

Observational Study

Efficacy of peroral endoscopic myotomy *vs* other achalasia treatments in improving esophageal function

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Abstract

AIM: To assess and compare the esophageal function after peroral endoscopic myotomy (POEM) *vs* other conventional treatments in achalasia.

METHODS: Chart review of all achalasia patients who underwent POEM, laparoscopic Heller myotomy (LHM) or pneumatic dilation (PD) at our institution between January 2012 and March 2015 was performed. Patient demographics, type of achalasia, prior treatments, pre- and post-treatment timed barium swallow (TBE) and high-resolution esophageal manometry (HREM) findings were compared between the three treatment groups. Patients who had both pre- and 2 mo post-treatment TBE or HREM were included in the final analysis. TBE parameters compared were barium column height, width and volume of barium remaining at 1 and 5 min. HREM parameters compared were basal lower esophageal sphincter (LES) pressures and LES-integrated relaxation pressures (IRP). Data are presented as mean \pm SD, median [25th, 75th percentiles] or frequency (percent). Analysis of variance, Kruskal-Wallis test, Pearsons χ^2 test and Fishers Exact tests were used for analysis.

RESULTS: A total of 200 achalasia patients were included of which 36 underwent POEM, 22 underwent PD and 142 underwent LHM. POEM patients were older (55.4 ± 16.8 years *vs* 46.5 ± 15.7 years, $P = 0.013$) and had higher BMI than LHM (29.1 ± 5.9 kg/m² *vs* 26 ± 5.1 kg/m², $P = 0.012$). More number of patients in POEM and PD groups had undergone prior treatments compared to LHM group (72.2% *vs* 68.2% *vs* 44.3% respectively, $P = 0.003$). At 2 mo post-treatment, all TBE parameters including barium column height, width and volume remaining at 1 and 5 min improved significantly in all three treatment groups ($P = 0.01$ to $P < 0.001$) except the column height at 1 min in PD group ($P = 0.11$). At 2 mo post-treatment, there was significant improvement in basal LES pressure and LES-IRP in both LHM (40.5 mmHg *vs* 14.5 mmHg and 24 mmHg *vs* 7.1 mmHg respectively, $P < 0.001$) and POEM groups (38.7 mmHg *vs* 11.4 mmHg and 23.6 mmHg *vs* 6.6 mmHg respectively, $P < 0.001$). However, when the efficacy of three treatments were compared to each other in terms of improvement in TBE or HREM parameters at 2 mo, there was no significant difference ($P > 0.05$).

CONCLUSION: POEM, PD and LHM were all effective in improving esophageal function in achalasia at short-term. There was no difference in efficacy between the three treatments.

Key words: Achalasia; Dysphagia; Heller myotomy; Peroral endoscopic myotomy; Manometry; Pneumatic dilation

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Core tip: This study evaluated and compared the efficacy of peroral endoscopic myotomy with laparoscopic Heller myotomy and pneumatic dilation in improving esophageal function in achalasia. Esophageal function was objectively assessed by timed barium esophagram and high resolution manometry at 2 mo follow-up. The results demonstrate that all three treatment modalities are effective in improving esophageal function at short term follow-up and there was no difference in efficacy between the three treatment modalities.

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INTRODUCTION

Achalasia is a rare primary esophageal motility disorder, with an incidence of about 1 per 100000 per

year^[1]. The disease is characterized by aperistalsis of the esophageal body and impaired relaxation of the lower esophageal sphincter (LES), caused by progressive destruction and degeneration of neurons in the myenteric plexus. Typical symptoms of achalasia are dysphagia, regurgitation of undigested food, retrosternal pain, and weight loss. The disease is irreversible and all the current treatments of achalasia are aimed at palliation of symptoms^[2]. Established treatment options include disruption of the LES by endoscopic pneumatic dilation (PD) and laparoscopic Heller myotomy (LHM). Both treatments are considered the "standard of care" and have similar excellent short-term results, as demonstrated in a large, randomized, controlled trial^[3]. Because of submucosal fibrosis after treatment and the natural course of the disease, symptoms can recur, leading to a need for retreatment in some patients. LHM has been shown to provide more durable long-term symptom relief than PD and is considered the preferred treatment^[4]. Recently, peroral endoscopic myotomy (POEM) is emerging as an alternative to LHM. POEM has the advantages of minimal invasiveness of an endoscopic procedure and the precision of a surgical myotomy^[5].

