

Title

Peroral Endoscopic Myotomy for Esophageal Achalasia: Outcomes of the first over
100 Patients With Short-term Follow-up

Authors

Hironari Shiwaku,^{*} Haruhiro Inoue,[†] Kanefumi Yamashita,^{*} Toshihiro Ohmiya,^{*}
Richiko Beppu,^{*} Ryo Nakashima,^{*} Shinsuke Takeno,^{*} Takamitsu Sasaki,^{*}
Satoshi Nimura,[‡] Yuichi Yamashita^{*}

Affiliations

^{*}Department of Gastroenterological Surgery, Faculty of Medicine, Fukuoka University,
Fukuoka, Japan;

[†]Digestive Disease Center, Showa University Koto Toyosu Hospital, Tokyo, Japan; and

[‡]Department of Pathology, Faculty of Medicine, Fukuoka University, Fukuoka, Japan

Address all correspondence and reprint requests to:

Hironari Shiwaku

Department of Gastroenterological Surgery, Faculty of Medicine, Fukuoka University,

Fukuoka, Japan

Tel: +81-92-801-1011. Fax: +81-92-863-9759. E-mail: hiro.shiwaku@gmail.com

Running title

POEM for 100 patients of achalasia

Conflicts of interest

None of the authors have any conflicts of interest associated with this work.

Sources of funding

This study did not receive any financial support in the form of funding.

Keywords:

achalasia, POEM, 100 cases, balloon dilatation

Abbreviations :

POEM: Peroral Endoscopic Myotomy

ASA-PS: American Society of Anesthesiologists physical status

GERD: gastroesophageal reflux disease

LES: lower esophageal sphincter

IRP: integrated relaxation pressure

EGJ: esophagogastric junction

FSSG: frequency scale for the symptoms of GERD

Abstract

BACKGROUND:

POEM is a recently developed achalasia treatment method, which combines the efficacy of surgical myotomy with the benefits of endoscopic procedures. Very few studies have focussed on the efficacy and usefulness of POEM in over 100 cases.

METHODS:

The first 100 adult patients treated according to standard POEM technique in a single center and followed up for 3 months were identified and included in this study (men, 42; women 58; mean age, 48.2 ± 18.8 ; range, 9–91 years) The pre- and postoperative assessments included Eckardt scores, manometry, endoscopy, and monitoring pH.

RESULTS:

One hundred and three patients underwent POEM for achalasia between September 2011 and December 2014, and 100 patients were followed up 3 months after POEM. The average age of the 100 patients, including 42 men and 58 women, with achalasia, was 48.2 ± 18.8 (range, 9–91) years. Mean operative time was 150.8 ± 49.3 minutes (75–370 minutes). Adverse events over Grade IIIb by the Clavien–Dindo classification were not encountered. The mean preoperative and postoperative lower esophageal

sphincter pressures were 43.6 ± 26.2 and 20.9 ± 12.7 mmHg, respectively, indicating a statistically significant decrease after POEM ($P < 0.05$). The mean preoperative and postoperative integrated relaxation pressure (IRP) values were 33.5 ± 15.2 and 15.3 ± 6.5 mmHg ($P < 0.05$). Furthermore, the Eckardt score significantly decreased from 5.9 ± 2.5 preoperatively to 0.8 ± 0.9 postoperatively ($P < 0.05$).

Clinical success was documented in 99% of the patients. Short-term outcomes after POEM were extremely good and independent of the age, type of achalasia, and previous treatment method. The investigation time as revealed by 24-h pH with a pH < 4 was on average 3.5% (3/86) in patients not on proton pump inhibitors (PPIs). Nine patients were diagnosed with symptomatic gastroesophageal reflux disease (GERD); patients with reflux esophagitis and symptomatic GERD improved with PPIs treatment.

CONCLUSIONS:

Our results confirm the efficacy of POEM in a large patient series, and support POEM as one of the first-line achalasia therapies in the near future.

Introduction

Esophageal achalasia is an esophageal motility disorder of an unknown cause and is characterised by achalasia of the lower esophageal sphincter (LES) and impaired peristalsis of the esophageal body[1]. Conventionally, if pharmacological therapy fails to adequately control the symptoms of esophageal achalasia, Heller–Dor surgery is considered. However, with recent advances in endoscopic treatment techniques and devices, Inoue et al. have developed Peroral Endoscopic Myotomy (POEM), allowing adequate incision of the muscle layer alone without scarring the body surface, which has advanced treatment strategies for esophageal achalasia [2]. Although there have been numerous reports regarding the efficacy and usefulness of POEM, very few studies have included over 100 cases [3-5]. We herein report the outcomes of POEM in 100 cases of esophageal achalasia at our hospital.

