Thieme

Per-oral endoscopic myotomy for achalasia cardia: outcomes in over 400 consecutive patients

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ABSTRACT

Background and study aims Per-oral endoscopic myotomy (POEM) has emerged as an efficacious treatment modality for the management of achalasia cardia (AC) and non-achalasia spastic esophageal motility disorders. Initial results are encouraging. We analyzed the safety and efficacy of POEM in a large cohort of patients with AC.

Patients and methods The data from patients who underwent POEM (from January 2013 to June 2016) was prospectively collected and analyzed. Clinical success was defined as Eckardt score ≤ 3 after POEM procedure. Objective parameters including high-resolution manometry (HRM) and timed barium swallow (TBS) were analyzed and compared before and after the procedure. Gastroesophageal reflux was analyzed using 24-hour pH impedance study and esophagogastro-duodenoscopy.

Results A total of 408 patients (mean age 40 years, range 4 – 77 years) underwent POEM during the specified period. POEM could be successfully completed in 396 (97 %) patients. Clinical success rates at 1, 2 and 3 years were 94 %, 91 % and 90 %, respectively. Mean Eckardt score was 7.07 ± 1.6 prior to POEM and 1.27 ± 1.06 after POEM (P = 0.001) at 1 year. Significant improvement in esophageal emptying on TBE (> 50 %) was documented in 93.8 % patients who completed 1-year follow up. Pre-procedure and post-procedure mean lower esophageal sphincter pressure was 45 ± 16.5 mmHg and 15.6 ± 6.1 mmHg, respectively (P = 0.001). Technical and clinical success were comparable in naïve vs prior treated cases (97.3 % vs 96.8 %, P = 0.795) (95.7 % vs 92.6 %, P = 0.275). GERD was documented in 28.3 % patients with 24-hour pH-impedance study and erosive esophagitis was seen in 18.5 % of patients who underwent POEM.

Conclusions POEM is safe, effective and has a durable response in patients with achalasia cardia. Prior treatment does not influence the outcomes of POEM.

Introduction

Achalasia cardia (AC) is the most common primary motility disorder of the esophagus, characterized by absent esophageal peristalsis along with incomplete relaxation of lower esophageal sphincter (LES). The causative mechanism of AC is not well known. However, genetic predisposition along with autoimmunity to some viral agent (e.g herpes virus) may be responsible for the degeneration of myenteric neurons [1]. No currently available treatment options result in regeneration of myenteric neurons to bring back esophageal motility. However, lowering LES pressure can significantly reduce symptoms and improve quality of life. To achieve this outcome (LES pressure reduction), therapeutic techniques have been modified from time to time. Graded pneumatic balloon dilatation (PBD) has replaced conventional one-time dilatation and open Heller's myotomy has cleared the way for laparoscopic Heller's myotomy (LHM) with fundoplication.

Young patients (< 40 years) and those with spastic achalasia (type III AC) do not respond as well to PBD [2, 3]. Moreover, repeated dilatations may be required in these patients. LHM is efficacious with durable response [4, 5]. However, it is invasive

with definite morbidity. Per-oral endoscopic myotomy (POEM) has emerged as a minimally invasive endoscopic treatment modality with excellent short-term results [6–8]. However, the experience is limited when compared to PBD or LHM. Long-term efficacy and incidence of gastroesophageal reflux disease (GERD) after POEM have not been well studied.

In this study we analyzed medium-term outcomes with POEM in a large cohort of patients with AC at a single tertiary care center.

Patients and methods

In this study we analyzed the prospectively collected data on all patients who underwent POEM at our center. All eligible patients presenting with AC were offered POEM from January 2013 to March 2016.

Exclusion criteria included patients unfit for general anesthesia, presence of esophageal varices, oral anti-coagulation and very young children (<4 years or <15 kg weight).

Diagnosis and sub-typing of AC were established using high-resolution manometry (HRM). Esophagoduodenoscopy (EGD) and timed barium swallow (TBS) were done prior to POEM in all patients. In the presence of esophageal candidiasis, oral antifungals were given for 7 to 10 days prior to POEM. Symptom severity was recorded using Eckardt score which has scores for dysphagia, regurgitation, chest pain, and weight loss (range 0 to 12).

All intraoperative events including procedure time and complications were recorded prospectively. All patients were kept nil per oral for 1 day after the procedure. Thin barium esophagogram was done on the second postoperative day to look for any leak. Patients were started on liquid diet on Day 2 and on a soft diet from Day 3 onward.

All patients were evaluated for symptoms (Eckardt score) at pre-specified intervals: 6 months, 1 year, 2 years, and 3 years after the procedure. Objective parameters including TBS, HRM and EGD were recorded in addition to symptom assessment at the 1-year visit.