Both PD and LHM improve parameters of objective esophageal function, such as LES pressures on high resolution esophageal manometry (HREM), esophageal emptying on timed barium esophagram (TBE) and esophagogastric junction (EGJ) distensibility^[6]. Objective improvement in these parameters regardless of symptoms is predictive of long-term favorable response. For example, patients with LES-Integrated relaxation pressures (IRP) of > 10 mmHg after treatment were shown to have a significantly higher risk for retreatment during follow-up^[7-9]. Vaezi *et al*^[10] have shown that patients with incomplete esophageal emptying after PD on TBE had a 90% risk for treatment failure within 1 year, whereas the treatment success rate remained about 90% in patients with complete emptying. Therefore, these parameters are useful not only to objectively determine esophageal function post-treatment, but also for predicting the need for retreatments.

Since POEM is relatively new, only short- and intermediate-term treatment success rates are available. There were several studies that showed objective improvement in esophageal function assessed by HREM and TBE findings after POEM^[11-15]. Bhayani *et al*^[16], reported that improvement in HREM parameters after POEM was comparable to LHM. To date, there are several studies comparing the improvement in esophageal function between either PD and LHM or POEM and LHM. However, there are no studies comparing the outcomes between all three treatment modalities. Hence, the aim of this study was to compare objective improvement in esophageal function among achalasia patients who underwent POEM, LHM and PD at our institution.

MATERIALS AND METHODS

This study was approved by the Institutional Review Board at the Cleveland Clinic. We reviewed medical records of all adult achalasia patients who underwent one of the three treatment modalities at our institution between January 2012 and March 2015. A written informed consent was obtained from all patients prior to the treatments. Patient demographics, type of achalasia, prior treatments, pre- and 2-mo post-treatment TBE and HREM parameters were compared between the three treatment groups. All patients undergoing either POEM or LHM had TBE and HREM performed before and at two months post-treatment as part of our standard clinical practice. Most of the patients who underwent PD had TBE and HREM performed before and TBE alone performed at two months post-treatment.

LHM procedure

In our patients, LHM was performed with anterior approach and thoracic esophagus was mobilized and full-thickness myotomy was performed along distal 4-6 cm of esophagus and was extended 2-3 cm on to the gastric wall. Subsequently a partial anterior fundoplication (Dor fundoplication) was performed. Patients underwent barium swallow study next day to exclude perforation and liquid diet was initiated and gradually advanced over the next few days.

PD procedure

A standard upper endoscopy was performed under sedation by monitored anesthesia care and esophagus was cleared of any residual food debris. A guidewire was placed into the antrum and under fluoroscopic guidance, and a Rigiflex balloon (Boston Scientific, MA, United States) of either 30 mm or 35 mm diameter was passed and positioned across the gastroesophageal junction and inflated for few seconds until the "waist" was obliterated. A 30 mm balloon was used when patients underwent PD for the first time, and a 35 mm balloon was used for patients undergoing subsequent PD. All patients underwent a barium swallow post-procedure to exclude a perforation and were discharged home on clear liquid diet with gradual advancement of diet.

POEM procedure

All POEM procedures were performed under general anesthesia in an operating room using standard steps as described by Inoue *et al.*^[5]. The steps were (1) creation of a submucosal tunnel starting approximately 12 cm proximal to the LES and extending distally to about 2-4 cm into the stomach side. The submucosal tunnel was usually created on anterior esophageal wall except in post-Heller patients in whom it was created on the posterior esophageal wall; (2) Myotomy of the circular muscle fibers starting 3-4 cm distally from

the first incision and 2-4 cm into the stomach wall; and (3) Closure of the entry site of the submucosal tunnel by using endoscopic clips. Next day, patients underwent a soluble contrast swallow radiograph to exclude transmural perforations. If swallow study is unremarkable, patients were started on clear liquid diet, discharged home and were advised to advance diet gradually over the next 1-2 wk.

