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# Peroral Endoscopic Myotomy for Esophageal Motility Disorders

Jun Young Kim and Yang Won Min

Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Peroral endoscopic myotomy (POEM) is one of the most clinically successful tunnel-based minimally invasive endoscopic treatments. The classic indications of POEM include achalasia of all types, including failed prior treatments, and expanded indications include the non-achalasia esophageal motility disorders, such as esophagogastric junction outflow obstruction, diffuse esophageal spasm, and jackhammer esophagus. For achalasia treatment, POEM has achieved a comparable surgical efficacy and a safety outcome and, therefore, has emerged as a first-line treatment. For non-achalasia esophageal motility disorders, POEM has also shown high clinical response rates. The complication rate of POEM for esophageal motility disorders is low and most complications are managed with conservative treatment. Currently, POEM is a representative procedure of natural orifice transluminal endoscopic surgery, which has shown a good clinical efficacy with low complication rates for esophageal motility disorders including achalasia. However, further studies are needed to treat non-achalasia motility disorder via POEM. **Clin Endosc 2020;53:638-645**

**Key Words:** Achalasia; Esophageal motility disorders; Natural orifice transluminal endoscopic surgery; Peroral endoscopic myotomy

## INTRODUCTION

Achalasia and non-achalasia motility disorders, such as esophagogastric junction outflow obstruction (EGJOO), diffuse esophageal spasm (DES), jackhammer esophagus (JHE), and esophageal motility disorders, are rare diseases of unknown etiologies. Based on the comprehensive factors of patient history, endoscopy, barium esophagography, and high-resolution manometry (HRM), esophageal motility disorders are diagnosed.<sup>1</sup> The aim of an ideal therapy for these disorders is to revert the swallow function to normal and maintain the patient free of symptoms without pathological reflux.<sup>2</sup> The conventional treatment includes Botox injections, pneumatic balloon dilation, and laparoscopic Heller myotomy.

my.<sup>3,4</sup> Since Inoue et al. first reported a new endoscopic technique, named peroral endoscopic myotomy (POEM) for the treatment of achalasia in 2010, POEM has been performed as the primary treatment for achalasia worldwide with the number of procedures increasing exponentially.<sup>5</sup> Recently, obstructive physiology at the esophagogastric junction (EGJ) or distal esophagus has also been recognized as an important aspect of non-achalasia motility disorders and, therefore, is now a rendered treatment formerly reserved for achalasia.<sup>6</sup> In this aspect, the POEM procedure has been widely adopted for treating non-achalasia motility disorders. POEM not only has an advantage over surgical myotomy with reduced perioperative morbidity and mortality but also facilitates a calibrated myotomy and can be extended proximally to include the whole affected smooth muscle segment of the esophagus. Under the concept of targeting obstructive physiology regardless of the specific disease entity, POEM has gradually been introduced as a treatment for non-achalasia esophageal motility disorders (Table 1).<sup>7,8</sup>

In this paper, we focus on the current procedure, recent clinical outcomes in achalasia and non-achalasia motility disorders (EGJOO, JHE, and DES), and the complications of POEM.

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Correspondence: Yang Won Min

Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 06351, Korea

Tel: +82-2-3410-3409, Fax: +82-2-3410-6983, E-mail: yangwonee@gmail.com

ORCID: <https://orcid.org/0000-0001-7471-1305>

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**Table 1.** Indications of Peroral Endoscopic Myotomy for Esophageal Motility Disorders

Diseases	Classifications
Achalasia	Type I-III achalasia
Special achalasia	Sigmoid achalasia Achalasia with diverticulum
Recurrent achalasia	Failed prior treatment (LHM, PD, POEM, Botox injection)
Non-achalasia esophageal motility disorders	JHE/nutcracker esophagus EGJOO DES

DES, diffuse esophageal spasm; EGJOO, esophagogastric junction outflow obstruction; JHE, jackhammer esophagus; LHM, laparoscopic Heller myotomy; PD, pneumatic dilatation; POEM, peroral endoscopic myotomy.

## PROCEDURE

### Pre-procedure preparation

Before the procedure, a fluid diet and fasting are required.<sup>9</sup> To reduce the aspiration risk during intubation, residual contents in the esophagus are cleared by endoscopy using endoscopic retrieval devices, such as a net, under conscious sedation before general anesthesia. There is no consensus on whether a soluble antibiotic content should be added during endoscopic cleaning.<sup>9,10</sup>

### Mucosal incision

In patients with achalasia, the submucosal injection site is approximately 6–10 cm proximal to the EGJ. However, for non-achalasia motility disorders, it is necessary to determine

the site and length of the affected segments of abnormal contractions based on the results of HRM. The position of the mucosal incision on the oral side should be at least 2 cm higher than the initial end of the abnormal contraction.

