic Myotomy for Treatment of Esophageal Achalasia

Effective: October 1, 2019

Next Review: June 2020
Last Review: August 2019

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Peroral endoscopic myotomy (POEM) is a novel endoscopic procedure that uses the oral cavity as a natural orifice entry point to perform myotomy of the lower esophageal sphincter (LES) in patients with achalasia.

MEDICAL POLICY CRITERIA

Peroral endoscopic myotomy is considered investigative as a treatment for esophageal achalasia.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES

1. Gastroesophageal Reflux Surgery, Surgery, Policy No. 186

BACKGROUND

ACHALASIA
Esophageal achalasia is characterized by prolonged occlusion of the lower esophageal sphincter (LES) 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. Treatment options for achalasia have traditionally included pharmacotherapy such as injections with botulinum toxin, pneumatic dilation, and laparoscopic Heller myotomy (LHM).[1,2] Although the latter two are considered the mainstay of treatment because of higher success rates and relative long-term efficacy compared with pharmacotherapy and botulinum toxin injections, 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. One-year response rates of 86% and rates of major mucosal tears requiring subsequent intervention of 0.6% have been reported.[3]

PERORAL ENDOSCOPIC MYOTOMY

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 LES. This procedure has the intent of reducing the total number of incisions needed and, thus, reducing the overall invasiveness of surgery.

The POEM procedure was developed in Japan by Dr. Haruhiro Inoue, and is performed with the patient under general anesthesia.[2,4] After 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. POEM differs from laparoscopic surgery, which involves complete division of both circular and longitudinal LES muscle layers. The dysfunctional muscle fibers that prevent the LES from opening are cut in order to allow food to enter the stomach more easily.

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

EVIDENCE SUMMARY

In order to isolate the specific therapeutic effects of POEM and adequately control for placebo effects and individual patient differences (clinical and demographic, known and unknown), well-designed randomized clinical trials (RCTs) that compare POEM with the current standard of care are necessary.

The RCT is the most rigorous and reliable study design for demonstrating a causal relationship between the therapy under investigation and the health outcomes of interest. This form of study is necessary in order to understand whether an intervention such as POEM can positively impact the health outcomes of patients with achalasia. Although informative, evidence from observational, nonrandomized studies describing POEM outcomes is of limited utility in establishing causal relationships. Therefore, well-designed, RCTs are needed to establish whether treatment with POEM improves health outcomes in patients with achalasia compared to established, standard surgical treatments.

SYSTEMATIC REVIEWS
Several systematic reviews have evaluated the outcomes of POEM in nonrandomized studies. Three systematic reviews only selected studies comparing POEM to an alternative surgical treatment.[5-7]

In 2017, Awaiz compared the safety and effectiveness of POEM and laparoscopic Heller myotomy (LHM) in a systematic review and meta-analysis of seven comparative trials totalling 483 patients (LHM = 250, POEM = 233).[7] The review was conducted in accordance with PRISMA methodology, and study methodological quality was assessed using the Modified Newcastle-Ottawa scale. Several variables were found to have a high degree of heterogeneity, including prior endoscopic treatment, long-term GERD, operating time, and length of hospital stay – which limits generalizability of conclusions. Although evidence suggests POEM may be superior to LHM in short-term follow-up, the Awaiz concluded that meaningful comparison of POEM to LHM is impossible in the absence of data beyond one year.

Studies by Zhang (2016)[5] and Marano (2016)[6] included the same time period in their review. Because the Marano review assessed more patients and studies, only their results are summarized here. The study evaluated outcomes for 486 patients (196 receiving POEM, 290 receiving laparoscopic Heller myotomy [LHM]) from 11 studies. None were randomized. Reviewers rated all studies to have 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 length of stay was shorter for POEM.

Four recent reviews have summarized outcomes of both comparative studies and case series.[8-11]

Schlottmann (2017) compared POEM to laparoscopic Heller myotomy (LHM) in 53 and 21 studies of POEM and LHM, respectively.[11] Mean follow-up was significantly longer for studies of LHM (41.5 vs. 16.2 mo, P < 0.0001). Short-term results show that POEM is more effective than LHM in relieving dysphagia, but it is associated with a very high incidence of pathologic reflux (OR for GERD symptoms 1.69, 95% CI 1.33-2.14, P < 0.0001; GERD evidenced by erosive esophagitis OR 9.31, 95% CI 4.71-18.85, P < 0.0001; and GERD evidence by pH monitoring OR 4.30, 95% CI 2.96-6.27, P < 0.0001). Length of hospital stay was also 1.03 days longer after POEM (P = 0.04).