HREM procedure

HREM was performed by using the following protocol: a 36-channel, solid-state catheter system with high-fidelity circumferential sensors at 1-cm intervals was advanced through the nasal canal (Sierra Scientific Instruments Inc., Los Angeles, CA, United States). Pressure data of ten, 5 mL swallows of water were recorded and analyzed by using a dedicated computerized analysis system. All relevant parameters were analyzed according to the Chicago classification. Diagnostic criteria for achalasia were incomplete relaxation of LES (IRP > 15 mmHg) and aperistalsis of the esophageal body. Achalasia was classified into type I, if there was 100% peristalsis without esophageal pressurization, type II if there was pan-esophageal pressurization > 30 mmHg in $\geq 20\%$ of swallows and as type III when there were premature contractions in $\geq 20\%$ of swallows.

TBE procedure

Patients were instructed to drink the maximum volume of dilute barium sulfate contrast (45% weight in volume) that they could tolerate without regurgitation or aspiration (mostly between 100 and 250 mL) over a period of 30 to 45 s. With the patient in upright position, radiographs of the esophagus were taken at 1 and 5 min after the last swallow. Height and width of the barium column were measured using a calibrated ruler. Estimated esophageal barium volume was calculated as a simple cylinder ($\pi r^2 \times \text{height of barium column}$, $r = \text{barium width divided by } 2$).

Statistical analysis

Data are presented as mean \pm SD, median (25th, 75th percentiles) or frequency (percent). A univariable analysis was performed to assess differences between treatment groups. Analysis of variance (ANOVA) or the non-parametric Kruskal-Wallis tests were used for continuous or ordinal variables and Pearson's chi-square tests were used for categorical factors. When the overall test suggested a difference between at least 2 of the groups, post-hoc comparisons were done at a significance level of 0.017 (0.05/3 tests) to adjust for multiple comparisons. In addition, analysis of covariance was performed to assess the association between treatment and outcomes while adjusting for possible confounders. For each outcome, a logarithm transformation $\ln[(y-1) + \min(y)]$ was modeled as the dependent variable with age at time of treatment, body mass index (BMI) and having had previous treatments

Table 1 Patient characteristics *n* (%)

Factor	PD (<i>n</i> = 22)		LHM (<i>n</i> = 142)		POEM (<i>n</i> = 36)		<i>P</i> value
	<i>n</i>	Summary	<i>n</i>	Summary	<i>n</i>	Summary	
Age at diagnosis (yr)	22	47.5 ± 17.0	142	45.8 ± 15.6	36	52.6 ± 17.2	0.078 ^a
Age at current treatment (yr)	22	50.3 ± 17.9	142	46.5 ± 15.7 ³	36	55.4 ± 16.8 ²	0.013 ^a
Gender	22		142		36		0.19 ^c
Female		11 (50.0)		71 (50.0)		12 (33.3)	
Male		11 (50.0)		71 (50.0)		24 (66.7)	
Ethnicity	22		141		36		0.85 ^d
White		17 (77.3)		118 (83.7)		31 (86.1)	
Black		4 (18.2)		19 (13.5)		4 (11.1)	
Other		1 (4.5)		4 (2.8)		1 (2.8)	
BMI (kg/m ²)	22	27.1 ± 6.9	142	26.0 ± 5.1 ³	36	29.1 ± 5.9 ²	0.012 ^a
Achalasia sub-type	14		120		34		0.023 ^d
Subtype 1		5 (35.7)		30 (25.0)		13 (38.2)	
Subtype 2		6 (42.9)		82 (68.3)		18 (52.9)	
Subtype 3		2 (14.3)		1 (0.83)		3 (8.8)	
Achalasia variant		1 (7.1)		7 (5.8)		0 (0.0)	
Prior treatments							
Received any prior treatment	22	15 (68.2)	140	62 (44.3) ³	36	26 (72.2) ²	0.003 ^c
Months from last to current treatment	14	17.7 [2.3, 87.5]	54	6.3 [3.2, 28.5]	25	14.7 [6.4, 20.2]	0.29 ^b
Botulinum toxin injection	22	1 (4.5)	140	16 (11.4)	36	8 (22.2)	0.11 ^c
PD	22	9 (40.9) ²	140	19 (13.6) ^{1,3}	36	11 (30.6) ²	0.002 ^c
LHM	22	7 (31.8) ²	140	1 (0.71) ^{1,3}	36	10 (27.8) ²	< 0.001 ^c
Botulinum toxin injection and regular endoscopic balloon dilation	22	2 (9.1)	140	1 (0.71)	36	0 (0.0)	0.050 ^d
Regular endoscopic balloon dilation	22	3 (13.6)	140	34 (24.3) ³	36	2 (5.6) ²	0.031 ^c

