

# Is Peroral Endoscopic Myotomy a Potential Therapy for Esophageal Absent Contractility?

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**Aim:** Peroral endoscopic myotomy (POEM) is recommended for the endoscopic treatment of achalasia and esophageal junction outflow obstruction (EGJO); however, absent contractility, a subtype of peristalsis disorders classified by the Chicago Classification of esophageal motility v3.0, has no effective treatment. The purpose of this study was to assess the efficacy of POEM in absent contractility, in the part of the patients presents with dysphagia.

**Methods:** We conducted a single-center retrospective study at a tertiary referral center. We included 30 patients who mainly complain with dysphagia, and they underwent POEM from January 2013 to December 2018. The data of high-resolution esophageal manometry was collected before and after POEM. They were divided into 3 groups: EGJO, Achalasia, and Absent contractility according to the Chicago Classification of esophageal motility v3.0 before POEM. Telephone follow-up was made in February 2019 to obtain Eckardt scores and weight changes.

**Results:** We found that both Eckardt scores and integrated relaxation pressure decreased post-POEM in the 3 groups ( $P < 0.05$ ). Eckardt score was significantly lower in the EGJO group than in the Absent contractility group ( $P = 0.004$ ) post-POEM. The difference of Eckardt Score was higher in the EGJO group ( $P = 0.010$ ) and the Achalasia group ( $P = 0.007$ ) than in the Absent contractility group, as was weight gain ( $P = 0.023$ ;  $P = 0.002$ ).

**Conclusions:** These findings suggest that POEM is an effective endoscopic procedure for patients with EGJO and achalasia. Furthermore, POEM can significantly improve symptoms in patients with absent contractility, although less so than for the other 2 groups. POEM is a potential therapy for absent contractility patients presenting with dysphagia.

**Key Words:** peroral endoscopic myotomy, absent contractility, achalasia, esophagogastric junction outflow obstruction, high-resolution esophageal manometry

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Peroral endoscopic myotomy (POEM) is an endoscopic procedure consisting of a longitudinal myotomy of the circular esophageal and gastric muscle to reduce lower esophageal sphincter (LES) pressure.<sup>1</sup> According to the Chicago Classification of esophageal motility v3.0,<sup>2</sup> achalasia and esophageal junction outflow obstruction (EGJO) are defined by elevated median integrated relaxation pressure (IRP), usually  $> 15$  mm Hg. High IRP means high LES pressure in the first 10 seconds after swallow. Since 2008, when Inoue and colleagues first performed POEM on patients with achalasia, it has become a reliable choice for achalasia in addition to medical treatments, botulinum toxin injections, pneumatic balloon dilatation, and surgery-Heller myotomy. Achalasia resolves well post-POEM.<sup>3,4</sup> EGJO had a similar good response post-POEM,<sup>5</sup> so POEM performs well for patients with high LES pressure.

Achalasia and EGJO mainly causes dysphagia, regurgitation, and chest pain, while absent contractility is the third reason for dysphagia, followed by normal and achalasia.<sup>6</sup> Absent contractility is characterized by normal median IRP and 100% failed peristalsis. Regarding absent contractility, the mechanism and pathogenesis has been discussed rarely in the literature, and no effective treatment has been identified.<sup>7</sup> Smooth swallowing include pharyngeal opening, food passing down by peristaltic esophagus and gravity, LES relaxation. Lower LES pressure help swallowing in dysphagia patients. Therefore, in this study, we performed POEM on patients with absent contractility to determine whether POEM improves their symptoms, by comparing Eckardt scores and weight changes before and after POEM. We also compared high-resolution esophageal manometry (HREM) data, weight gain, Eckardt score, and General characteristic with achalasia and EGJO to identify similarities and differences.