Objective assessment of GERD was done by 24-hour pH-impedance at 3 months. Patients were asked to stop any PPI medications 5 days before the proposed date of the test. On the test day calibrated pH probe was placed transnasally, which was connected to a pH data acquisition device (ZepHr pH monitor with ComforTEC disposable catheters, Sandhill Scientific, Highlands Ranch, CO, USA). The pH measurements were recorded for 24 hours. Acid reflux episode was defined as a pH fall of less than 4. Twenty-four-hour esophageal acid exposure of <4.2 % was considered normal. Of all the parameters recorded in the report, total number of reflux episodes (normal<73) and composite DeMeester Score were taken into account for evaluation of GERD. DeMeester score >14.7 was considered as indicative of GERD.

Clinical success was defined as an Eckardt score ≤3 after POEM. In cases with persistent symptoms or relapse of symptoms (Eckardt score >3), additional treatment was offered including PBD or botulinum toxin injection (BTI) or re-POEM.

Adverse events (AE) were defined as those requiring a specific intervention such as insufflation-related events requiring drainage or transiently withholding the procedure and those leading to prolonged hospitalization. Along with clinical assessment, end tidal CO_2 and fluoroscopy were used to decide whether the POEM procedure should be temporarily withheld. Fluoroscopy was also used in cases with significant abdominal distension and rise in end tidal CO_2 (>45 mmHg). The procedure was temporarily withheld in cases of retroperitoneal air or high end-tidal CO_2 (>50 mmHg). Capnoperitoneum associated with significant abdominal distension was drained using a standard intravenous cannula.

Technique

All patients with non-sigmoid AC were kept on a liquid diet for 1 day prior to the procedure. In patients with sigmoid AC, only clear liquids were allowed for 2 to 3 days prior to the procedure. Intravenous antibiotics were started on the day of the procedure and continued for 2 days thereafter. Subsequently patients were switched to oral antibiotics for up to 7 days.

The POEM procedure was carried out under general anesthesia with patient in supine position. An upper gastrointestinal endoscope equipped with water jet (Olympus GIF HQ 190; Olympus Corp., Tokyo, Japan) was used for the procedure. A transparent cap with tapered end (DH-28GR; Fujifilm, Tokyo, Japan) was used in the initial 250 cases. In subsequent cases a standard transparent cap from Olympus was used in addition to the tapered cap. The selection of site and length of myotomy (anterior at 2 o'clock position vs posterior at 5 o'clock position) was left to the endoscopist's (DNR, ZA and MR) discretion. However, patients with spastic esophageal disorders (i.e Type III AC, jackhammer esophagus and distal esophageal spasm) were subjected to longer myotomies. A posterior approach (5 o'clock position) was used in patients who had undergone LHM previously.

The POEM procedure was carried out using the following steps-

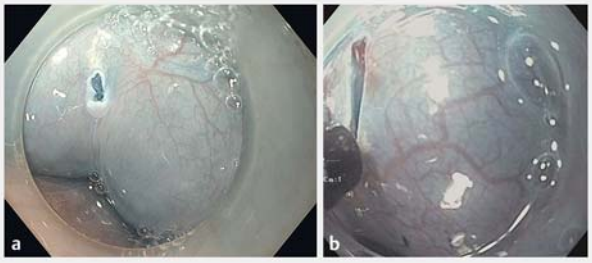
Step 1. Submucosal injection was given using a solution of saline mixed with indigo-carmine dye to raise a wheal.

Step 2. A small incision (a few millimeters long) was made with a needle knife and enlarged vertically up to ~2 cm with an insulated tip knife (KD-611L; Olympus, Tokyo, Japan) (▶ **Fig. 1a, b**).

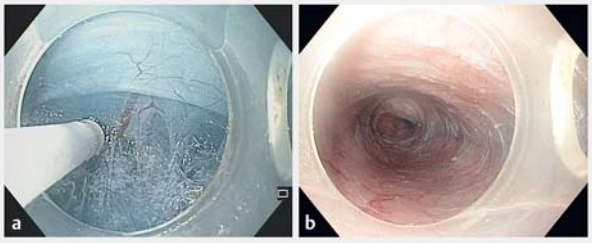
Step 3. Subsequently, entry into the tunnel was facilitated by clearing submucosal fibers along the edges and leading apex of mucosal incision using a triangular tip knife (Triangle Tip Knife, KD-640 L, Olympus, Japan).

Step 4. A submucosal tunnel was created by dissecting the fibers using spray coagulation with a triangular tip knife (▶ **Fig. 2a b**). Intervening vessels were coagulated with a coagrasper (Coagrasper G, FD-412LR, Olympus, Japan) in soft coagulation mode (80 W, effect 5) (▶ **Fig. 3a b**).

