Current Status of Peroral Endoscopic Myotomy

Young Kwan Cho and Seong Hwan Kim

Division of Gastroenterology and Hepatology, Department of Internal Medicine, Eulji University College of Medicine, Seoul, Korea

Peroral endoscopic myotomy (POEM) has been established as an optional treatment for achalasia. POEM is an endoluminal procedure that involves dissection of esophageal muscle fibers followed by submucosal tunneling. Inoue first attempted to use POEM for the treatment of achalasia in humans. Expanded indications of POEM include classic indications such as type I, type II, type III achalasia, failed prior treatments, including Botulinum toxin injection, endoscopic balloon dilation, laparoscopic Heller myotomy, and hypertensive motor disorders such as diffuse esophageal spasm, jackhammer esophagus. Contraindications include prior radiation therapy to the esophagus and prior extensive esophageal mucosal resection/ablation involving the POEM field. Most of the complications are minor and self-limited and can be managed conservatively. As POEM emerged as the main treatment for achalasia, various adaptations to tunnel endoscopic surgery have been attempted. Tunnel endoscopic surgery includes POEM, peroral endoscopic tumor resection, gastric peroral endoscopic pyloromyotomy. POEM has been widely accepted as a treatment for all types of achalasia, even for specific cases such as achalasia with failed prior treatments, and hypertensive motor disorders.

**Key Words:** Peroral endoscopic myotomy; Achalasia; Natural orifice transluminal endoscopic surgery; Heller myotomy

**INTRODUCTION**

The annual incidence of achalasia is 1 per 100,000, with a prevalence of 10 per 100,000 people, which makes it a very rare disease. Symptoms of achalasia include dysphagia for solids and liquids, chest pain, loss of weight, heartburn, and aspiration pneumonia. The Eckardt score is used to assess the degree of achalasia symptoms. Esophageal manometry, the gold standard test for the diagnosis of achalasia, reveals incomplete relaxation of the lower esophageal sphincter (LES) and aperistalsis of the esophageal body. Various treatment options for achalasia aim at relieving symptoms by reducing resting pressure in the LES. Conventional treatments include oral pharmacologic therapies with nitrate and calcium channel blockers, botulinum toxin injection, pneumatic dilation, and surgical myotomy. As endoscopic submucosal dissection (ESD) emerged as a treatment for gastric neoplasm with the development of endoscopic techniques and devices, the submucosal layer became a manipulatable region. As the ESD technique and endoscopic submucosal surgery evolved, natural orifice transluminal endoscopic surgery (NOTES) was also introduced. Peroral endoscopic myotomy (POEM) represents a NOTES approach to Heller myotomy. POEM is an endoscopic procedure to divide the circular muscles mainly in the esophageal muscle fibers across the esophagogastric junction (EGJ) and into the stomach. Pasricha et al. first suggested the feasibility of POEM in a porcine model. Inoue et al. were the first to try POEM for treating achalasia in humans. Since then, the use of POEM has quickly spread worldwide. This paper will focus on the current procedure, outcomes, complications, and future aspects of POEM.