## METHODS

### Patients

Thirty patients were included in this study who mainly complain with dysphagia. All of them receive HREM and were divided into 3 groups, they underwent POEM, and recheck HREM after POEM in half a year to 1 year during 2013 and 2018 in Ningbo Medical Center, Li Huili Hospital. Telephone follow-up was conducted in February 2019. This study was approved by the Ethical Review Committee of our institution. Written and informed consent was obtained from all patients. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in an a priori approval by the institution's human research committee. Patients were divided into 3 groups depending on the HREM results. EGJO, Achalasia, and Absent contractility. We recorded the following data: age, sex, smoke, alcohol consumption, *Helicobacter pylori* (HP) infection, disease course, Eckardt

score, and weight. We also recorded the following esophageal dynamic test data: LES length (LESL), upper esophageal sphincter (UES), and IRP. Regarding endoscopic surgery, we recorded the following: esophageal length, myotomy position, esophageal tunnel, and complications.

### Equipment and Instruments

We used the Netherlands MMS Solar GI gastrointestinal dynamic inspection system to perform the studies (MMS USA, Inc.), and the Japan Olympus company GIF Q260J Electronic endoscope to perform POEM, and the NM-4L-1 needle to submucosal injection, and the KD-650L Dual knife/ KD-640L TT Knife for mucous membrane and muscle incision, and the HX-610-90/HX-610-135 clip for closing the wound, and the FD-410LR hot biopsy forceps and Germany ERBE Company VIO 200D Electrosurgical workstation (APC2, EIP2) for hemostasis.

### Statistical Analysis

SPSS 22.0 software (SPSS Inc., Chicago, IL) was used for description and comparative statistical analysis. Statistical counting data were compared using simple cross tab ( $\chi^2$  test and Fisher exact test). For measurement data, we used the Kruskal-Wallis 1-way analysis of variance (ANOVA).  $P < 0.05$  was regarded as statistically significant.

## RESULTS

### Age, Sex, Smoking History, Alcohol Consumption, HP Infection, and Disease Course

There were 7 patients in the EGJOO group, mean age— $52.3 \pm 18.3$  years, including 4 women, 1 smoker, 1 history of alcohol consumption, and 6 with history of HP infection. Mean disease course was  $3.7 \pm 1.4$  years. There were 17 patients in the Achalasia patients group, mean age— $40.8 \pm 12.9$  years, including 11 women, 2 smokers, no drinkers, and 7 with history of HP infection. Mean disease course was  $6.2 \pm 5.4$  years. There were 6 patients in the absent contractility patients, mean age— $63.8 \pm 14.6$  years, including 3 women, 2 smokers, 1 drinker, and 2 with a history of HP infection. The mean disease course was  $3.7 \pm 2.4$  years (Table 1).

No significant differences were found in terms of sex, history of smoking, drinking, HP infection among the 3 groups (Fisher value  $> 0.05$ , Fisher exact test). No differences were found in ages and disease courses among the 3 groups ( $P > 0.05$ , Kruskal-Wallis 1-way ANOVA). Achalasia group patients were younger than Absent contractility group patients, and Achalasia group patients had much lower weight than EGJOO and Absent contractility group patients ( $P < 0.05$ , Kruskal-Wallis 1-way ANOVA) (Table 1).

### Endoscopic Surgery Characteristics

All patients underwent gastroduodenoscopy and timed barium radiography before and after POEM. Figure 1 shows an endoscopic picture and barium radiography before and post-POEM. POEM consists of 4 steps: mucosal incision, submucosal tunnel construction, myotomy of the LES and gastric muscle bundles, and wound surface closure (Fig. 2). Six patients underwent myotomy from the right wall, and from the posterior wall of the esophagus in the other 24 patients. The average esophageal length was 40.3 cm.