A systematic review by Akintoye (2016) evaluated outcomes for 2373 patients from 36 studies.[8] Clinical success rates were achieved in 98% of patients (95% confidence interval [CI], 97% to 100%) and mean Eckardt scores decreased from baseline at 1, 6, and 12 months. (The Eckardt score grades 4 major symptoms of achalasia [dysphagia, regurgitation, retrosternal pain, weight loss] each on a 0 [none] to 3 [severe] scale, for a maximum score of 12; total scores of ≥4 represent treatment failure.[12])

A systematic review by Crespin (2016) evaluated outcomes for 1299 patients from 19 studies.[9] Improvements in Eckardt scores were statistically significant in all studies. The most frequently reported complications were mucosal perforation, pneumothorax, pneumoperitoneum, and subcutaneous emphysema.

A systematic review by Patel (2016) evaluated outcomes for 1122 patients from 22 studies.[10] Eckardt scores dropped from 6.8 at baseline to 1.2 postoperatively. There were improvements in lower esophageal sphincter (LES) pressure and symptoms.
RANDOMIZED CONTROLLED TRIAL

In 2019, Ponds reported results of a randomized multicenter trial comparing POEM (n=67) to pneumatic dilation (n=66), conducted at 6 hospitals in the Netherlands, Germany, Italy, Hong Kong, and the United States.\textsuperscript{[13]} Adult patients (mean age, 48.6 years; 56\% men) with newly diagnosed achalasia and an Eckardt score greater than 3 who had not undergone previous treatment were included (130 of the 133 randomized patients received treatment). At 2 years follow-up, treatment success (defined as an Eckardt score $\leq$3 and the absence of severe complications or re-treatment) occurred in 58 of 63 patients (92\%) in the POEM group vs 34 of 63 (54\%) in the pneumatic dilation group, a difference of 38\% ([95\% CI, 22\%-52\%]; P<.001). Fourteen other secondary endpoints were reported, none of which were statistically significantly different. In total, 7 serious adverse events occurred, 2 of which were related to pneumatic dilation, and 5 were unrelated to the study. One pneumatic dilation patient experienced perforation after dilation and required 13 days of hospitalization, and another patient as admitted for one night with severe chest pain assumed to be related to perforation. In total, adverse events were more common after POEM than pneumatic dilation (67\% of patients vs 22\%). POEM patients experienced reflux esophagitis, reflux symptoms, Candida esophagitis, ulcer at the esophagogastric junction that healed after PPI treatment, and peri-procedural mucosal tear that was managed conservatively and healed at endoscopy performed 1 week later. In the pneumatic dilation group, reported adverse events included reflux esophagitis, reflux symptoms, Candida esophagitis, and belching/dyspepsia. Limitations of this study included the lack of a strict intention-to-treat analysis. Patients who were randomized and did not go on to receive treatment were not included in final analysis. However, sensitivity analysis suggests this would not have had a significant effect on final outcomes. Longer-term follow-up is not available for this study, since primary outcomes were assessed at two-years. Given the pathophysiology of achalasia, the authors pointed this out as a limitation. Lastly, the trial was not blinded, which is commonly the case for new surgical and endoscopic procedures.

NONRANDOMIZED STUDIES

Comparative Studies

A number of comparative nonrandomized studies have compared the safety and efficacy of POEM with a standard of care treatment for achalasia. Those not included in the aforementioned meta-analyses are summarized here.

In 2016, Sanaka reported retrospective two-month post-treatment outcomes for 200 achalasia patients treated with POEM (N = 36), pneumatic dilation (N = 22), and LHM (N=142).\textsuperscript{[14]} Patients underwent treatment between January 2012 and March 2015, and were not statistically significantly different between groups for age at diagnosis, gender, ethnicity, months from last to current treatment, and use of botulinum toxin injection as a prior treatment. As compared to LHM, patients in the POEM group were significantly older (55.4 years versus 46.5 years, p = 0.012); and PD and POEM patients had more prior treatments than the LHM patients (68, 72, and 44 percent, respectively). Eckardt symptom scores were assessed; and to objectively assess esophageal function, lower esophageal sphincter (LES) pressures on high resolution esophageal manometry (HREM), and esophageal emptying on timed barium esophagram (TBE) were assessed pre- and at two-months post-treatment. All three treatments showed improvement in HREM and TBE at follow-up, and there was no difference in measurements between groups.
Noncomparative Studies

In recent years, many case series reported improved clinical outcomes following POEM with follow-up ranging from two-months to a mean of 30 months.[15-23] Among them, several specifically evaluated post-operative reflux.[15,19,21,23] In one study, POEM was not associated with clinically significant refractory GERD[23]; in another study, a high rate of reflux on pH testing was associated with POEM, though the objective pH measurement did not correlate with subjective patient symptom surveys[21]. Several authors concluded that the preliminary data suggest POEM may be a minimally invasive, safe, and efficacious treatment option for achalasia, however, large, prospective randomized studies are necessary to make conclusions.

