J Gastrointest Surg (2016) 20:1789–1796
DOI 10.1007/s11605-016-3232-x

ORIGINAL ARTICLE

A Matched Comparison of Per Oral Endoscopic Myotomy to Laparoscopic Heller Myotomy in the Treatment of Achalasia

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Received: 24 May 2016 / Accepted: 2 August 2016 / Published online: 11 August 2016

Abstract
Background Per oral endoscopic myotomy (POEM) is increasingly utilized to treat patients with achalasia. Early results have demonstrated significant improvement of symptoms, but there are concerns about postoperative reflux. With only limited comparative data available, we sought to compare POEM to laparoscopic Heller myotomy (LHM) with partial fundoplication.
Methods This is a retrospective review of 42 POEM and 84 LHM patients undergoing primary myotomy for achalasia. Patients were matched by achalasia type, by Eckardt and dysphagia scores, and by quality of life (QOL) metrics. Analysis at 6–12-month follow-up evaluated these metrics, PPI use, pH, manometric, and endoscopic data.
Results We matched 25 patients with achalasia types I (6), II (13), and III (6). Follow-up was longer for LHM at 158.1 (36.5–272.9) weeks versus 36.2 (22.2–41.2) weeks ($p = 0.001$). Eckardt scores, QOL metrics, and dysphagia significantly improved in both groups. DeMeester scores and total percent time less than 4 were abnormal in both groups and comparable ($p = 0.925$ and $p = 0.838$). Esophagitis was seen in 53.4 % (POEM) and 31.6 % (LHM) (Yates' $p = 0.91$), and PPI use was equivalent at 36 %.
Conclusion Early clinical outcomes are excellent with POEM and comparable to the standard of care LHM. Long-term follow-up is required as concerns for reflux persist.

Keywords Achalasia · Esophagus · Gastroesophageal reflux · Fundoplication · Endoscopy · POEM

Introduction

Achalasia is a rare disease of the esophagus with an incidence ranging from 0.6 to 1.6 per 100,000 that is characterized by absent peristalsis of the esophageal body and lower esophageal sphincter dysfunction due to inflammatory degeneration of the myenteric plexus.[1] Clinically, patients with achalasia present with progressive solid and liquid food dysphagia, weight loss, and regurgitation. There is no known cure for achalasia, and therapies have been directed at disrupting the lower esophageal sphincter to reduce its pressure and thus enable more effective swallowing. Until recently, the two most comparable and effective therapies were pneumatic dilation and laparoscopic Heller myotomy (LHM) with or without fundoplication.[2]

Recently, this standard has been challenged by the introduction of per oral endoscopic myotomy (POEM). POEM has been rapidly introduced into clinical practice around the world after promising initial reports.[3, 4] A review of early single-center case series has demonstrated that POEM is feasible in the treatment of achalasia and other dysmotility disorders[5] and results in significant improvement in swallowing function with a low complication rate and minimal morbidity.[6–8] The most significant concern is the risk and degree to which patients will experience gastroesophageal reflux disease (GERD) since POEM is not followed by a fundoplication. In

Oral Presentation
Digestive Disease Week/SSAT
May 24, 2016, San Diego, CA, USA

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the largest POEM series, the rate of endoscopic esophagitis after POEM is greater than 56 %.[9] However, in the limited number of studies comparing LHM and POEM, the rate and severity of GERD has been similar between the two.[10, 11] Our objective was to compare our LHM with fundoplication and POEM experiences in terms of clinical and objective outcomes with a focus on reflux rates and complications to provide additional comparative data to the POEM experience.

Materials and Methods

We performed a retrospective, single-center review of a prospectively collected database of patients with idiopathic achalasia undergoing surgery at Swedish Medical Center from March 2004 to March 2016. We included consecutive patients who underwent primary LHM with fundoplication or POEM. We included only achalasia types I, II, and III. We excluded patients with other dysmotility disorders such as esopha gogastric junction (EGJ) outflow obstruction, jackhammer esophagus, or diffuse esophageal spasm (DES); patients with less than 6 weeks of follow-up, prior myotomies, and robotic myotomies; and patients less than 18 years of age. Patients that could not be matched were also excluded from analysis. The institutional review board of Swedish Medical Center approved this study. Patients were informed that their de-identified data would be included in our review board-approved esophageal database. Individual patient consent was waived due to the limited risk to any individual patient and the retrospective analysis.