Submucosal tunnels began at 12.7 cm proximal to the esophageal junction (EGJ) and extending 2.9 cm into the proximal stomach. Average tunnel length was 11.7 cm. Complications were recorded: 3 perforations, no bleeding,

**TABLE 1.** General Characteristics of the 3 Group (N = 30)

Parameters	EGJ			P
	Outflow Obstruction (n = 7)	Achalasia (n = 17)	Absent Contractility (n = 6)	
Demographic features				
Sex ratio (female/male)	4/3	11/6	3/3	0.08
Age (median) (y)	52.3 (34.0-70.6)	40.8 (27.9-53.7)*	63.8 (49.2-78.5)*	0.01
Weight (kg)	64.6 (55.0-74.2)	54.5 (45.9-63.2)	63.3 (57.8-68.8)	0.02
Clinical features				
Smoke condition (smoker/nonsmoker)	1/6	2/15	2/4	0.56
Alcohol consumption (drinker/nondrinker)	1/6	0/17	1/5	0.18
HP infection (infected/not-infected)	6/1	7/10	2/4	0.10
Disease course (y)	3.7 (2.3-5.1)	6.2 (0.9-11.6)	3.7 (1.2-6.1)	0.65
Eckardt score	7.6 (4.6-10.6)	7.9 (5.5-10.3)	6.3 (5.3-7.3)	0.42

Weight: adjusted  $P > 0.05$  between one another.

\* $P = 0.013$ , Achalasia patients were younger than Absent contractility patients.

EGJ indicates esophageal junction; HP, *Helicobacter pylori*.

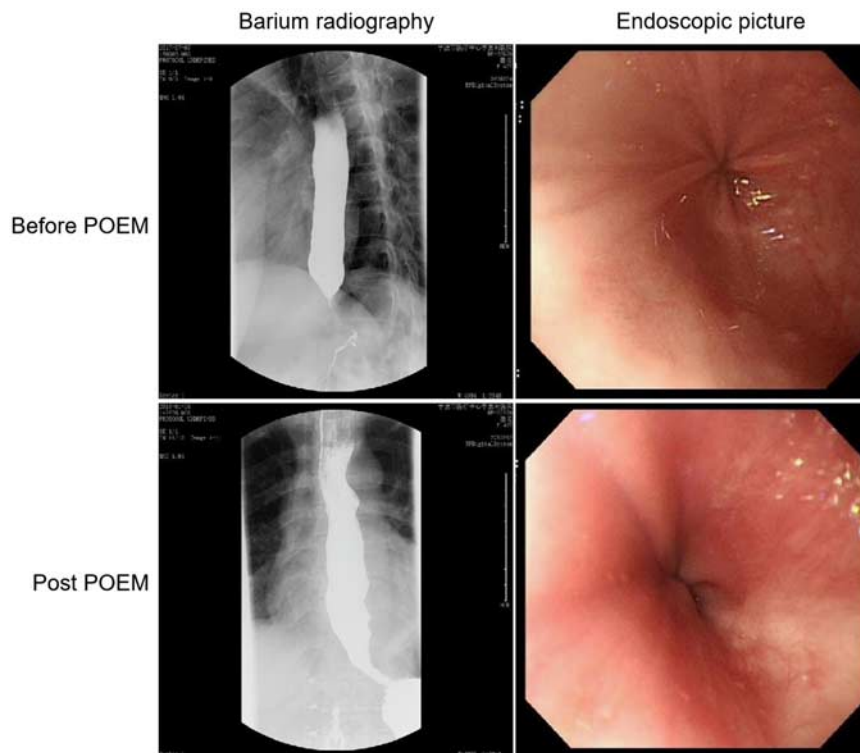
and no esophageal stenosis. All complications were resolved with conservative medical therapy.