¹Significantly different from PD; ²Significantly different from LHM; ³Significantly different from POEM. Values presented as Mean ± SD, Median [P25, P75] or N (column %). *P*-value: a = ANOVA, b = Kruskal-Wallis test, c = Pearson's χ^2 test, d = Fisher's Exact test. PD: Pneumatic dilation; LHM: Laparoscopic Heller myotomy; POEM: Peroral endoscopic myotomy.

as the independent variables. No adjustments were done for type of achalasia because (1) it was missing for > 15% of patients and (2) it is a 5 level variable. All analyses were performed using SAS version 9.4 (The SAS Institute, Cary, NC, United States) and a *P*-value < 0.05 was considered statistically significant. The statistical methods of this study were reviewed by Rocio Lopez, MS, Biostatistician from Department of Biostatistics, Cleveland Clinic, Cleveland, OH, United States.

RESULTS

A total of 200 achalasia patients were included of which 36 underwent POEM, 22 underwent PD and 142 underwent LHM. Baseline patient characteristics are summarized in Table 1. Patients who underwent POEM were significantly older compared to LHM patients (55.4 years vs 46.5 years, *P* = 0.013). POEM patients also had higher BMI compared to LHM patients (29.1 kg/m² vs 26 kg/m², *P* = 0.012). PD and POEM patients have had more prior treatments performed compared to LHM patients (68%, 72% and 44%, *P* = 0.003).

Pre-treatment and 2-mo post-treatment TBE and HREM findings in the three treatment groups are summarized in Tables 2 and 3. There was no significant difference in pre-treatment TBE and HREM parameters in all three treatments groups (*P* > 0.05). Post-treatment, there was significant improvement in TBE and HREM parameters in all three treatment groups.

Both basal LES and LES-IRP pressures improved significantly after both POEM and LHM (*P* < 0.05). HREM was not routinely performed in all PD patients post-treatment and hence that data is not available. Actual LES-IRP at 2 mo decreased to less than 10 mmHg in 66/92 patients (71.7%) in LHM group, 19/26 patients (73.1%) in POEM group and 0/3 patients (0%) in PD group (*P* not significant). TBE parameters such as barium column height, width and volume remaining at both 1 min and 5 min improved significantly in all the three treatment groups (*P* < 0.05) except column height at 1 min in TBE group (*P* = 0.11). Actual barium column height at 5 min on TBE at 2 mo decreased by more than 50% in 73/131 patients (55.7%) in LHM group, 16/34 patients (47.1%) in POEM group and 7/20 patients (35%) in PD group (*P* not significant). Eckardt symptom scores improved significantly in both POEM and LHM patients (although only 7 patients had these available both pre- and post-treatment in LHM group). Eckardt scores were not available in PD group.

Details of multivariate analysis assessing pre- and post-treatment differences in HREM and TBE parameters in all three treatment groups are shown in Table 4. The degree of improvement in TBE parameters did not significantly differ among the three treatment groups (*P* > 0.05). Similarly, there was no significant difference in improvement in HREM parameters between the POEM and LHM groups (*P* > 0.05). Only 3 patients in the PD group had HREM testing done pre- and post-treatment, hence this group was not included

Table 2 High-resolution esophageal manometry and timed barium swallow findings: Univariable analysis