After patients were identified from the database and charts reviewed, patients were matched according to achalasia subtype, Eckardt score, QOLRAD score, Dysphagia Severity score, and GERD-HRQL score in descending order. Eckardt score was the second matching factor, and we accepted a score variance of one to allow for adequate recruitment. Patients were compared by their QOLRAD, Dysphagia Severity, and GERD-HRQL scores, and the most congruent pairs were matched for analysis.

Our primary outcomes were the subjective response to surgery as measured by four subjective metrics: Eckardt score, QOLRAD (Quality of Life in Reflux and Dyspepsia) score, GERD-HRQL (GERD Health-Related Quality of Life questionnaire) score, and Dysphagia Severity score and the objective evidence of reflux as determined by pH testing and esophagitis on upper endoscopy. Our secondary outcomes were morbidity, re-intervention rates, proton pump inhibitor (PPI) use, and manometric data.

Patient Evaluation

All patients underwent a thorough history and physical as well as symptom assessment by standardized and validated quality of life (QOL) tests pre- and postoperatively at 2 weeks, 6 weeks, 6 months, and 1 year. Preoperative assessment included upper endoscopy, timed barium swallow, and manometry. The majority of patients were evaluated with high-resolution manometry and classified according to the Chicago classification into achalasia types I, II, and III. A few patients in the LHM group underwent standard pull through manometry and were classified in retrospect into achalasia types I, II, and III when sufficient data was available. Postoperatively, patients were requested to undergo the same objective tests between 6 and 12 months after myotomy.

The Eckardt score was used as the primary criterion for establishing the severity of achalasia. This cumulative score ranges from 0 to 12 with a lower score indicating minimal severity. It is based on four metrics—weight loss, dysphagia, retrosternal chest pain, and regurgitation. The frequency of each symptom (none, occasionally, daily, or with each meal) and the extent of weight loss (none, less than 5 kg, between 5 and 10 kg, and more than 10 kg) are scored from 0 to 3. QOLRAD is a comprehensive 25-item questionnaire for patients with gastroesophageal reflux disease or upper esophageal symptoms.[12] It assesses the impact of upper gastrointestinal symptoms on five major components that influence QOL—vitality, sleep, food choices, physical functionality, and social functionality. Scores range from 1 to 7, and a higher score is indicative of a better QOL. The GERD-HRQL score is a disease-specific score that measures the severity of GERD.[13] It consists of 10 questions, each revolving around symptoms of heartburn and potential side effects of GERD or surgery such as dysphagia and bloating. This score is based on a Likert scale that ranges from 0 to 5 for each question, making for results between 0 and 50. Lower scores are more reflective of a better QOL. Lastly, to assess the swallowing ability, a modified Dakkak Dysphagia Severity score was utilized.[14] It grades the patient's ability to ingest varying consistencies of food ranging from thin and thick liquids to soft foods, hard fruits, and even tough to swallow foods like breads and meats. The score ranges from 0 to 45, and a higher score is indicative of better swallowing and less dysphagia.

Surgical Techniques

All patients were prepared with a full liquid diet beginning 3 days before surgery and clear liquids for the 24 h immediately before surgery. They received nystatin 100,000 units swish and swallow QID for 3 days before surgery. POEM patients also received a single dose of dexamethasone 6 mg IV at the induction of anesthesia.