### The Efficacy of POEM

We evaluated Eckardt scores, weights, and manometric data before and after POEM. Figure 3 shows the HREM graphic of the 3 groups before and after POEM. In EGJOO patients, the mean before-POEM Eckardt score was  $7.6 \pm 3.0$ , and the after-POEM Eckardt score was  $0.8 \pm 0.8$ , significantly lower than before-POEM ( $P = 0.001$ ). IRP was significantly lower after POEM as well ( $P = 0.001$ ), from  $16.1 \pm 1.3$  to  $4.7 \pm 2.0$ . In the Achalasia group, mean Eckardt score was  $7.9 \pm 2.4$  before POEM and  $1.7 \pm 1.0$  after POEM ( $P = 0.000$ ). IRP was significantly lower after POEM ( $P = 0.000$ ), from  $21.0 \pm 6.8$  to  $4.4 \pm 2.1$ . In the Absent contractility group, Eckardt score decreased from  $6.3 \pm 1.0$  to  $4.0 \pm 1.7$  ( $P = 0.015$ ), and IRP decreased from  $10.8 \pm 1.3$  to  $3.7 \pm 0.8$  ( $P = 0.002$ ). These data suggest that POEM caused both IRP and Eckardt scores to decrease; furthermore, POEM effectively treat patients with EGJ outflow obstruction, achalasia, and absent contractility who complain of dysphagia (Table 2).

### The Differences Among the 3 Groups

To evaluate the differences among the 3 groups, we compared Eckardt scores, weights, and esophageal dynamic test data. There were no significant differences among the 3 groups before POEM in terms of Eckardt score, LES (mm Hg), LESL (cm), or UES (mm Hg) ( $P > 0.05$ ). IRP was different among the 3 groups because of the CC3.0 classification. The IRP in the EGJOO and Achalasia groups were higher than 15 mm Hg, whereas the Absent contractility



**FIGURE 1.** Endoscopic picture and barium radiography before and post-POEM (magnification  $\times 20$ ). POEM indicates peroral endoscopic myotomy. [full color online](#)

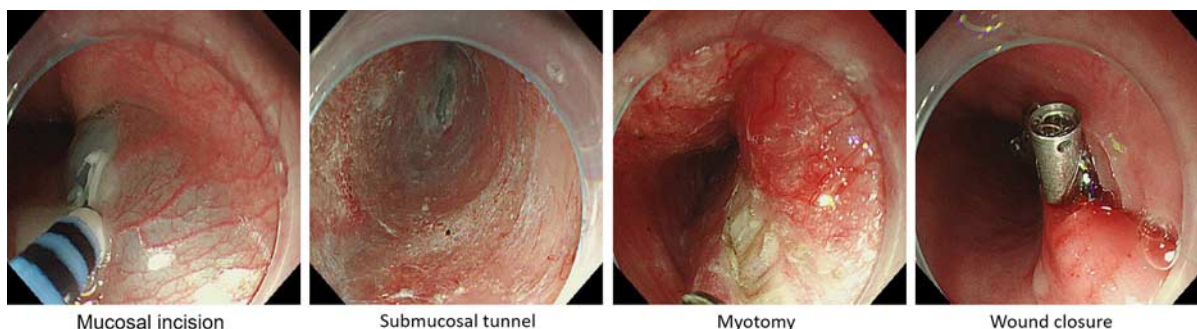
group had normal IRP,  $<15$  mm Hg. After POEM, no significant differences were found in terms of LES (mm Hg), LESL (cm), and UES (mm Hg) ( $P > 0.05$ ) among the 3 groups. Eckardt scores were significantly lower in the EGJOO group than in the Absent contractility group ( $*P = 0.004$ ) post-POEM. The difference of Eckardt score was greater in the EGJOO and Achalasia groups than in the Absent contractility group ( $**P = 0.010$ ;  $\#P = 0.007$ ), as was the case for weight gain (kg) ( $^aP = 0.023$ ,  $^bP = 0.002$ ). These data suggest that POEM is more efficacious in patients with EGJOO and achalasia than in patients with absent contractility (Table 2).