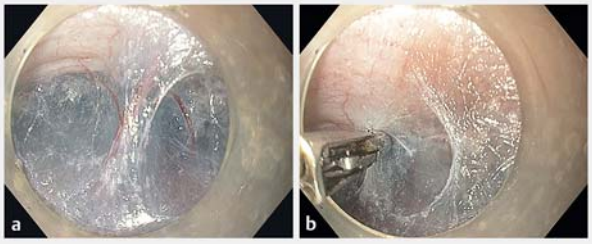
Step 5. The tunnel was extended across the gastroesophageal junction (GEJ) for at least 2 cm. Extension across the GEJ was confirmed by visualizing blanched gastric mucosa, characteristic vascular pattern, aberrant longitudinal muscle fiber



▶ **Fig. 1** **a** Small mucosal incision made with a needle knife. **b** Extension of mucosal incision with an insulated tip knife



▶ **Fig. 2** **a** Submucosal tunneling with use of a triangular tip knife. **b** Completion of submucosal tunneling.



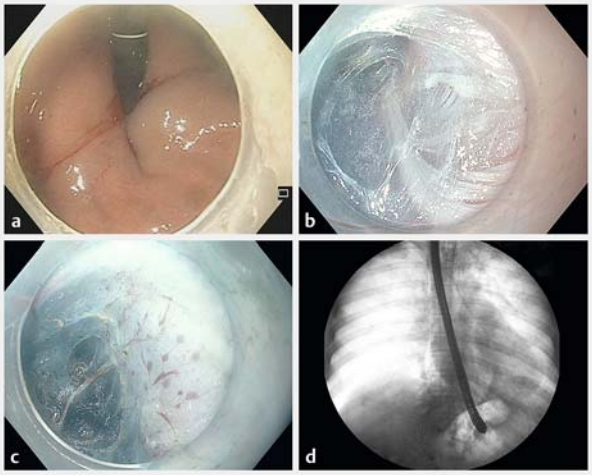
▶ **Fig. 3** **a** Perforator vessel encountered during submucosal tunneling. **b** Coagulation of the same vessel with Coagrasper.

and/or the position of the tip of endoscope fluoroscopically (▶ **Fig. 4a – d**).

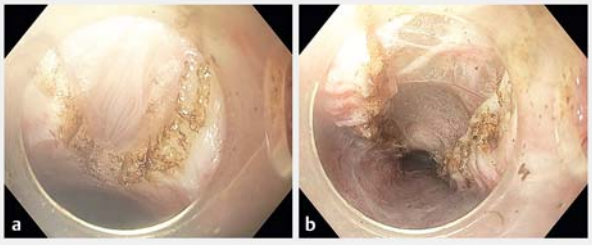
Step 6. Circular-only myotomy was done in the proximal esophagus and full-thickness myotomy was carried out from 2 to 3 cm above the GEJ up to the gastric end of the tunnel (▶ **Fig. 5a, b**).

Step 7. After the completion of myotomy, the esophageal and gastric mucosa were carefully inspected for any inadvertent injury. Any mucosotomy was closed with endoclips.

Step 8. The mucosal incision was closed using endoclips (EZ Clip, HX-610-090 L, Olympus, Japan) in distal to proximal fashion .



▶ **Fig. 4** Gastroesophageal junction (GEJ) markers. **a** Blanched gastric mucosa suggestive of extension across GEJ. **b** Aberrant longitudinal muscle fibers indicating the proximity of GEJ. **c** Short spindle vessels on the gastric end of the submucosal tunnel. **d** Visualisation of the gastroscope under fluoroscopy to confirm extension beyond the GEJ.



▶ **Fig. 5** Myotomy with a triangular tip knife. **a** Longitudinal muscle fibers visible after selective circular myotomy. **b** Full-thickness myotomy at the lower end of the tunnel.

Statistics

The data were analyzed and compared before and after the POEM procedure. The data are presented as median (range) or mean ± standard deviation. Student's paired *t*-test was used for continuous variables and proportion test for categorical variables. A *P* value < 0.05 was considered statistically significant.

Results

Patient characteristics

A total of 423 patients underwent POEM in our department during the study period (▶ **Table 1**). Of them, 15 patients who were diagnosed with non-achalasia spastic esophageal disorders including Jackhammer esophagus and distal esophageal spasm were excluded from the final analysis. Four hundred and eight patients (mean age 40 years, range 4 – 77 years, 231 men) were classified as AC according to Chicago classification-type I (n = 128), type II (n = 259) and type III (n = 20). Prior treatment

▶ **Table 1** Demographics of study patients.