Factor	PD (n = 22)		LHM (n = 142)		POEM (n = 36)		P value
	n	Summary	n	Summary	n	Summary	
Pre-treatment							
Eckardt score	2	7.0 (7.0, 7.0)	9	6.0 (5.0, 7.0)	36	6.5 (5.0, 8.0)	0.77
HREM							
Basal mean pressure (mmHg)	2	31.9 (10.6, 53.2)	86	40.5 (27.2, 51.7)	24	38.7 (27.0, 48.7)	0.89
LES-IRP pressure (mmHg)	3	29.1 (12.0, 34.5)	92	24.0 (17.5, 34.4)	26	23.6 (20.2, 33.4)	0.92
TBE							
Height in 1 min (cm)	22	10.2 (7.0, 13.6)	133	9.5 (7.2, 15.0)	34	9.8 (4.0, 14.5)	0.43
Width in 1 min (cm)	22	3.4 (2.5, 4.0)	133	3.0 (2.5, 4.0)	34	3.4 (2.0, 4.4)	0.93
Volume remaining at 1 min (cc)	22	67.3 (44.0, 126.2)	133	71.6 (41.1, 131.9)	34	52.8 (37.7, 119.2)	0.44
Height in 5 min (cm)	20	6.5 (4.0, 10.5)	131	8.0 (5.0, 12.5)	34	5.3 (2.5, 10.0)	0.063
Width at 5 min (cm)	20	2.7 (2.0, 3.6)	131	2.5 (2.0, 3.7)	34	2.5 (1.5, 4.0)	0.83
Volume remaining at 5 min (cc)	20	40.8 (15.5, 73.1)	131	49.1 (15.7, 91.6)	34	25.4 (11.3, 62.8)	0.12
2-mo post-treatment							
Eckardt score	4	4.5 (2.0, 6.0)	50	1.00 (0.00, 2.0)	36	1.00 (0.00, 2.0)	0.073
HREM							
Basal mean pressure (mmHg)	2	22.0 (18.8, 25.1)	86	14.5 (7.6, 22.7)	24	11.4 (8.2, 20.2)	0.32
LES-IRP pressure (mmHg)	3	10.8 (10.5, 19.4)	92	7.1 (3.9, 10.7)	26	6.6 (3.3, 11.1)	0.18
TBE							
Height in 1 min (cm)	22	8.0 (5.8, 11.0)	133	6.7 (4.5, 10.2)	34	6.3 (2.1, 9.5)	0.39
Width in 1 min (cm)	22	2.0 (1.5, 2.5)	133	2.0 (1.2, 2.5)	34	1.6 (0.50, 2.5)	0.28
Volume remaining at 1 min (cc)	22	25.4 (14.1, 41.7)	133	20.4 (6.0, 49.8)	34	12.8 (0.79, 47.7)	0.31
Height in 5 min (cm)	20	2.2 (0.00, 6.5)	131	2.5 (0.00, 6.2)	34	2.3 (0.00, 6.9)	0.94
Width at 5 min (cm)	20	1.05 (0.00, 2.6)	131	1.00 (0.00, 2.1)	34	0.50 (0.00, 2.0)	0.97
Volume remaining at 5 min (cc)	20	4.1 (0.00, 30.2)	131	2.7 (0.00, 21.2)	34	0.54 (0.00, 18.8)	0.98
Post - pre treatment difference							
Eckardt score	-	-	7	-6.0 (-8.0, -2.0)	36	-6.0 (-7.0, -4.0)	0.75
HREM							
Post-Pre basal mean pressure (mmHg)	2	-10.0 (-34.4, 14.5)	86	-25.1 (-36.8, -12.1)	24	-19.6 (-43.1, -11.9)	0.78
Post-Pre LES-IRP pressure (mmHg)	3	-9.7 (-23.7, -1.5)	92	-15.2 (-26.4, -8.3)	26	-14.2 (-24.5, -7.8)	0.60
TBE							
Post-Pre height at 1 min (cm)	22	-0.90 (-5.5, 1.9)	133	-2.5 (-7.0, 0.30)	34	-2.8 (-8.5, 1.5)	0.73
Post-Pre width at 1 min (cm)	22	-1.4 (-2.0, -0.30)	133	-1.00 (-2.0, -0.20)	34	-1.5 (-2.1, 0.00)	0.79
Post-Pre volume at 1 min (cc)	22	-40.2 (-81.2, -14.1)	133	-35.8 (-101.8, -10.4)	34	-29.5 (-100.7, -0.29)	0.74
Post-Pre height at 5 min (cm)	20	-0.75 (-5.4, 0.05)	131	-4.7 (-10.0, 0.00)	34	-2.0 (-7.5, 1.9)	0.069
Post-Pre width at 5 min (cm)	20	-0.90 (-2.3, 0.00)	131	-1.5 (-2.2, -0.20)	34	-1.00 (-2.4, 0.00)	0.86
Post-Pre volume at 5 min (cc)	20	-14.0 (-45.9, -2.6)	131	-31.3 (-66.1, -5.5)	34	-17.0 (-37.7, 0.00)	0.14

Values presented as Median (P25, P75) with Kruskal-Wallis tests. PD: Pneumatic dilation; LHM: Laparoscopic Heller myotomy; POEM: Peroral endoscopic myotomy; HREM: High resolution esophageal manometry; TBE: Timed barium esophagram; LES: Lower esophageal sphincter; IRP: Integrated relaxation pressure.

in the multivariate analysis on HREM.