POEM procedures were performed in the operating room using the stepwise approach previously described.[15] Briefly, after an initial endoscopy to determine the key landmarks, an endoscopic over-tube (US Endoscopy, Mentor, OH) was placed followed by insertion of the functional lumen imaging

catheter, Endoflip (Crospon, Dangan, Ireland), to measure baseline compliance and distensibility measurements. A mucosal lift was performed with 3–4 mL dilute methylene blue 5 cm above the anticipated myotomy. A 1.5-cm mucosotomy was performed at the 2 o'clock position, and the submucosal space was entered. Dissection down to the gastroesophageal junction (GEJ) was performed with the hybrid waterjet knife (Erbe, Marietta, GA). The tunnel was taken 2 cm past the GEJ and its extent and location confirmed via a pediatric endoscope, which was passed alongside the working endoscope in the native esophagus and placed in retroflexion while the working endoscope was in the tunnel. The inner circular musculature was divided from 3 to 4 cm above to 2 cm below the GEJ. The adequacy of the myotomy was confirmed by endoscopy and endoluminal catheter measurements. The muco sotomy was then closed with endoscopic clips or suturing. Peak airway pressures were followed closely throughout the procedure, and Veress needle decompression was performed when patients developed peak airway pressures >35 mmHg and abdominal distension.

LHM was performed in low lithotomy and reversed Trendelenburg with five incisions. The esophageal hiatus was entered after transection of the pars flaccida at the 10 o'clock position adjacent to the right crus. The anterior mediastinal dissection was continued around to the 2 o'clock position to expose the esophagus and vagus nerve. The anterior fat pad was reflected off of the esophagus including the anterior vagus nerve. Once the GEJ was identified, the myotomy was performed with electrocautery along the 1 o'clock position, extending 4 cm above the GEJ and 2 cm onto the gastric cardia in a slight hockey stick configuration towards the greater curve. Adequacy of the myotomy was confirmed via endoscopy, and a Dor fundoplication was created by bringing the apex of the gastric myotomy to the apex of the esophageal myotomy. Three sutures were placed with two from the left crural edge at the 1 and 3 o'clock positions to the left edge myotomy and then to the anterior edge of the gastric myotomy and one from the opposite edge of the stomach to the myotomy edge and the right crus at the 11 o'clock position. A final suture goes from the stomach edge to the myotomy at the 9 o'clock position. If a Toupet fundoplication is used, the short gastric arteries are divided and the hiatus closed loosely. Then, the posterior fundus is marked 6 cm along the greater curve and a making suture of 2-0 silk placed one third of the way posterior. The posterior fundus was brought through the retro esophageal window and shoe-shined with the anterior fundus. The edge of each fundus is sutured to the corresponding myotomy edge with three, 2-0 silk sutures.

Statistical analysis was performed with SPSS software (IBM Analytics, Armonk, NY, USA). Continuous variables were compared with Student's t test. Categorical variables were compared using chi-square tests. A p value of less than 0.05 was considered statistically significant.

Results

We identified 42 patients who underwent POEM from July 2014 through March 2016 and excluded 13 patients (Fig. 1) due to insufficient follow-up,[5] prior myotomies,[4] and diagnosis other than achalasia[3] and one due to missing preoperative manometry. We also identified 84 patients who underwent LHM with fundoplication from March 2004 through March 2016. The 29 POEM patients were then matched according to Eckardt and the three QOL metrics to patients undergoing LHM. Four POEM patients had adequate follow-up but were unable to be matched accordingly due to a lacking counterpart in the LHM group leaving 25 for comparison.

The two groups were comparable in age, gender, and ASA class. BMI was significantly lower in the LHM group