No. of patients	423
Mean age, years (+ SD,range)	40 ± 13.8 (4 – 77)
Male: female	231:177
Disease duration (months)	18.6 (3 – 106)
Indication of POEM	
▪ Achalasia cardia	408
– Type I	128
– Type II	259
– Type III	20
▪ Distal esophageal spasm	9
▪ Jack Hammer esophagus	6
Previous therapy	
▪ Botulinum injection	3
▪ Pneumatic balloon dilatation (PBD)	162
▪ Heller's Myotomy (LHM)	19
▪ Combined (PBD and LHM)	5
▪ POEM	3

POEM-peroral endoscopic myotomy

history was noted in 189 patients (46 %) including – PBD (162), LHM (19), LHM and PBD both (5), and botulinum toxin injection (3).

Procedure characteristics

An anterior approach (~2 o'clock) was used in majority of patients (320/408; 78 %), whereas 88 (22 %) patients underwent POEM via posterior approach (~5 o'clock position). All patients who had previously undergone LHM were treated with posterior myotomy.

The median time of POEM procedure was 76.6 min (30 min to 180 min). Median length of total myotomy was 13 cm (range 6 – 21). The median length of myotomy on the esophageal and gastric sides was 10 cm (range 3 – 18) and 3 cm (range 1 – 4), respectively.

Technical and clinical success

The technical success rate for the POEM procedure was 97 % (396/408) in patients with AC (▶ **Table 2**). There was no difference in the technical success rates in naïve vs prior treated cases (97.3 % vs 96.8 %, $P = 0.795$). POEM could not be completed in 12 patients due to excessive submucosal fibrosis (9 patients) and inadvertent enlargement of mucosal incision (3 patients). Of the 9 patients with submucosal fibrosis, 4 cases were treatment-naïve and 5 had a history of prior treatment (PBD-3, LHM-2). The majority of patients with submucosal fibrosis underwent PBD (6 patients), whereas 2 patients received botulinum toxin injection and 1 patient with end-stage achalasia underwent esophagectomy. In the 3 patients with inadvertent

▶ **Table 2** Operative findings, adverse events and postoperative follow-up.

Operating time (min) Mean ± S.D. (Range)	76.6 ± 29.1 (30 – 180)
Site of myotomy	
▪ Anterior	320 (78 %)
▪ Posterior	88 (22 %)
Length of myotomy (cm)	13 (6 – 21)
▪ Esophageal (cm)	10 (3 – 18)
▪ Gastric (cm)	3 (1 – 4)
Adverse events	
▪ Significant mucosal bleeding	0
▪ Mucosal injury	18 (4.5 %)
▪ Capnothorax	5 (1.2 %)
▪ Capnoperitoneum requiring drainage	52 (13.1 %)
▪ Retroperitoneal air requiring temporary stoppage of procedure	70 (17.6 %)
▪ Pneumomediastinum	1 (0.2 %)
▪ Pneumopericardium	1 (0.2 %)
Other events (not requiring intervention)	
▪ Subcutaneous emphysema	91 (23 %)
▪ Pleural effusion	1 (0.2 %)
No. of clips, median (range)	6 (3 – 22)
Technical Success	396/408 (97 %)
Reasons for technical failure	
▪ Submucosal fibrosis	9 (2.2 %)
▪ Mucosal incision enlargement	3 (0.7 %)
Hospital stay, mean (range)	3 (2 – 5 days)
30 days readmission rate	1 (Bronchopneumonia)

mucosal incision enlargement, POEM was successfully completed via posterior approach after 4 to 8 weeks.

Of the 396 patients who successfully underwent POEM, 261 (66 %), 172 (43.4 %) and 51 (9.6 %) patients completed 1, 2 and 3 years of follow-up, respectively. The median follow-up duration was 17 months (range: 2 – 42 months).

The clinical success rates (Eckardt < 4) at 1, 2 and 3 years were 94 % (246/261), 91 %(157/172) and 90.2 % (46/51), respectively. At 1 year, the mean Eckardt score significantly decreased from 7.07 ± 1.6 at baseline to 1.27 ± 1.06 ($P = 0.001$). The clinical success rate in treatment-naïve cases was 95.7 % (134/140) as compared to 92.6 % (112/121) in previously treated patients at 1 year and was not clinically significant (P-0.275).

In intention to treat analysis (including patients with technical failure and lost to follow up), the clinical success rates were 88.5 % (246/278), 84.4 %(157/186) and 46/58 (79.3 %) at 1, 2 and 3 years respectively (▶ **Table 3**).

▶ **Table 3** Number of patients lost to follow-up and those with clinical or technical failure.