The anterior (12–2 o'clock orientation) or posterior (5–6 o'clock orientation) side wall of the esophagus is selected as the point for the mucosal incision, tunnel direction, and myotomy site.<sup>11</sup> An incision length of  $\leq 3$  cm is recommended because of gas-related complications during the procedure.<sup>12</sup>

### Submucosal tunneling

Submucosal tunneling is extended distally via the endoscopic submucosal dissection technique up to 2–3 cm into the gastric cardia. For beginners, a timely exit of the endoscope from the tunnel cavity and entrance into the esophageal cavity for observation is necessary to establish a straight tunneling and linear myotomy. Indicators of the locations within the submucosal tunnel are listed in Table 2.<sup>13</sup>

### Myotomy

Myotomy is performed from the oral side, 2 cm below the mucosal entry site to 2–3 cm below the EGJ. The circular muscle bundles are cut gradually until the longitudinal muscle is identified. At the EGJ, the tissue planes and tunneling spaces become narrowed. For long-term efficacy, an adequate linear lower esophageal sphincter (LES) incision is very important. Therefore, the relaxation of the EGJ should be observed before completing the myotomy procedure. Full-thickness myotomy, which dissects the entire circular and longitudinal muscle layer, can be an alternative option.<sup>14</sup> A comparison with classic selective circular myotomy showed comparable efficacy with post-procedural low integrated relaxation pressure (IRP) and more gastroesophageal reflux disease (GERD).<sup>15</sup>

The length of the myotomy should be individualized and disease-specific, based on the intraoperative endoscopic iden-

**Table 2.** Various Location Indicators within the Submucosal Tunnel by the International Peroral Endoscopic Myotomy Survey<sup>13</sup>

Sign	Location	Usefulness
Insertion depth		Moderately useful
Palisade vessels	Distal esophagus	Moderately useful
Narrowing of submucosal tunnel	Gastroesophageal junction	Moderately useful
Lower esophageal sphincter circular bundles	Lower esophageal sphincter	Very useful
Submucosa of the cardia (large space, more/larger vessels)	Gastric cardia	Very useful
Luminal side of the cardia (blue discoloration of the mucosa)	Gastric cardia	Very useful
Transillumination double-scope technique	Gastric cardia	Very useful
Injection markers in the submucosa of the cardia	Gastric cardia	Not useful/uncertain

tification of the high-pressure zone as well as comparison with the preoperative HRM and contrast study results. The average myotomy length is 6–10 cm in classic achalasia. However, a longer myotomy is occasionally needed in type III achalasia, DES, or JHE.<sup>11,16,17</sup> Currently, including the LES in the myotomy is reasonable.<sup>18</sup> After esophageal body myotomy, contractility is significantly reduced and, therefore, may result in post-operative dysphagia caused by induced ineffective esophageal motility.<sup>19</sup> Also, some cases of DES and JHE progress to achalasia and require additional treatment if the LES is spared.<sup>20-22</sup> Therefore, LES myotomy is currently considered for treating these motility disorders. Although LES myotomy increases the risk of reflux as a side effect, most of these associated complications are clinically insignificant and easily managed with proton pump inhibitors (PPIs).<sup>23</sup>

**Tunnel closure**

Before closing the tunnel opening, no immediate complications of bleeding, damaged vessels, overt perforation, and liquid residue in the tunnel should be ensured. The mucosal incision site is closed from the distal to the proximal side with the endoclips.

**Post-procedure examination**

A chest X-ray is performed immediately after the procedure to rule out immediate complications. If there are signs of perforation such as pneumoperitoneum or pneumomediastinum, empirical antibiotics are administered intravenously. Barium esophagogram or endoscopy should be performed to rule out complications such as bleeding or leakage before restarting the diet. After confirming the absence of any complication, a soft diet is started, and if the diet is tolerable, the patient can be discharged.