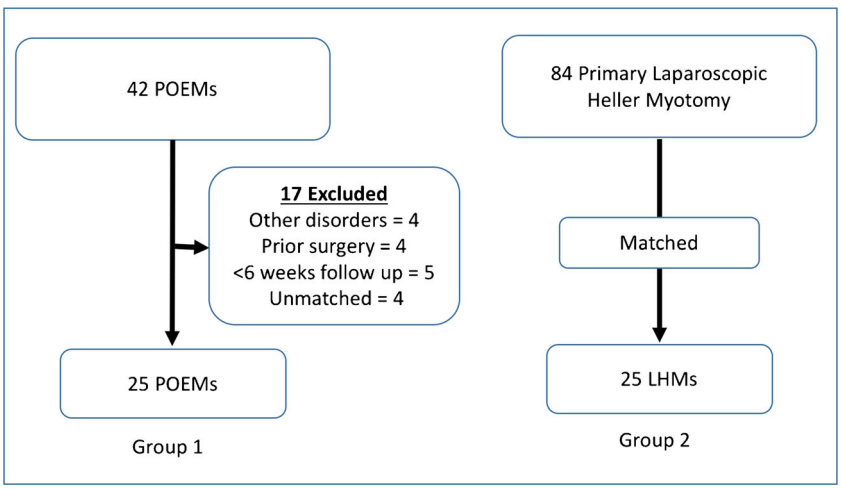

Fig. 1 Inclusion

Table 1 Demographics

Median (IQR)	POEM	LHM	*p* value
Age	59 (55–62)	54 (39–66)	0.316
Gender	13 M/12 F	12 M/13 F	0.778
BMI	25.1 (23–30.8)	23.6 (20.3–26.5)	0.049
ASA class	1 = 12 % 2 = 56 % 3 = 32 %	1 = 36 % 2 = 46 % 3 = 18 %	Yates' 0.541
Achalasia			
Type I Type II	6 13	6 13	NA
Type III	6	6	

($p = 0.049$) (Table 1). In the LHM group, Dor fundoplication was performed in 18 and Toupet fundoplication in 7 cases.

Since matching was based on preoperative Eckardt scores and all three QOL metrics, they did not differ between groups (Table 2). The average preoperative Eckardt score was 6.6 (±2.3), QOLRAD was 3.9 (±1.4), and Dysphagia Severity was 13.8 (±11.3). Median follow-up was significantly longer in the LHM group at 158.1 weeks (IQR 36.5–272.9) versus the POEM group at 36.2 weeks (IQR 22.2–41.2) ($p < 0.001$). Treatment success, as based on Eckardt score less than 3, was 91 % (POEM) and 84 % (LHM) ($p = 0.444$). On follow-up, all four metrics, Eckardt, Dysphagia Severity, QOLRAD, and GERD-HRQL scores, significantly improved in both groups and outcomes were comparable.

All patients in the POEM group underwent successful endoscopic myotomy. There were no major adverse events. One patient in the POEM group required stent placement for an intraoperative mucosotomy at the GEJ in the POEM group. The stent was successfully removed after 2 days, and barium esophagogram did not show a leak. Needle decompression of the abdominal distension was performed in 13 patients (52 %). There were seven inadvertent mucosotomies in the POEM group. These were all identified intraoperatively and closed without further consequence. In the LHM group, one patient underwent revision on POD 2 for an incomplete myotomy. There were three inadvertent mucosotomies in the LHM group ($p = 0.157$) also identified intraoperatively and closed without further consequence. Operative time was 152.3 min (±45.2) in the POEM group and 171.1 min (±34.9) in the LHM group (p value = 0.133).

Postoperative 48-h pH testing was performed in 33.3 % of POEM and 27.7 % of LHM patients ($p = 0.575$). Of these studies, 50 % in the POEM group were abnormal (DeMeester score >14.7) versus 30 % in the LHM group ($p = 0.369$). The average DeMeester score and total percent time less than 4 were comparable at 36.0 (POEM) and 34.2 (LHM) and 9.5 % (POEM) and 10.85 % (LHM), respectively. Interestingly, upright time was more than doubled in the LHM group, but this did not reach statistical significance ($p = 0.395$) (Fig. 2). When we examined the extent of upright and supine reflux in those patients that had abnormal pH studies, we found a trend in the POEM group towards having more supine reflux ($p = 0.06$) although absolute values did not differ between groups (Fig. 3).

Postoperative upper endoscopy was performed in 50 % (POEM) and 73 % (LHM) of patients ($p = 0.087$). On these studies, esophagitis rates were noted to be 53.8 % (POEM) and 31.6 % (LHM) with an equal distribution between LA grades A, B, and C (Yates' p value = 0.910) (Table 3). PPI use was equal between both groups at 34.6 %.

Preoperative and postoperative manometric findings can be seen in Table 4. Initial lower esophageal sphincter (LES) length, LES basal pressure, and residual pressures were comparable between groups. All prior mentioned metrics significantly decreased for the POEM group whereas LES basal pressure and LES residual pressure significantly decreased for the LHM group. LES length decreased in the LHM group, but this was not statistically significant. There was a trend towards lower resting pressures in the LHM group at 12.67 mmHg versus POEM at 20 mmHg ($p = 0.055$). Both groups had normalization of the residual pressures.