Follow-up	Clinical failure	Technical ailure	Lost to follow-up
1 year	15/261 (5.7 %)	11/278 (3.9 %)	6/278 (2.1 %)
2 years	15/172 (8.7 %)	9/186 (4.8 %)	5/186 (2.6 %)
3 years	5/51 (9.8 %)	4/58 (6.8 %)	3/58 (5.1 %)

▶ **Table 4** Clinical success among Type I, type II and type III achalasia.

	Type I AC	Type II AC	Type III AC	*P* value
1 year	74/81 (91.3 %)	158/164 (96.3 %)	14/16 (87.5 %)	>0.05
2 years	50/55 (90.9 %)	100/109 (91.7 %)	7/8 (87.5 %)	>0.05
3 years	14/16 (87.5 %)	29/31 (93.5 %)	3/4 (75.0 %)	>0.05

▶ **Table 5** Comparison of objective data before and after POEM procedure.

	Pre-POEM	Post-POEM (1 year)	Post-POEM (2 years)	Post-POEM (3 years)	*P* value
Eckardt score (n-408)	7.07 ± 1.6	1.27 ± 1.06	1.12 ± 0.77	1.2 ± 0.85	<0.0001
LES pressure (mean ± SD)	45 ± 16.5	15.6 ± 6.1	–	–	<0.0001
Integrated relaxation pressure (mean ± SD)	26.7 ± 12.9	9.6 ± 6.5			<0.0001
Timed Barium (> 50 % emptying at 5 minutes)	–	93.8 % (213/227)	–	–	

LES-Lowe esophageal sphincter

There was no significant difference in clinical success among three subtypes of AC (I, II, III) at each follow-up visit (1, 2, 3 years) (▶ **Table 4**).

Three patients with clinical failure at one year successfully underwent a re-POEM via alternative route.

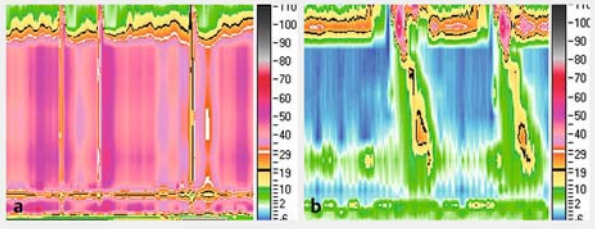
Objective data

Objective data including HRM and TBS were available for 227 out of 261 patients (87 %) who completed 1-year follow-up (▶ **Table 5**). Mean LES pressure at 1 year after POEM was 15.6 ± 6.1 mmHg and significantly less than the pre-procedure LES pressure (45 ± 16.5 mm Hg). Mean integrated relaxation pressures (IRP) before and after POEM were 26.7 ± 12.9 and 9.6 ± 6.5, respectively (P<0.0001). Partial restoration of esophageal motility was also observed in previously aperistaltic segments in 6 patients (▶ **Fig. 6a, b**). These findings were interpreted as ineffective esophageal motility i. e. distal contractile integral <450 mmHg·s·cm in ≥ 50 % swallows as per the Chicago classification of esophageal motility disorders, v3.0.

Of 227 patients, 213 (93.8 %) had more than 50 % reduction in barium column height at 5 minutes (▶ **Fig. 7a, b**).

Adverse events

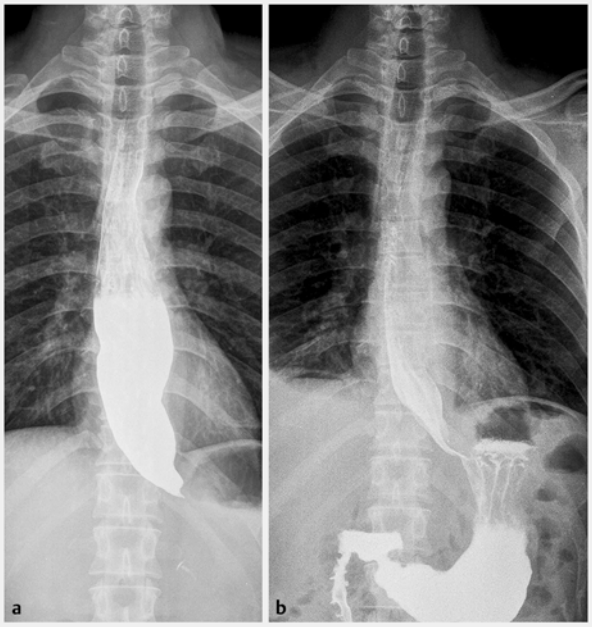
AEs included mucosal perforation, gas-related and other AEs (▶ **Table 2**). Gas-related events not requiring an intervention, such as drainage or temporary stoppage of procedure, were not considered as AEs. Mucosal perforation was noticed in 18 (4.5 %) cases. The majority of the perforations (15/18) occurred within 3 cm of the GEJ. All the perforations were successfully closed by clips and no leak was identified on barium swallow performed on the second postoperative day.