**CLINICAL OUTCOMES**

**Achalasia**

The treatment success of POEM for achalasia has been defined by some parameters listed in Table 3.<sup>24-27</sup> Based on these parameters, POEM has demonstrated clinical and functional efficacy.<sup>28-31</sup> Since the first human POEM in 2008, the procedure has been performed for over 10 years, and the efficacy and safety of POEM for achalasia is evident. Its short-term curative efficacy is reported to be 90%–100%, with a long-term follow-up success rate of over 80% (Table 4).<sup>9,13,16,17,28,29,32-45</sup> Also, compared with conventional achalasia treatments such as laparoscopic Heller myotomy and pneumatic dilatation, POEM had better clinical outcomes (Table 5).<sup>30,38,46-50</sup> A me-

ta-analysis comparing POEM (5,834 patients) and Heller myotomy (1,958 patients) showed that the clinical symptom remission rates at 1 year and 2 years after POEM were higher than those after Heller myotomy (1 year: 93.5% vs. 91.0%,  $p=0.01$ , 2 years: 92.7% vs. 90.0%,  $p=0.01$ ).<sup>51</sup> Although POEM is comparable to laparoscopic Heller myotomy in the efficacy and safety for the treatment of achalasia, long-term data comparing the outcomes are needed. In studies comparing patients who underwent POEM and pneumatic dilatation, the former showed significantly higher clinical success rates at long-term follow-up.<sup>48,52</sup>

The outcomes of POEM in patients with failed previous treatments also showed good results (Table 6).<sup>53-58</sup> In patients with failed prior pneumatic dilatation, POEM showed no significant difference in outcomes compared with treatment-naïve patients.<sup>56</sup> A study comparing the treatment efficacy of POEM for patients with failed prior Heller myotomy and treatment-naïve patients revealed that the clinical response rate was lower (81% vs. 94%), and the rate of adverse events was not significantly different.<sup>58</sup> After failed POEM, repeat POEM procedures showed a clinical success rate of 85% without serious adverse events, indicating efficaciousness with safety<sup>57</sup>; however, further studies are needed. The most important cause of recurrence after myotomy is inadequate or incomplete myotomy with an insufficient incision below the EGJ.<sup>59</sup> An inexperienced endoscopist, a longer duration of the disease ( $\geq 10$  years), and a history of previous treatment failure are also associated with a risk for recurrence.<sup>36,60,61</sup> POEM seems to be a promising alternative option for patients with other failed treatments, including endoscopic and surgical myotomies.

**Table 3.** Parameters for Clinical Success after Peroral Endoscopic Myotomy for Achalasia

Measurement tool	Parameters for success
Eckardt score	$\leq 3$
Timed barium esophagogram	Adequate emptying
Manometry	
Lower esophageal pressure	Decrease after procedure (descending amplitude was greater than 50%)
Integrated relaxation pressure	$\leq$ Upper normal limit
During POEM procedure	Distensibility using EndoFLIP

EndoFLIP, endoscopic functional luminal imaging probe; POEM, peroral endoscopic myotomy.

**Table 4.** Clinical Outcomes of Peroral Endoscopic Myotomy for Achalasia and Non-Achalasia Esophageal Motility Disorders

Study	Type of motility disorder	Patient (n)	Clinical responses (%)	Mean follow-up (mo)	Major complication (%)
Li et al. (2013) <sup>32</sup>	Achalasia	238	95.0	8.5	0
Cai et al. (2014) <sup>33</sup>	Achalasia	100	96.5	11.5	0
Stavropoulos et al. (2013) <sup>13</sup>	Achalasia	100	97.0	13.3	0
Ramchandani et al. (2016) <sup>29</sup>	Achalasia	220	92.0	13.4	0
Chen et al. (2015) <sup>34</sup>	Achalasia (pediatric)	27	100.0	24.6	0
Inoue et al. (2015) <sup>35</sup>	Achalasia	500	91.0	36.0	3.2
	DES	9	100.0		
Li et al. (2018) <sup>36</sup>	Achalasia	564	87.1	49.0	6.4
Teitelbaum et al. (2018) <sup>37</sup>	Achalasia (type I)	8	88.0	65.0	4.7
	Achalasia (type II)	15	80.0		
	EGJOO	5	60.0		
	DES	1	100.0		
Werner et al. (2019) <sup>38</sup>	Achalasia	112	83.0	24.0	2.7
Brewer Gutierrez et al. (2020) <sup>39</sup>	Achalasia <sup>a)</sup>	146	95.2	55.0	5.5 <sup>b)</sup>
Shiwaku et al. (2020) <sup>40</sup>	Achalasia <sup>a)</sup>	1,346	94.7	12.0	0
Khashab et al. (2015) <sup>16</sup>	Achalasia (type III)	54	96.3	7.8	7.4 <sup>b)</sup>
	DES	9	100.0		22.2 <sup>b)</sup>
	JHE	10	70.0		20.0 <sup>b)</sup>
Sharata et al. (2015) <sup>28</sup>	Achalasia <sup>a)</sup>	75	97.8	16	6.0 <sup>b)</sup>
	DES, NE, isolated hypertensive non-relaxing LES	25	70.8		
Khan et al. (2017) <sup>41</sup>	Achalasia <sup>a)</sup> (type III)	116	92.0	3–36	11.0 <sup>b)</sup>
	JHE	37	72.0		16.0 <sup>b)</sup>
	DES	18	88.0		14.0 <sup>b)</sup>
Khashab et al. (2018) <sup>17</sup>	DES, JHE	35	84.9	9.1	20.0 <sup>b)</sup>
	EGJOO	15	93.3	6.5	13.3 <sup>b)</sup>
Filicori et al. (2019) <sup>42</sup>	DES	11	91.0	48.0	10.0 <sup>b)</sup>
	EGJOO	14			
	Hypercontractile esophagus	15			
Bernardot et al. (2020) <sup>43</sup>	NAEMD (JHE, SED, EGJOO)	30	63.2	6	26.7 <sup>b)</sup>
	Achalasia (type I, II)	30	95.5		20.0 <sup>b)</sup>
	Achalasia (type III)	30	87.0		33.4 <sup>b)</sup>