Table 2 Eckardt score and quality of life metrics

Mean (SD)	POEM		LHM		Between groups *p* value
Eckardt (pre/post)	6.5 (2.48)	1.04 (1.36)	6.6 (2.1)	1 (1.32)	Pre = 0.883
	$p = <0.001$		$p = <0.001$		Post = 0.911
QOLRAD (pre/post)	4.07 (1.51)	6.4 (1.08)	3.68 (1.39)	6.57 (0.74)	Pre = 0.423
	$p = <0.001$		$p = <0.001$		Post = 0.542
DSS (pre/post)	12.86 (12.54)	37.33 (9.33)	14.6 (10.3)	37.66 (10.59)	Pre = 0.646
	$p = <0.001$		$p = <0.001$		Post = 0.938
GERD-HRQL (pre/post)	17.2 (10.15)	5.35 (7.39)	21.71 (14.37)	4.15 (5.47)	Pre = 0.279
	$p = <0.001$		$p = <0.001$		Post = 0.546

DSS Dysphagia Severity score

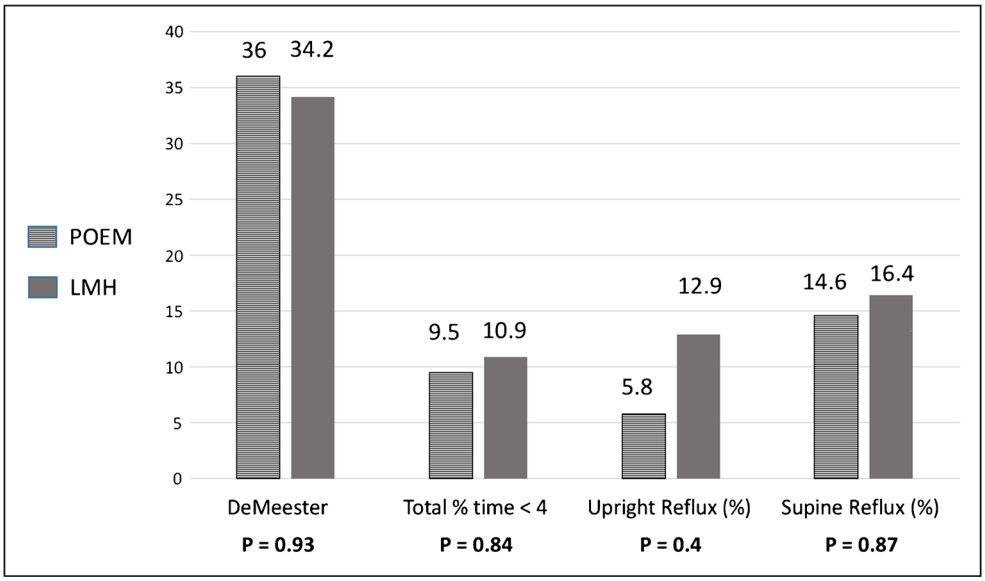

Fig. 2 pH data in all POEM and Heller patients

Discussion

There are two major findings in this study. The first is that patients with achalasia undergoing POEM or LHM with fundoplication have significant and comparable palliation of dysphagia as measured by Eckardt and Dysphagia Severity scores. In studies comparing these two procedures, similar changes in the Eckardt scores are also seen from preoperative scores of 6 or 7 down to 1 or 2 after both procedures.[10, 16] The degree of improvement is similarly seen when POEM is examined separately. In a single-center study of over 500 patients who underwent POEM, Eckardt scores improved from 6 (IQR 5–8) to 1 (IQR 0–2) ($p = <0.001$) at 3 years.[9] A recent meta-analysis of comparative studies between POEM and LHM identified 486 patients, 196 POEM and 290 LHM, and showed that there was no difference in improvement of Eckardt scores between the two groups (difference in means −0.659, 95 % CI −1.70 to 0.38, $p = 0.217$).[17] Although there is published evidence that POEM may have more favorable early outcomes in comparison to LHM, with Eckardt scores