▶ **Fig. 6 a, b** High-resolution manometry before POEM and after POEM. Note the appearance of peristaltic wave after POEM (▶ **Fig. 8b**).

Other events included bleeding and gas-related events. All the intraprocedural bleeding events were controlled with coagrasper (Coagrasper G, FD-412LR, Olympus, Japan) (▶ **Fig. 3**). There were no major bleeding episodes requiring blood transfusion. None of the patients had delayed bleeding.

The gas-related AE events included capno-thorax in 5 (1.2 %), capno-peritoneum in 52 (13.1 %) and retroperitoneal air in 70 (17.6 %) patients (▶ **Fig. 8a, b**). All gas-related events were suspected clinically and confirmed by fluoroscopy. Capno-mediastinum and capno-pericardium were noted in 1 patient each. Capno-peritoneum was managed with drainage using conven-



▶ **Fig. 7** **a** Pre-POEM barium swallow showing complete retention of barium at 5 minutes. **b** Post-POEM barium swallow showing free flow of barium with complete emptying at 5 minutes.

tional intravenous cannula. Other insufflation-related AEs were managed by temporarily discontinuing the POEM procedure until CO_2 was absorbed. Capno-pericardium was incidentally discovered while confirming for the gastric extension of submucosal tunnel. Although it was not associated with hemodynamic compromise, the procedure was withheld for about 15 minutes until CO_2 was absorbed.

In addition to the gas-related AEs, 1 patient required readmission within 2 weeks of POEM due to bronchopneumonia which responded to antibiotics.

Other events

Other events which did not require an intervention included subcutaneous emphysema in 91 (23 %) patients and mild right pleural effusion in 1 patient (▶ **Fig. 8c**).

Development of pseudodiverticulae was noted in 5 patients on follow-up endoscopy at 1 year (▶ **Fig. 9**). However, it was an incidental observation and the clinical significance of same is unknown.

Gastroesophageal reflux disease

GERD was assessed by clinical symptoms, EGD and pH-impedance analysis (▶ **Table 6**). Clinical symptoms of GERD were detected in 44 out of 261 patients (16.8 %). Twenty-four-hour pH-impedance results were available for 92 patients at 3 months after POEM. A De Meester score of >14.7 suggestive of GERD was found in 26 patients (28.3 %).

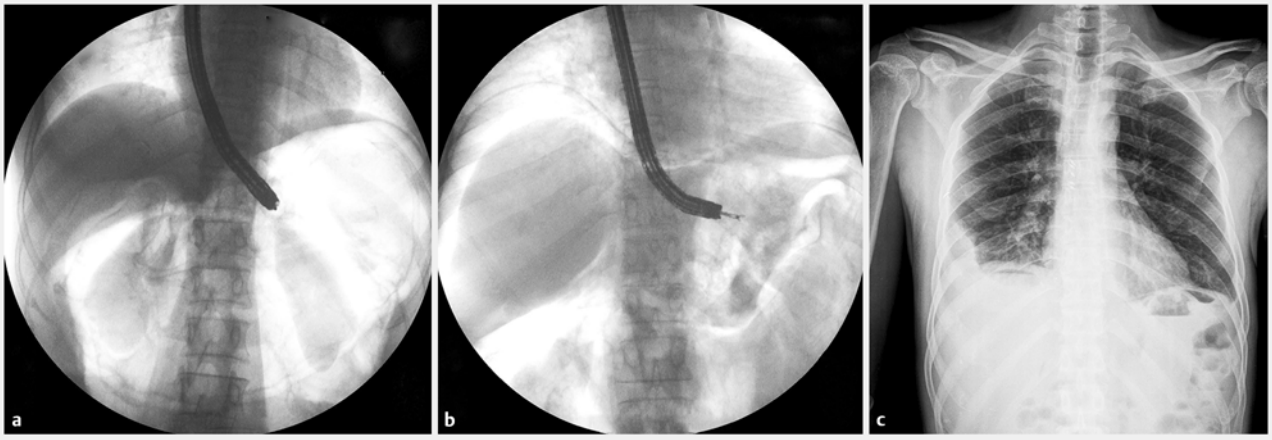
EGD detected erosive esophagitis in 41 patients (18.1 %; 41/227). Mild (LA grade A-26, LA grade B-11) and severe esophagitis (LA grade C-3 and D-1) was found in 37 and 4 patients respectively.