**DISCUSSION**

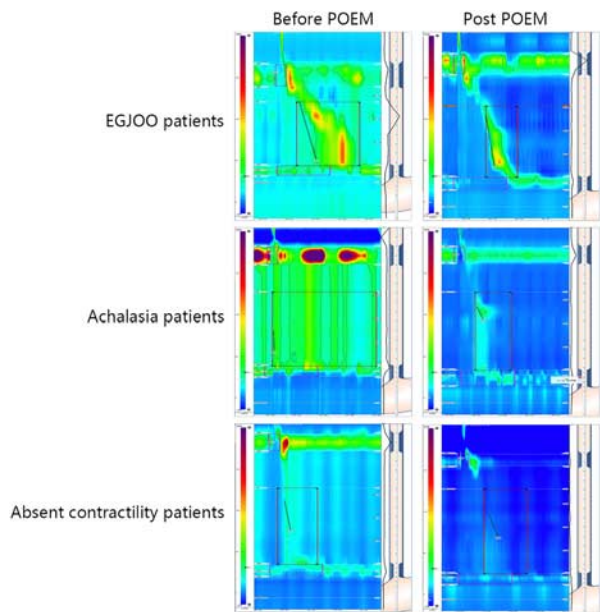
The Chicago Classification 3.0<sup>2</sup> categorizes esophageal motility disorders into 4 groups: disorders of esophagogastric junction outflow, including EGJOO and achalasia; major

disorders of peristalsis, including absent contractility, distal esophageal spasm, and hypercontractile esophagus; Minor disorders of peristalsis; and normal esophageal motility. Absent contractility is characterized by normal, median IRP and 100% failed peristalsis. Achalasia should be considered when IRP values are borderline. Achalasia shows elevated IRP  $> 15$  mm Hg, and can be divided into 3 subtypes. EGJOO shows elevated IRP  $> 15$  mm Hg, but does not meet the criteria for achalasia.

Many patients suffer from clinical dysphagia. Almost all types of esophageal motility disorders has been detected in dysphagia patients.<sup>6,8</sup> About 49% are normal, 7.1% have absent contractility, 8.3% have achalasia I-III, and 5.2% EGJOO. Males are 5 times more affected than females, and erosion and application of calcium antagonists are risk factors.<sup>6</sup> EGJOO, hypermotility, and hypomotility result in a gradient of decreasing dysphagia and increasing reflux burden.



**FIGURE 2.** POEM procedure graphic (magnification  $\times 20$ ). POEM indicates peroral endoscopic myotomy. [full color online](#)



**FIGURE 3.** HREM graphic of 3 groups before and after POEM. EGJOO indicates esophageal junction outflow obstruction; HREM, high-resolution esophageal manometry; POEM, peroral endoscopic myotomy. full color online

Hypomotility has the highest global symptoms, while symptoms of absent contractility are similar to those of minor motor disorders.<sup>9</sup> Current treatment for esophageal motility disorders are not clearly established. Pharmacotherapy, including L-type calcium channel blockers (nifedipine), isosorbide dinitrate, sildenafil, antidepressants, and other neuromodulators may be effective for dysphagia; nevertheless, weak evidence and side-effects restrict their widespread use.<sup>7,10</sup>

For esophageal hypomotility disorders, the cholinergic agonist bethanechol and the cholinesterase inhibitors pyridostigmine and edrophonium have been reported to increase peristaltic amplitude in healthy volunteers and some patients with ineffective esophageal motility. Buspirone

and capsaicin can increase LES pressure or peristalsis amplitude.<sup>11-13</sup> There is no specific treatment to restore or improve peristalsis.<sup>14</sup>

Esophageal hypermotility disease, including EGJ outflow obstruction and achalasia, has similar treatment. Botulinum toxin injection, pneumatic dilation, and myotomy have been reported to be effective.<sup>10</sup> Pérez-Fernández et al<sup>15</sup> reported that over one third of the EGJOO patients show spontaneous resolution of the symptoms; therefore, invasive treatment should be considered with caution. Myotomy is an original approach involving division of the muscle fibers of the LES using either thoracoscopy or endoscopy. POEM is effective and reliable for achalasia,<sup>16</sup> and was more effective than laparoscopic Heller myotomy in terms of relieving dysphagia, although it was associated with high incidence of pathologic reflux.<sup>17</sup> A recent meta-analysis showed POEM can also be used for esophageal spastic disease, including type III achalasia, diffuse esophageal spasm, and excessive contraction of the esophagus.<sup>18</sup>