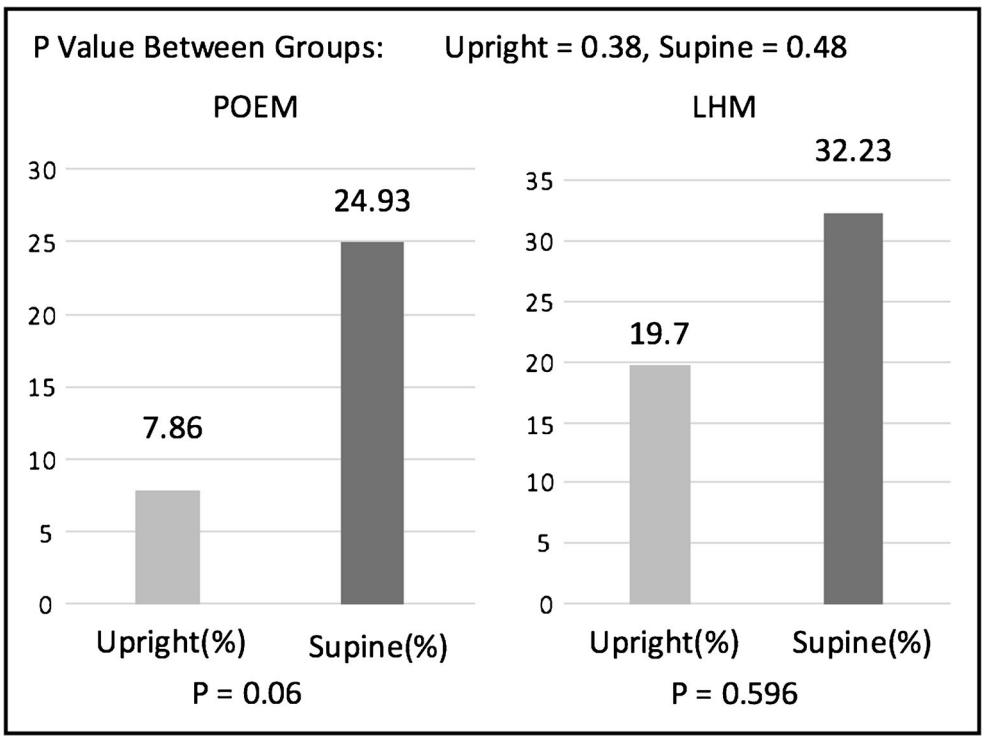

Fig. 3 Upright and supine reflux in pH-positive patients

Table 3 Esophagitis rates

	POEM	LHM	*p* value
EGD	(*N* = 13)	(*N* = 19)	0.087
Esophagitis			
None	6 (46.2 %)	13 (68.4 %)	Yates' 0.910
LA A	3 (23.1 %)	2 (10.5 %)	
LA B	2 (15.4 %)	2 (10.5 %)	
LA C	2 (15.4 %)	2 (10.5 %)	

being 0.8 versus 1.8 ($p = 0.001$), by 6 months of follow-up, there does not appear to be a difference and both groups have comparable Eckardt scores. [10]

The second major finding, and perhaps more important, in this study was that after POEM and LHM with fundoplication, patients have similar GERD-HRQL scores and objective postoperative testing with abnormal DeMeester scores and percent time pH <4. These results are similar and consistent with recently published data on POEM where esophagitis rates have been quoted as high as 63 % and pH positive rates have ranged from 38 to 46 %.[7, 18] In the studies that have directly compared POEM to LHM, the reflux rates have been inconsistent in their description, with one study showing 39 % of POEM patients had a positive postoperative pH study whereas 32 % of LHM had a positive study ($p = 0.7$). Another smaller study documented that 26 % of LHM patients compared to 15.2 % of POEM patients had symptomatic GERD ($p = 0.311$). However, the comparative studies are all limited by small numbers, a large series is likely to magnify these small differences, and it is possible they will be more significant. In fact, in a recent meta-analysis, there was a significant trend towards reduction in symptomatic GERD rates favoring LHM (OR = 1.81, 95 % CI 1.11–2.95, $p = 0.017$)[17] and may reflect a subtle difference that we were not able to detect with a small sample size.