DISCUSSION

Our study showed that all three treatment modalities for achalasia namely PD, LHM and POEM were effective in improving esophageal function evaluated at 2 mo post-treatment. All three treatments resulted in significant improvement in esophageal emptying on TBE. Both POEM and LHM led to significant decrease in LES pressures on HREM. More importantly, this is the first study that demonstrates efficacy of all three treatments and that there was no significant difference in efficacy between the three treatments on short term follow-up.

Pre and post-treatment physiologic evaluation of esophageal function in achalasia by HREM is very important to assess the improvement after treatment

and also to predict long term response. HREM parameters such as LES-IRP were shown to correlate with symptom scores of achalasia^[17,18]. Several studies in achalasia patients treated with PD and LHM have shown that the HREM parameters also predict long term need for retreatment^[6-9,19]. As such LES-IRP of greater than 10 mmHg after treatment was predictive of requiring retreatment on follow-up. In our study, LES-IRP decreased significantly after treatment in all three treatment modalities (although only 3 patients in PD group had HREM post-treatment). Post-treatment LES-IRP was only 7.1 mmHg and 6.6 mmHg in LHM and POEM groups respectively, and hence we predict our patients would have excellent long term efficacy. Teitelbaum *et al*^[12] have shown that decreased LES-IRP at 2 mo after POEM persisted at 1 year as well, which supports our long-term prediction in our POEM and LHM groups.

Table 3 Improvement in high resolution esophageal manometry and timed barium esophagram parameters in each treatment group

Factor	n	PD (n = 22)		P value
		Pre-Treatment	Post-treatment	
HREM ¹				
TBE				
Height at 1 min (cm)	22	10.2 (7.0, 13.6)	8.0 (5.8, 11.0)	0.11
Width at 1 min (cm)	22	3.4 (2.5, 4.0)	2.0 (1.5, 2.5)	< 0.001
Volume at 1 min (cc)	22	67.3 (44.0, 126.2)	25.4 (14.1, 41.7)	< 0.001
Height at 5 min (cm)	20	6.5 (4.0, 10.5)	2.2 (0.00, 6.5)	0.026
Width at 5 min (cm)	20	2.7 (2.0, 3.6)	1.05 (0.00, 2.6)	< 0.001
Volume at 5 min (cc)	20	40.8 (15.5, 73.1)	4.1 (0.00, 30.2)	0.001
		LHM (n = 142)		
Factor				
HREM				
Basal mean pressure (mmHg)	86	40.5 (27.2, 51.7)	14.5 (7.6, 22.7)	< 0.001
LES-IRP pressure (mmHg)	92	24.0 (17.5, 34.4)	7.1 (3.9, 10.7)	< 0.001
TBE				
Height at 1 min (cm)	133	9.5 (7.2, 15.0)	6.7 (4.5, 10.2)	< 0.001
Width at 1 min (cm)	133	3.0 (2.5, 4.0)	2.0 (1.2, 2.5)	< 0.001
Volume at 1 min (cc)	133	71.6 (41.1, 131.9)	20.4 (6.0, 49.8)	< 0.001
Height at 5 min (cm)	131	8.0 (5.0, 12.5)	2.5 (0.00, 6.2)	< 0.001
Width at 5 min (cm)	131	2.5 (2.0, 3.7)	1.00 (0.00, 2.1)	< 0.001
Volume at 5 min (cc)	131	49.1 (15.7, 91.6)	2.7 (0.00, 21.2)	< 0.001
		POEM (n = 36)		
Factor				
Eckardt score	36	6.5 (5.0, 8.0)	1.00 (0.00, 2.0)	< 0.001
HREM				
Basal mean pressure (mmHg)	24	38.7 (27.0, 48.7)	11.4 (8.2, 20.2)	< 0.001
LES-IRP pressure (mmHg)	26	23.6 (20.2, 33.4)	6.6 (3.3, 11.1)	< 0.001
TBE				
Height at 1 min (cm)	34	9.8 (4.0, 14.5)	6.3 (2.1, 9.5)	0.01
Width at 1 min (cm)	34	3.4 (2.0, 4.4)	1.6 (0.50, 2.5)	< 0.001
Volume at 1 min (cc)	34	52.8 (37.7, 119.2)	12.8 (0.79, 47.7)	< 0.001
Height at 5 min (cm)	34	5.3 (2.5, 10.0)	2.3 (0.00, 6.9)	0.017
Width at 5 min (cm)	34	2.5 (1.5, 4.0)	0.50 (0.00, 2.0)	< 0.001
Volume at 5 min (cc)	34	25.4 (11.3, 62.8)	0.54 (0.00, 18.8)	0.003