**POEM PROCEDURE**

Patients are evaluated before undergoing POEM; after the procedure is performed, postoperative complications and effica-
cy of POEM should be evaluated. Assessment of the severity of symptoms and special tests may be needed for evaluation of the patient prior to the procedure. The Eckardt score is used to assess the degree of achalasia symptoms. The Eckardt score was evaluated from 0 to 3 points for weight loss, dysphagia, posterior sternal pain, and reflux symptoms. Higher the score, greater the severity of the symptoms, and it is also helpful to determine the therapeutic effect (Table 1). Esophageal manometry, esophagography, and endoscopy are used for the diagnosis of achalasia. Patients suspected of achalasia require at least two tests for diagnosis and in some cases all three tests are necessary. The esophagogram findings include delayed passage of barium, esophageal enlargement, esophageal ataxia, and narrow gastric esophageal junction, which is characterized by a “bird beak” appearance and helps to determine the presence of sigmoid type achalasia. The role of endoscopy in the diagnosis of achalasia is to exclude mechanical obstruction; pseudoachalasia mistaken for achalasia. On high resolution manometry, achalasia has been classified into three types. Type I has incomplete LES opening and aperistalsis, type II has panesophageal pressurization, and type III has no normal peristalsis, but distal esophageal spasm. Patient maintains a liquid diet for 2 days before the procedure. Intravenous antibiotics should be prescribed for three days until the procedure day, following additional oral antibiotics for three or four days. The POEM procedure is carried out under general anesthesia. Carbon dioxide gas should be used during the procedure to decrease the risk of complications including mediastinal emphysema and air embolization. An upper gastrointestinal endoscope equipped with water jet and transparent cap is used. Triangle-tip knife (TT knife; Olympus Medical Systems, Tokyo, Japan), Hybrid Knife (ERBE, Tübingen, Germany) have been used for POEM. TT knife has the advantage of facilitating selective dissection of the circular muscle layer, whereas Hybrid knives have the advantage of being infusible and shortening the procedure time. For electrosurgery, an electrosurgical unit is used. The site of mucosal incision in the anterior approach is at the 2 o'clock position, mainly, but in the posterior approach, the 5 o'clock position is used in patients who have undergone laparoscopic Heller myotomy (LHM). The length of myotomy should be at least 7 cm, with 2 cm extending into the gastric side, and even longer in spastic esophageal disorders (SEDs) such as Type III achalasia. The detailed procedure of POEM is as follows (Fig. 1).

Step 1. Submucosal injection- Submucosal injection is performed using a solution of saline mixed with indigocarmine dye to create separation between the mucosa and submucosa.

Step 2. Mucosal incision- Mucosal incision is made in the 2-o’clock position, with a knife, up to 2 cm vertically in order to close easily.

Step 3. Submucosal tunneling- A submucosal tunnel is formed using a triangle tip knife and passed over the EGJ and 3 to 4 cm down into the cardia.

Step 4. Myotomy- Myotomy is performed from the proximal esophagus up to 2 to 3 cm below the EGJ, to a point 2 cm below the mucosal entry.

Step 5. Closure- The mucosal incision site is closed with endoclips.

Barium esophagogram and endoscopy should be performed on postoperative day 1 to rule out complications such as presence of leakage, bleeding in the tunnel. After confirming the absence of any complication, liquid diet will be initiated, and if the patient tolerates the diet, he will be discharged. Eckardt score, esophageal manometry, esophagogram, endoscopy will be checked to evaluate the efficacy of POEM after discharge. A decrease in the Eckardt score by more than 3 points is considered as a clinical success.

### Table 1. Eckardt Score

| Score | Weight loss (kg) | Dysphagia | Retrosternal pain | Regurgitation |
|-------|-----------------|-----------|------------------|--------------|
| 0     | None            | None      | None             | None         |
| 1     | <5              | Occasional| Occasional       | Occasional   |
| 2     | 5–10            | Daily     | Daily            | Daily        |
| 3     | >10             | Each meal | Each meal        | Each meal    |

INDICATIONS AND CONTRAINDICATIONS

Inoue et al. first reported the POEM trial for achalasia in humans. The application of POEM was limited to achalasia initially. There have been attempts since then, for use of the technique beyond the classic indication. Sharata et al. reported safety and effectiveness of POEM after preoperative endoscopic balloon dilatation or botulinum toxin injection, Zhou et al. reported safety and effectiveness of POEM for failed Heller myotomy. Importantly, POEM has the advantage of the ability to access the entire length of the esophageal body, an extensive myotomy being possible without limitation. Owing to these advantages, the application of POEM in SEDs including diffuse esophageal spasm and jackhammer esophagus has been attempted, which requires a more extensive than achalasia. Shiwaku et al. and Ko et al. reported the feasibility of POEM for diffuse esophageal spasm and jackhammer esophagus respectively. As the applications of POEM increase, an expanded indication of POEM is suggested in the International Peroral Endoscopic Myotomy Survey (IPOEMS) study, which includes the classic indication for achalasia and past history of...
failed treatments. Moreover, contraindications of POEM have been mentioned in the IPOEMS study, which include previous radiation therapy to the esophagus, past history of wide esophageal mucosal resection or ablation involving the POEM field, and various conditions with high morbidity (Table 2).