Despite these encouraging initial results, the concern for long-term outcomes and reflux rates remain at the forefront of the POEM discussion. With multiple recent reports having raised public concern about long-term use of PPIs and the known risks of esophageal cancer with long-standing reflux, our treatment goal should be to keep reflux rates at a minimum while palliating the patients' dysphagia. The beneficial effect of the fundoplication can be seen when analyzing the data of transthoracic and laparoscopic myotomies performed without a fundoplication, as these patients exhibit reflux rates of 47.6 to 60 %.[19, 20] Comparatively, adding an anterior Dor fundoplication after laparoscopic myotomy reduced the rate of pathologic reflux from 48 to 9 % in a recent randomized trial.[19] In this trial, myotomy with fundoplication resulted in a postoperative DeMeester score of 6.5 (compared to 31.5 without a fundoplication). However, when counseling patients about the choices of procedure, it is important to recognize that even though fundoplication reduces GERD, a reasonable number of patients will still have GERD despite undergoing partial fundoplication.

We observed that patients are often asymptomatic as seen by the low GERD-HRQL score in both of our groups yet there was a high proportion with objective evidence of GERD. In long-term studies, only 21.3 % of patients who underwent POEM complained of GERD symptoms[9] and up to 53.8 % of patients with positive pH studies are found to be asymptomatic.[21] This is likely reflective of the insensate esophagi that are encountered in advanced achalasia. Because of this discordance with symptoms and objective testing, we advocate postoperative pH testing in all patients with achalasia for several reasons. First, although the treatment of acid reflux is fairly well tolerated by patients, there are increasing concerns for serious side effects with long-term PPI use.[22, 23] Magnesium and vitamin deficiencies as well as osteoporosis and fractures,[24] increasing rates of clostridium difficile infections,[25] and correlations with cardiac[22, 26] and renal disease[23] as well as possibly dementia have been associated with prolonged PPI use.[27] Confirmatory pH testing postoperatively ensures that patients who have GERD regardless of symptoms are treated appropriately and if after POEM could undergo partial fundoplication. Second, failure to

Table 4 Manometric data

Mean (SD)	POEM (*N* = 7)		LHM (*N* = 8)		Between groups *p* value
LES length (pre/post)	3.57 (0.98)	1.91 (0.83)	3.12 (1.1)	2.34 (0.93)	Pre = 0.206
	$p = <0.001$		$p = 0.155$		Post = 0.439
LESP (pre/post)	46.08 (18.56)	20.03 (5.84)	40.86 (28.86)	12.67 (7.63)	Pre = 0.463
	$p = <0.001$		$p = <0.001$		Post = 0.055
LESrP (pre/post)	31.3 (17.01)	11.67 (6.53)	23.93 (18.5)	9.64 (7.14)	Pre = 0.161
	$p = <0.001$		$p = <0.001$		Post = 0.574

LESP lower esophageal sphincter pressure, *LESrP* lower esophageal residual pressure

identify and control or limit ongoing reflux insults to the esophageal mucosa combined with poor bolus clearance is a setup in the short term for stricture formation and in the longer term for the development of Barrett's esophagus and esophageal cancer.[28]

There are several limitations to our study. First and foremost, this is a retrospective study with a small patient cohort, which is prone to type II errors. Second, our postoperative objective manometric and pH data was incomplete. Third, patient follow-up can be difficult for this group of patients who have already undergone multiple investigations and procedures and are usually feeling improved.

Conclusion

Patients undergoing POEM or LHM with partial fundo plication for achalasia will have a significant improvement in the ability to swallow and leads to an overall improvement in the quality of life with high patient satisfaction. Its effect and efficacy on the LES as measured by manometry shows improved relaxation while maintaining a normal LES resting pressure. Although PPI use was equivalent and DeMeester score and percent time less than 4 were comparable between groups, there remains concern for persistent reflux in both groups which warrants discussion with the patient preope ratively.

Acknowledgments Dr. Schneider's fellowship is supported by the Ryan Hill Foundation and the Foundation for Surgical Fellowships.

Drs. Schneider, Louie, Warren, Farivar, Schembre, and Aye have substantially contributed towards, reviewed, and approved this paper. They agree to be accountable towards ensuring accuracy and integrity of this work.

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