¹HREM data not available in PD group. Values presented as Median (P25, P75) with Wilcoxon signed rank test. PD: Pneumatic dilation; LHM: Laparoscopic Heller myotomy; POEM: Peroral endoscopic myotomy; HREM: High resolution esophageal manometry; TBE: Timed barium esophagram; LES: Lower esophageal sphincter; IRP: Integrated relaxation pressure.

Esophageal emptying assessed by a TBE is a complementary test to HREM for functional assessment of esophageal physiology. Similar to LES-IRP, post-treatment improvement in esophageal emptying is a predictor of the need for retreatment in achalasia^[3,10]. Vaezi *et al*^[10] have shown that successful esophageal emptying, defined as at least 50% reduction of barium column after treatment, was associated with long-term remission of symptoms. In that study, patients with sub-optimal esophageal emptying after PD required retreatments on long-term follow-up. In our study, barium column height decreased by more than 50% in all three treatments groups at 2 mo follow-up, reinforcing the efficacy of all three treatments. In our POEM patients, Eckardt scores improved significantly paralleling the improvement in LES pressures. However, we suspect to have had similar decrease in Eckardt scores in LHM and PD groups if they were available, since LES pressures decreased significantly in those patients as well. There was also no significant difference in esophageal emptying between the three treatment groups, reinforcing comparable efficacy of

all three treatment modalities.

In our study, there were some notable differences in patient characteristics among PD, LHM and POEM groups. Patients in POEM and PD treatments groups were older, had higher BMI, and more likely to have received prior treatments. This is likely due to the selection bias of a particular treatment modality for different patients at our institution. Usually younger patients and fit surgical candidates were offered LHM due to its well established long term durability record. Older and somewhat less ideal surgical candidates were preferentially offered either PD or POEM. Initially the following subsets of patients were considered for POEM: (1) Obese patients, patients with upper abdominal surgical scars *i.e.*, hostile abdomen and those with prior failed LHM, in whom LHM is technically difficult or less desirable; and (2) patients over 60 years of age (not younger patients since long term cumulative effects of gastroesophageal reflux disease (GERD) after POEM are not yet known). However, we do not believe that this selection bias should have affected the results of our study significantly.

Table 4 High resolution esophageal manometry and Timed barium esophagram findings: Adjusted analysis¹

Outcome	PD	LHM	POEM	P value
Eckardt score	²	-5.7 (-6.7, -4.5)	-5.6 (-6.1, -5.2)	0.94
HREM				
Post-Pre basal mean pressure (mm Hg)	²	-27.5 (-30.3, -24.5)	-33.1 (-38.0, -27.6)	0.084
Post-Pre LES-IRP pressure (mm Hg)	²	-20.1 (-22.2, -17.9)	-20.9 (-24.7, -16.5)	0.76
TBE				
Post-Pre height at 1 min (cm)	-2.7 (-5.1, -0.05)	-4.6 (-5.5, -3.7)	-5.4 (-7.1, -3.5)	0.21
Post-Pre width at 1 min (cm)	-1.4 (-1.9, -0.77)	-1.3 (-1.5, -1.03)	-1.7 (-2.2, -1.2)	0.28
Post-Pre volume at 1 min (cc)	-81.8 (-112.4, -44.3)	-79.3 (-92.7, -64.8)	-95.6 (-119.4, -67.6)	0.58
Post-Pre height at 5 min (cm)	-5.8 (-7.7, -3.7)	-6.0 (-6.8, -5.2)	-5.8 (-7.3, -4.1)	0.95
Post-Pre width at 5 min (cm)	-1.6 (-2.4, -0.74)	-1.5 (-1.8, -1.1)	-1.9 (-2.5, -1.3)	0.47
Post-Pre volume at 5 min (cc)	-68.2 (-89.9, -43.5)	-51.2 (-60.9, -41.0)	-64.6 (-82.0, -45.3)	0.28