POEM is now widely used to treat achalasia, and plays an important role in other esophageal hypermotility diseases. In the present study, we asked whether it can be applied to other esophageal motility disease that cause dysphagia. Our cohort included 6 patients with absent contractility who suffered from dysphagia and were willing to try POEM. All these patients showed improved symptoms post-POEM. Absent contractility is defined as normal IRP and 100% failed peristalsis, with food descent depending on gravity. When we incise the muscle of the LES, IRP significantly decreased ( $P=0.002$ ), and food passed through the esophagus faster and more easily because of lower resistance in the LES. In achalasia and EGJOO, partial recovery of peristalsis after POEM accelerated the speed,<sup>19</sup> helping to explain why symptoms improved less in absent contractility patients than in achalasia and EGJOO patients; other reasons are worth exploring. Of the 6 volunteers, 1 Eckardt score remained 5 after POEM; in 3 patients, scores improved by 2 points, 1 improved by 5, and 1 improved by 3. Though statistically valid, the small number of participants is a limitation to the interpretation of our results. We call for more clinical trials to verify the effectiveness of POEM for patients with absent contractility who primarily suffer from dysphagia.

**TABLE 2.** Eckardt Scores, Manometric Features, and Weight Gain (N=30)

Groups	Parameters	EGJ Outflow Obstruction	Achalasia	Absent Contractility	P
Before POEM	Eckardt Score	7.6 ± 3.0	7.9 ± 2.4	6.3 ± 1.0	0.424
	LES (mm Hg)	21.0 ± 10.6	29.8 ± 11.1	29.3 ± 5.9	0.236
	LESL (cm)	2.5 ± 0.8	2.8 ± 0.6	2.4 ± 0.6	0.230
	UES (mm Hg)	43.0 ± 24.6	53.3 ± 37.3	49.5 ± 20.1	0.864
	IRP	16.1 ± 1.3	21.0 ± 6.8	10.8 ± 1.3	0.000
Post-POEM	Eckardt Score	0.8 ± 0.8*	1.7 ± 1.0	4.0 ± 1.7*	0.005
	LES (mm Hg)	21.3 ± 12.2	16.1 ± 18.3	22.3 ± 10.4	0.169
	LESL (cm)	2.4 ± 0.9	2.6 ± 0.6	2.0 ± 0.4	0.155
	UES (mm Hg)	58.3 ± 24.7	39.9 ± 22.6	42.3 ± 16.1	0.269
	IRP	4.7 ± 2.0	4.4 ± 2.1	3.7 ± 0.8	0.458
Weight gain (kg)		8.1 ± 6.8 <sup>a</sup>	8.7 ± 6.8 <sup>b</sup>	1.7 ± 1.0 <sup>ab</sup>	0.003
Difference of Eckardt score		6.9 ± 2.4 <sup>**</sup>	6.2 ± 2.0 <sup>#</sup>	2.3 ± 1.6 <sup>***</sup>	0.004

EGJ indicates esophageal junction; IRP, integrated relaxation pressure; LES, lower esophageal sphincter; LESL, lower esophageal sphincter length; POEM, peroral endoscopic myotomy; UES, upper esophageal sphincter.

<sup>a</sup> $P=0.023$ , patients in the EGJ outflow obstruction group gain more weight than in the absent contractility group.

<sup>b</sup> $P=0.002$ , patients in the achalasia group gain more weight than in the absent contractility group.

\* $P=0.004$ , post-POEM Eckardt score is significantly different between the EGJ outflow obstruction group and the absent contractility group.

\*\* $P=0.010$ , Eckardt score differences is much more obvious in the EGJ outflow obstruction group than the absent contractility group.

<sup>#</sup> $P=0.007$ , Eckardt score differences is much more obvious in the achalasia group than the absent contractility group.

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