Discussion

In this study we demonstrated the safety, efficacy and durability of response to POEM in a large number of subjects with AC with medium-term follow-up.

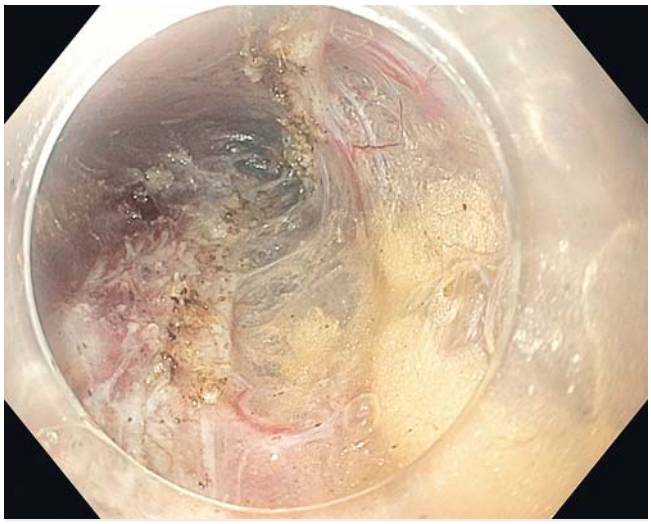
AC is an incurable disease and the currently available treatments aim at palliation of dysphagia by reducing LES pressures.

The mainstay of endoscopic management in AC is PBD or POEM. The surgical treatment of choice is LHM with partial fundoplication. In the European achalasia trial, LHM and graded PBD were equal in efficacy at 2 and 5 years follow-up. However, a quarter of patients in the PBD group required additional dilatations [5]. Therefore, it appears that the response to PBD is less durable than that for LHM and reintervention requirement is frequent [4].



▶ **Fig. 8** Gas-related and other pulmonary adverse events during POEM. **a** Retroperitoneal gas outlining both kidneys. **b** Intraperitoneal gas (air under diaphragm). **c** Mild right-sided pleural effusion.

▶ **Fig. 9** Pseudo-diverticulum at lower end of the esophagus after posterior POEM in one of the patient.



▶ **Fig. 10** Glistening peritoneal fat suggesting extension of the submucosal tunnel across the GEJ.

▶ **Table 6** Incidence of GERD after POEM procedure.

	No. of patients
Clinical symptoms (at 1 year follow up)	44/261 (16.8 %)
Esophagitis by EGD	41/227 (18.1 %)
▪ Grade A/B esophagitis	26/11
▪ Grade C/D esophagitis	3/1
De-Meester score > 14.7	26/92 (28.3 %)

GERD, gastroesophageal reflux disease; EGD, esophagogastroduodenoscopy

In contrast to LHM, endoscopic myotomy is newer and studies with long-term follow-up are awaited. We have previously reported on short-term outcomes of POEM in over 200 patients with AC. The clinical success rate at 1 year was 92 % and there were no major AEs [9]. Technical and clinical success rates reported in previous studies wer 97 % (95 % CI: 94 – 98 %) and 93 % (407/428; 95 % CI: 90 – 95 %), respectively [10].

In the current study, we evaluated the efficacy of POEM at longer follow-up periods (i. e. at 1, 2 and 3 years). The clinical success rate at 1 year was 94 %, which was maintained when followed up to 3 years (90 %). Therefore, POEM is not only effective but the response is also durable. There is paucity of literature regarding the long-term efficacy of POEM. In a series of 500 patients the clinical efficacy rate at 3 years was 88.5 % [11]. In another study, clinical recurrences (later failures) were seen in 17.7 % cases with a total failure rate of 21.5 % at 2 years [12].

Objective testing (TBE and HRM) was available for 227 patients. There was significant reduction in post-POEM LES pressure and height of barium column in TBE. Besides reduction in LES pressures and IRP, partial restoration of esophageal motility was also observed in previously aperistaltic segments in 6 patients (▶ **Fig. 6a, b**). Similar findings have been noted in 1 of the recently published studies [13,14]. However, the clinical impact of the same remains to be seen.

The clinical success of POEM depends to a large extent on the adequacy of myotomy towards the gastric end of the submucosal tunnel [15]. In the initial few cases of learning curve, it may be difficult to correctly identify the GEJ. Moreover, the submucosal tunneling may be prematurely stopped due to the presence of large vessels toward the gastric side of the tunnel. Inadequate extension of the tunnel may lead to early or late recurrences. In a recent study, the outcomes were measured after excluding initial learning curve cases. At an average of 2.4 years post-POEM (range 12 – 52 months), the overall success rate was 92 % [16].