OUTCOME

Many studies have demonstrated the efficacy of POEM, since Inoue et al. first reported the use of POEM in humans (Table 3).20-30 There were four meta-analysis studies on the outcome of POEM, and all the four studies showed efficacy of POEM with a reduction in both the Eckart score and LES pressure.31-34 Technical success was 97%, and clinical success (Eckardt score ≤3) was 93%–98%, symptom relief was maintained at 1, 6 and 12 months after treatment and median follow up duration was 6–8 months.31,33 Non-randomized studies comparing POEM to LHM showed conflicting results.35-37 Meta-analysis studies showed that there were no differences between the two groups with regard to reduction in the Eckhart’s score, post-operative pain scores, analgesic requirements, length of hospital stay, adverse events, reflux symptoms, and esophagitis.31,33 In the future, randomized comparative studies of POEM and LHM are necessary. Ngamruengphong et al. reported a long term result of POEM for achalasia, with a clinical success rate of 91% in patients who were followed up for at least 2 years.39 According to the subtype of achalasia, there were no differences between type I, type II and, type III achalasia in terms of reduction in the Eckhart’s score, LES pressure, integrated relaxation pressure.39 Khan et al. reported a meta-analysis of POEM in SED including type III achalasia, diffuse esophageal spasm, and jackhammer esophagus.40 Clinical success rates of POEM for SED, type III achalasia, diffuse esophageal spasm, jackhammer esophagus were 87%, 98%, 88%, 72%, respectively.40

| Table 2. Expanded Indications and Contraindications of Peroral Endoscopic Myotomy |
|-----------------------------------------------|
| **Expanded indications**                     |
| Classic indication: type I, type II, type III achalasia |
| Failed prior treatments: botulinum toxin injection, endoscopic balloon dilation, laparoscopic Heller myotomy |
| Hypertensive motor disorders: diffuse esophageal spasm, jackhammer esophagus |
| **Contraindications**                         |
| Prior radiation therapy to the esophagus     |
| Prior extensive esophageal mucosal resection/ablation involving the POEM field |
| Severe pulmonary disease                     |
| Severe thrombocytopenia                       |
| Cirrhosis with portal hypertension but no significant esophageal varices |

POEM, peroral endoscopic myotomy.
COMPLICATIONS

Early complications include mucosal injury, esophageal perforation, substantial bleeding requiring interventions, subcutaneous emphysema, pneumothorax, pneumomediastinum, and pleural effusion. Late complications include symptomatic gastroesophageal reflux, erosive esophagitis and abnormal acid exposure following a 24-hour pH monitoring study (Table 4). Most of the complications are self-limited and can be managed conservatively. The mucosal defect can be closed by multiple clips, fibrin sealant, over-the-scope-clips and endoscopic suture device. Bleeding can be managed by endoscopic hemostasis. Pneumoperitoneum can be managed with Veress needle technique in most cases, and most cases of pleural effusion and pneumothorax resolve spontaneously. Severe pleural effusions require thoracotomy with drainage. Mediastinitis is an uncommon but major complication of POEM and it often requires surgical drainage. Delayed bleeding is rare and can be managed conservatively in most cases by observation and transfusion. Patients who have symptomatic gastroesophageal reflux can be satisfactorily managed with proton pump inhibitors and antacids. POEM has shown no mortality in published reports.

CONSIDERATIONS

Myotomy site

Which is better between anterior myotomy and posterior myotomy?

Anterior myotomy at the 2 o'clock position has the advan-

tage of reducing gastroesophageal reflux by avoiding damage to the angle of His and the sling muscle bundle along the greater curvature of the stomach. Posterior myotomy at the 5 o'clock position has the advantage of fast and convenient access to the EGJ with the landmark of the spinal cord and the angle of His. Posterior myotomy has been reported to be useful in failed surgical Heller myotomy, advanced sigmoid type achalasia with megaesophagus, and redoPOEM and POEM post-Heller myotomy due to provision of better recognition of the dissection plane. However, since no studies have compared anterior myotomy and posterior myotomy, prospective clinical trial studies are necessary.