DES, diffuse esophageal spasm; EGJOO, esophagogastric junction outflow obstruction; JHE, jackhammer esophagus; LES, lower esophageal sphincter; NAEMD, non-achalasia esophageal motility disorder; NE, nutcracker esophagus; SED, spastic esophageal disorder.

<sup>a)</sup>Previous failed treatment was included.

<sup>b)</sup>Minor complication rate was included.

**Table 5.** Comparison of Outcomes between Peroral Endoscopic Myotomy and Other Treatments for Esophageal Motility Disorders

Study	Treatment comparison	Patient (n)	Clinical responses (%)	Mean follow-up (mo)	Major complication (%)
Hungness et al. (2013) <sup>30</sup>	POEM vs. HM	18 vs. 55	89 (POEM)	6	17 <sup>b)</sup> vs. 13 <sup>b)</sup>
Bhayani et al. (2014) <sup>46</sup>	POEM vs. HM	37 vs. 64	95 vs. 90	6	13 <sup>b)</sup> vs. 18 <sup>b)</sup>
Kumbhari et al. (2015) <sup>47</sup>	POEM vs. HM	49 vs. 26	98 vs. 80	8.6 vs. 21.5	6 <sup>b)</sup> vs. 27 <sup>b)</sup>
Ponds et al. (2019) <sup>48 a)</sup>	POEM vs. PD	67 vs. 66	92 vs. 54	24	0 vs. 3
Shea et al. (2020) <sup>49</sup>	POEM vs. HM	44 vs. 97	73.3 vs. 65.4	18.2 vs. 45.0	N/A
Wirsching et al. (2019) <sup>50</sup>	POEM vs. HM	23 vs. 28	Mean Eckardt score 0 at follow up (both)	2.8 vs. 3.4	9 <sup>b)</sup> vs. 14 <sup>b)</sup>
Werner et al. (2019) <sup>38 a)</sup>	POEM vs. HM	112 vs. 109	83.0 vs. 81.7	24	2.7 vs. 7.3

HM, heller myotomy; N/A, not available; PD, pneumatic dilatation; POEM, peroral endoscopic myotomy.

<sup>a)</sup>Randomized trial.

<sup>b)</sup>Minor complication rate was included.

**Table 6.** Clinical Outcomes of Peroral Endoscopic Myotomy after Failed Prior Achalasia Treatment

Study	Prior treatment	Patient (n)	Clinical responses (%)	Mean follow-up (mo)	Major complication (%)
Onimaru et al. (2013) <sup>53</sup>	HM & PD	10	100.0	18.0	0.0
Zhou et al. (2013) <sup>54</sup>	HM	12	91.7	10.4	0.0
Vigneswaran et al. (2014) <sup>55</sup>	HM	5	100.0	5.0	20.0 <sup>a)</sup>
Ling et al. (2014) <sup>56</sup>	PD	21	92.3	12.0	0.0
Tyberg et al. (2017) <sup>57</sup>	POEM	46	85.0	N	17.0 <sup>a)</sup>
Ngamruengphong et al. (2017) <sup>58</sup>	HM	90	81.0	9.0	1.0

HM, heller myotomy; PD, pneumatic dilatation; POEM, peroral endoscopic myotomy.