The importance of accurately identifying the GEJ cannot be underestimated. In our study we used retroflexion of scope in the stomach to visualize blanched gastric mucosa, narrowing of tunnel followed by widening of submucosal space, change of vascular pattern and aberrant longitudinal muscle fibers as indicators of GEJ (▶ **Fig. 4a – d**). When in doubt, fluoroscopy was used to ensure passage of the scope across the GEJ [17]. Other methods have been described for identification of the GEJ such as placement of a clip at the GEJ and use of a second endoscope [18, 19]. In addition to the above methods, we found that visualization of glistening yellow gastric fat during myotomy was a certain indicator of entry into the stomach (▶ **Fig. 10**). This has not been described in literature before and needs to be studied further.

The clinical and technical success rates in patients with prior treatment were similar to treatment-naïve cases in our study (92.6 % vs 95.7 %). The impact of prior treatment such as PBD or LHM on the success of POEM appears to be minimal as found in previous studies [20 – 22]. However, significant submucosal fibrosis may be encountered in some of these patients, leading to technical difficulty or failure and prolonged procedure duration [23]. In the current study, we found significant submucosal fibrosis in 5 patients who had a history of previous treatment

with PBD and LHM. In difficult cases with adherent circular muscle fibers, simultaneous myotomy and submucosal dissection can be performed. Care should be taken to avoid loss of planes [24].

Options for failed cases after POEM include PBD, BTI, LHM and re-POEM via an alternate route. In our series the majority of patients in whom POEM failed underwent PBD. Re – POEM was successfully performed in 3 patients with 100 % clinical success at 1-year follow-up. Repeat POEM appears safe and effective as a salvage option after initial POEM failure [25].

The POEM procedure can be performed anteriorly (2 o'clock) or posteriorly (5 o'clock) and largely depends on the operator's preference. In our study, an anterior approach was used in 78 % and a posterior approach in 22 % of patients. A randomized trial is required to compare the safety, efficacy and AE between these 2 approaches.

There were no major AEs related to POEM procedure in our study. Intra-procedural bleeding and gas-related events are part of the procedure, occur frequently and are usually inconsequential [26]. For the same reason, routine chest computed tomography scan is not justified because of the high rate of minor and clinically irrelevant findings [27]. However, caution is advised if tension capno-pericardium develops as cardiac arrest has been reported with this particular gas-related event [28]. In our series, 1 patient developed capno-pericardium which resolved spontaneously after a waiting period of about 15 minutes. It is very important that the complete POEM procedure is carried out under CO_2 insufflation, as air takes a much longer time to be absorbed. The utility of underwater POEM to reduce such events remains to be determined [29].

We used endoclips to close all the inadvertent mucoscotomies. Mucosal perforations have been noted in 0 % to 25 % of cases in previous studies [30]. Besides endo-clipping, suturing may also be used to close mucosal defects in difficult cases, although it is more time-consuming than the former [31, 32].

GERD is an important long-term AE after esophageal myotomy. However, there are only a few studies that have objectively determined acid exposure after POEM. In our study abnormal esophageal acid exposure was found in about 28 % of patients. However, clinical symptoms and esophagitis were detected in fewer patients (17 % – 18 %). The available literature suggests that using a 24-hour pH study, GERD is present in about 40 % to 50 % of patients after POEM [16, 33, 34]. However, clinically relevant GERD (altered acid exposure with heartburn and/or esophagitis) is found in only one-third to one-quarter of all patients. Therefore, it appears that subjective symptoms are not a reliable indicator of postoperative reflux [35]. The decrease in integrated relaxation pressure after POEM may be a predictor of reflux esophagitis and needs further evaluation [36]. The majority of our patients underwent POEM via an anterior approach, which may theoretically lead to less GERD than a posterior approach. In accordance with our results, symptoms of GERD and reflux esophagitis developed in only about 7 % and 16 % of patients, respectively, after anterior myotomy in another study [36]. However, randomized trials are required to document clinically relevant differences in the occurrence of GERD between these 2 approaches.

The strengths of our study include the large study population, objective evaluation of treatment success and GERD and reasonable duration of follow-up. However, certain drawbacks are noteworthy. The number of patients completing 3-year follow-up was small, pH impedance study could not be performed in all cases and complete GERD evaluation (pH study and EGD) was not performed at a single point in time. We may have underestimated the incidence of gas-related events as fluoroscopy was not used in all cases.

Conclusions

In conclusion, POEM is safe, effective and durable for treatment of AC. The incidence of GERD does not appear to be higher than with LHM. However, randomized comparisons are required. Whether POEM should be offered as a first-line treatment to all patients with AC is a matter of debate. Long-term follow-up studies and randomized comparison with established modalities such as PBD and LHM will provide conclusive information in that regard.

Competing interests

None

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