Wang (2016) retrospectively reviewed outcomes for POEM (n=21) and pneumatic dilation (n=10) in patients ages 65 years and older.[24] 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.

Inoue (2015) reported outcomes on 500 consecutive patients a single Japanese institution.[25] Outcomes were available for variable proportion of patients at various time 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 1. Lower esophageal sphincter pressure ranged from 13.4 to 11.7. Between 16.8% and 21.3% of subjects reported symptoms of GERD. The overall complication rate was 3.2%.

In 2014, Ling reported quality-of-life outcomes in two (probably overlapping) patient cohorts 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 (PCS) and Mental Component Summary (MCS) 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 (standard deviation [SD]) PCS improved from 30 (13) to 65 (10), and mean MCS improved from 43 (10) to 67 (11) (Student t test, p<0.001 for both comparisons).[26] Incidence of intraoperative subcutaneous emphysema and pneumothorax was 14% and 5%, respectively; and postoperative esophagitis developed in 19%. In 87 previously untreated patients, mean (SD) PCS improved from 33 (11) to 69 (18) (Student t test, p<0.001), and mean (SD) MCS improved from 44 (13) to 67 (15) (Student t test, p=0.003).[27] Incidence of intraoperative subcutaneous emphysema and pneumothorax was 12% and 1%, respectively; postoperative esophagitis developed in 6%.

In 2012, Ren published the largest POEM series to date, highlighting POEM-specific complications.[28] In their series of 119 cases, 23% of patients developed subcutaneous emphysema intraoperatively and an additional 56%, postoperatively. Three of these patients required treatment with subcutaneous needle decompression. Additionally, 3% patients developed a pneumothorax intraoperatively and another 25% postoperatively. Postoperatively, the incidence of thoracic effusion was 49%, and of mild inflammation or segmental atelectasis of the lungs was 50%. All complications were resolved with conservative treatment.

At least two small case series evaluated the efficacy and feasibility of POEM for patients with failed Heller myotomy/achalasia recurrence; success rates have been reported in over 90% of cases up to 10 months after rescue POEM.[29,30] Studies have also compared different POEM techniques and comparable outcomes have been reported between patients undergoing full-thickness versus circular myotomy.[31] An international survey of 16 centers (7 in North
America, 5 in Asia, 4 in Europe, some of which were high-volume centers [≥30 POEMs per center]) reported 841 POEM procedures performed as of July 2012.[32]

### PRACTICE GUIDELINE SUMMARY

#### AMERICAN COLLEGE OF GASTROENTEROLOGY

In 2013, the American College of Gastroenterology issued a clinical guideline on the diagnosis and management of achalasia.[33] POEM was discussed as an emerging therapy, and stated to have promise as an alternative to the laparoscopic approach. The guideline further states that randomized prospective comparison trials are needed, and the procedure should be performed in the context of clinical trials.

#### AMERICAN SOCIETY OF GASTROINTESTINAL AND ENDOSCOPIC SURGEONS

In 2014, the American Society of Gastrointestinal and Endoscopic Surgeons issued evidence-based, consensus guidelines on the use of endoscopy in the evaluation and management of dysphagia, including esophageal achalasia.[34] There were no recommendations for peroral endoscopic myotomy, though the discussion included the following:

> “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.”

#### SOCIETY OF AMERICAN GASTROINTESTINAL AND ENDOSCOPIC SURGEONS

In 2011, the Society of American Gastrointestinal and Endoscopic Surgeons issued a consensus guideline on the surgical management of esophageal achalasia. The guideline stated that the POEM technique "is in its infancy and further experience is needed before providing recommendations."[35]

### SUMMARY

There is not enough research to know if peroral endoscopic myotomy (POEM) improves overall health outcomes for people with esophageal achalasia. No US based clinical practice guidelines based on research recommend POEM as a treatment of esophageal achalasia. Therefore, the use of POEM as a treatment of esophageal achalasia is considered investigational.

### REFERENCES


### CODES

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