Table 3. Efficacy of Peroral Endoscopic Myotomy

| Study                           | Patient (n) | Eckardt score (pre/post) | LES pressure (pre/post) (mm Hg) | Follow-up (mo) |
|---------------------------------|-------------|--------------------------|---------------------------------|----------------|
| Ling et al. (2014)²⁰           | 87          | 7.1/0.4                  | 32.4/3.8                        | 12             |
| Wang et al. (2015)²¹           | 46          | 8.4/2.7                  | 39.4/24.4                       | 3              |
| Liu et al. (2015)²²            | 3           | 6.83/0.46                | 29.5/10.3                       | 6              |
| Ramchandani et al. (2016)²³    | 220         | 7.2/1.18                 | 37.5/15.2                       | 12             |
| Costamagna et al. (2012)²⁴     | 11          | 7.1/1.1                  | 45.1/16.9                       | 1              |
| Inoue et al. (2015)²⁵          | 500         | 6.0/1.0                  | 25.4/13.4                       | 36             |
| Shiwaku et al. (2016)²⁶        | 100         | 5.9/0.8                  | 43.6/20.9                       | 3              |
| Lee et al. (2013)²⁷            | 13          | 6.4/0.4                  | 30.3/15.3                       | 3              |
| Teitelbaum et al. (2014)²⁸     | 41          | 7/1                      | 28/11                           | 12             |
| Sharata et al. (2015)²⁹        | 100         | 6/1                      | 44.3/22.2                       | 16             |
| Khashab et al. (2016)³⁰        | 60          | 8/1.19                   | 29/11                           | 4              |

Les, lower esophageal sphincter.

Table 4. Complications of Peroral Endoscopic Myotomy

| Early complication                  | %  |
|------------------------------------|----|
| Mucosal injury                     | 4.8|
| Esophageal perforation             | 0.2|
| Major bleeding                     | 0.2|
| Subcutaneous emphysema             | 7.5|
| Pneumothorax                       | 1.2|
| Pneumomediastinum                  | 1.1|
| Pneumoperitoneum                   | 6.8|
| Pleural effusion                   | 1.2|

| Late complication                  | %  |
|------------------------------------|----|
| Symptomatic GERD                   | 8.5|
| Esophagitis on EGD                 | 13 |
| Abnormal exposure on 24-hour pH study | 47 |

GERD, gastroesophageal reflux disease; EGD, esophagogastroduodenoscopy.
Myotomy depth

Which is better between circular muscle myotomy and full thickness myotomy?

There were no significant differences in symptom relief, procedure-related parameters and adverse events, manometry outcomes, and reflux complications between circular muscle myotomy and full thickness myotomy. Full-thickness myotomy is associated with a reduction in the procedure time but a higher rate of postoperative gastroesophageal reflux disease. Intentional full-thickness myotomy is not essential to treat achalasia.

FUTURE

A key point enabling the use of POEM is a submucosal tunneling technique that manipulates the submucosal layer. As POEM emerged as the main treatment of achalasia, various adaptations in tunnel endoscopic surgery have been attempted. Tunnel endoscopic surgery includes POEM, peroral endoscopic tumor resection (POET), and gastric peroral endoscopic pyloromyotomy (G-POEM). POET is a way to completely remove a submucosal tumor through submucosal tunneling, particularly for esophageal, EGJ and gastric cardia tumors originating from the muscularis propria. POET has shown promising results in terms of efficacy and safety, however, further studies are necessary. Since Khashab et al. first reported human G-POEM, it has been an emerging novel endoscopic technique as an incisionless pyloroplasty for refractory gastroparesis. Several studies have shown feasibility and promising results of G-POEM, however, it has limitations due to a restricted number of studies and lack of a formalized protocol. Thus, further large scale studies are necessary.

CONCLUSIONS

POEM is a safe and effective option for treating type I, type II, and type III achalasia, and even for specific cases such as achalasia with failed prior treatments, Botulinum toxin injection, endoscopic balloon dilation, LHM and hypertensive motor disorders. However, large-scale studies and long-term outcomes are required. POEM has expanded the scope of adaptation to tunnel endoscopic surgeries such as POET and G-POEM, which also require larger scale studies with long-term outcomes.

Conflicts of Interest

The authors have no financial conflicts of interest.

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