<sup>a)</sup>Minor complication rate was included.

### Esophagogastric junction outflow obstruction

EGJOO is characterized by an elevated median IRP greater than the upper normal limit with effective peristalsis, and types I-III achalasia should be excluded.<sup>1,62</sup> Less than 10% of this motility disorder is thought to be an early stage or variant of achalasia, and some patients will later progress to developing achalasia.<sup>63</sup> In a study comparing the efficacy of POEM for non-achalasia motility disorders, patients with EGJOO had a higher clinical success rate (93.3%) compared with those with other spastic esophageal disorders (SEDs) (84.9%) in the subgroup analysis (Table 4). The results were consistent with the clinical success rates reported in patients with achalasia who underwent POEM, while extensive myotomy was not essential in EGJOO.

### Other non-achalasia esophageal motility disorders (DES and JHE)

POEM indications have expanded to include SEDs such as DES, hypercontractile esophagus, and JHE.<sup>7,16,64</sup> Khan et al. conducted a systematic meta-analysis of POEM for SEDs and reported excellent therapeutic results with high efficacy and acceptable safety (Table 4).<sup>41</sup> In that study, the clinical success rates were 88% and 72% in DES and JHE, respectively. The clinical success of POEM for JHE was 20% lower than that for type III achalasia, which may be due to the extreme contractility of the esophageal body in JHE.

Although the current data show a considerable clinical success rate for POEM for non-achalasia esophageal motility disorders, there are still an insufficient number of studies and no expert consensus or guidelines for POEM for the treatment

of non-achalasia esophageal motility disorders. Therefore, when considering myotomy for the diseases, it is mandatory to deliberate whether it can be helpful and thoroughly discuss this with the patient before the procedure.

## COMPLICATIONS

POEM is a safe procedure, with a low complication incidence. Moreover, most of the complications can be managed with conservative treatment (Table 7).<sup>44,65</sup> Globally, almost zero mortalities or emergent conversions to open surgery have been reported, despite the performance of over 5,000 procedures.<sup>18</sup> The reported immediate adverse events range from light mucosal injury to esophageal perforation, bleeding, mediastinitis, peritonitis, pneumonia, insufflation-related events, pleural effusion, and atelectasis.<sup>66</sup>

The most important late complication of POEM is GERD. Compared with surgical Heller myotomy, the incidence of GERD following POEM is higher in most reports.<sup>45,51,67</sup> This may be because POEM is not performed with laparoscopic fundoplication. Inoue et al. reported that the incidence of GERD 2 months and 3 years after POEM was 16.8% and 21.3%, respectively.<sup>35</sup> In a study analyzing GERD after POEM by pH, endoscopy, and questionnaires according to the follow-up time, the pH result and endoscopic result positive for GERD were over 55% and 28%, respectively. However, the reflux symptoms were less than 15% at 12 months.<sup>31</sup> Once a PPI was administered, the percentages decreased to 3%, 1%, and

4% at 60 months, respectively. Patients with symptomatic gastroesophageal reflux can be effectively managed with PPIs.<sup>68</sup>

## CONCLUSIONS

POEM has been globally introduced for the treatment of achalasia and is increasingly being performed. It is a safe and effective treatment modality not only for the primary and failed prior treatment of achalasia but also for non-achalasia esophageal motility disorders, with the advantage of tailoring the length of the myotomy. However, there are still challenges in maintaining long-term efficacy and reducing GERD after POEM for achalasia. Therefore, more randomized trials are needed to confirm the long-term efficacy and primary role of POEM in non-achalasia motility disorders. In conclusion, POEM, a representative procedure for tunnel-based minimally invasive endoscopic treatment, has shown good potential for further development and future high quality; however, multicenter prospective studies with longer follow-up periods are required.

### Conflicts of Interest

The authors have no financial conflicts of interest.

### Author Contributions

Writing-original draft: Jun Young Kim  
Writing-review&editing: Yang Won Min

### ORCID

Jun Young Kim: <https://orcid.org/0000-0002-9015-9212>

**Table 7.** Early and Late Complications of Peroral Endoscopic Myotomy<sup>44,65</sup>

Early complications	Percentage (%)
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 complications	Percentage (%)
Symptomatic GERD	<15
Esophagitis on EGD	28
Abnormal exposure on 24-hour pH study	55

EGD, esophagogastroduodenoscopy; GERD, gastroesophageal reflux disease.

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