¹ANOVA analysis was used to obtain adjusted means. A logarithm transformation of each outcome [$\ln(y - 1 + \min(y))$] was modeled as the outcome variable with age at time of treatment, BMI and having had previous treatments as the independent variables. ²Data not available Only 3 patients in PD group had HREM testing done both pre- and post-treatment, hence this group was not included in the models. Values presented as mean (95%CI). PD: Pneumatic dilation; LHM: Laparoscopic Heller myotomy; POEM: Peroral endoscopic myotomy; HREM: High resolution esophageal manometry; TBE: Timed barium esophagram; LES: Lower esophageal sphincter; IRP: Integrated relaxation pressure.

There are some limitations in our study including its retrospective design and only short-term follow-up. The details of patients' symptoms such as Eckardt scores were not available in all our patients except in the POEM group. Only 3/22 patients had HREM after treatment in the PD group. Details about GERD, a common adverse effect of any achalasia treatment, were not available and hence were not included in this study. It is also beyond the scope of this paper and we acknowledge it as one of the limitations of our study. Evaluation of esophagogastric junction (EGJ) distensibility by EndoFlip is another parameter being used for assessing esophageal physiology and is a useful predictor of treatment outcomes^[6]. EGJ distensibility was however, not assessed in our patients. The main strength of our study lies in the real world scenario of treating patients with established achalasia and a large number of patients in the study. All patients had multi-disciplinary clinical evaluation by gastroenterologists, thoracic surgeons and radiologists, along with TBE and HREM before and after treatment. This is also the first study which compared the efficacy of all three standard treatments of achalasia in a large number of patients.

In conclusion, this study shows that all three treatments of achalasia namely POEM, LHM and PD lead to improvement in esophageal function as assessed by HREM and TBE in the short-term. These results support the selection of any of the three treatment modalities based on patient characteristics and availability of local expertise to perform these procedures. Larger, prospective studies with homogeneous patient populations and longer follow-up are required to compare the efficacy of these treatment modalities in achalasia.

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United States.

COMMENTS

Background

Achalasia is a primary esophageal motility disorder characterized by esophageal aperistalsis and impaired relaxation of lower esophageal sphincter. Standard treatments are palliative and include laparoscopic Heller myotomy (HLM) and endoscopic pneumatic dilation (PD). Recently peroral endoscopic myotomy is rapidly emerging as a standard treatment as well. This study evaluated and compared the efficacy of peroral endoscopic myotomy vs other standard treatments of achalasia in improving esophageal function.

Research frontiers

Peroral endoscopic myotomy is gaining popularity due to its minimal invasiveness of an endoscopic procedure and high precision of a surgical myotomy. There are several studies comparing peroral endoscopic myotomy with either PD or HLM. This study compared the efficacy of all three treatment modalities in improving esophageal function. The study findings help the peers in appropriate selection of each treatment modality based on local expertise and availability.

Innovations and breakthroughs

Recent innovations in the achalasia include emergence of peroral endoscopic myotomy as a standard treatment modality. Several studies have shown its effectiveness in palliation of symptoms comparable to other treatments such as PD and HLM. This study evaluated and compared the efficacy of all three standard treatments in improving esophageal function objectively by timed barium esophagram and high resolution esophageal manometry. Peroral endoscopic myotomy was effective and was comparable to other treatments in improving esophageal function in the short term in patients with achalasia.

Applications

This study results suggested that peroral endoscopic myotomy is effective not only in proving symptoms but also objective esophageal function in achalasia similar to PD and HLM. Furthermore, the study findings have practical implications in the sense that selection of one of the three treatment modalities may be done based on local expertise and patient choice.

Terminology

Achalasia is rare primary esophageal disorder characterized by esophageal peristalsis and impaired relaxation of lower esophageal sphincter. Treatment of achalasia is aimed at palliation of symptoms by disruption of lower esophageal sphincter. Standard treatments include endoscopic PD, HLM and recently

emerging incisionless peroral endoscopic myotomy.

Peer-review

There is paucity of data comparing the efficacy of all three treatment modalities of achalasia namely HLM, PD and peroral endoscopic myotomy in improving objective esophageal function. This study showed that all three treatments modalities are effective and comparable in the short term. These findings have important practical implications in the treatment of patients with achalasia.

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