METHODS

Patients

The data for our single-center POEM procedures were collected prospectively. The POEM procedure was approved by the institutional review board (IRB) of Fukuoka

University Hospital, and written informed consent was obtained from all patients prior to enrolment in the study. The inclusion criterion was a confirmed diagnosis of achalasia. Exclusion criteria were as follows: 1) patients unable to undergo general anesthesia and 2) patients who declined treatment with POEM.

Clinical Assessment before POEM

Clinical achalasia symptoms were assessed using the Eckardt scores [6]. Patients were weighed, and preoperative tests, including manometry, endoscopy, barium swallow, and computed tomography (CT), were performed.

Surgical Preparation Before POEM

Patients were admitted 1 day before the POEM procedure to perform esophagogastroduodenoscopy (EGD) to ensure all food remnants were removed from the esophagus prior to POEM.

POEM Equipment

A forward-viewing endoscope with an outer diameter of 9.8 mm (GIF-H260, Olympus Medical Systems, Japan), which is routinely employed for upper gastrointestinal (GI)

examinations, was used with a short ST hood (DH-28GR, Fujifilm, Japan). The main device was a triangle-tip knife (KD-640L, Olympus) that was used to create the submucosal tunnel as well as to divide circular muscle bundles. The coagulating forceps (FD-411QR Coagrasper, Olympus) were used to close up larger vessels prior to dissection and for hemostasis. Carbon dioxide (CO₂) was used for insufflation during the procedure (UCR, Olympus), and the VIO 300D electrogenerator (ERBE, Tübingen, Germany) was used for electrosurgery. Finally, hemostatic clips (HX-610-90L EZ Clip and HX-610-90S EZ Clip Olympus) were used for closure of the mucosal entry site.

The POEM Procedure (Figure 1)

The first case was performed by Haruhiro Inoue who pioneered the POEM technique for clinical practice, and the next 10 cases were operated upon under his supervision and as described by Inoue et al. [4].

POEM was performed under general anesthesia with CO₂ insufflation. After injection of an approximate amount of glycerol mixed with 0.3% indigo carmine into the submucosal layer, a longitudinal mucosal incision was made in the mucosal surface to access the submucosal space. In the case of anterior myotomy, submucosal tunnel was created in the 1- to 2-o'clock position on the ventral aspect of the esophagus to preserve the angle

of His and then extended past the esophagogastric junction (EGJ) for 2 to 3 cm onto the gastric cardia.

For posterior myotomy, submucosal tunnel was created in the 5- to 6-o'clock position not to approach the aorta, and the submucosal tunnel was extended past the EGJ for 2 to 3 cm onto the gastric cardia, similar to anterior myotomy [7]. In cases of POEM for failed surgical myotomy, a new submucosal tunnel on the opposite side of the previous myotomy was created to avoid the fibrosis [8, 9].

A proximal-to-distal circular myotomy was performed with care to preserve the longitudinal muscle layers of the esophagus and stomach. Preservation of the longitudinal muscle sheet potentially avoids unnecessary injury to the structures adjacent to the esophagus.

The secure incision of the LES was identified by the following points [10]:

- length from incisor teeth to esophagogastric junction as a reference position for the scope
- narrowing of the esophageal lumen closer to the LES and then opening wide in the stomach when creating a submucosal tunnel
- change from palisade vessels (anatomically equivalent to the LES) to increased irregularity and augmentation of the vessels underlying the mucosa as viewed

from the submucosal tunnel

- smooth endoscope passage through the LES inside the true esophageal lumen and mucosa of stomach is seen from the esophageal lumen after the myotomy
- in anterior myotomy, the branch of the left gastric artery and oblique muscle in the submucosal tunnel of the gastric side (sometimes, this cannot be confirmed)
- in difficult cases, to identify the secure incision of the LES by abovementioned points, using a small caliber transluminal scope inserted through the natural lumen to observe real-time dissection [11].

After spraying an antibiotic (80 mg gentamycin) into the tunnel, the mucosotomy was closed using endoscopic clips.

During the procedure, POEM was performed with CO₂ insufflation every 30 min, and the upper abdomen was palpated to monitor severe pneumoperitoneum. In cases of excessive distention of the abdominal wall by severe pneumoperitoneum or poor ventilation reported by the anesthesiologist, the procedure was stopped and the abdomen was tapped if necessary.

The operation time was defined from insertion of the scope to its removal.

Postprocedural Management

Intravenous antibiotics were administered for 3 days after the procedure. Endoscopy was performed to confirm mucosal integrity on the first day after surgery, and barium swallow examination was performed to confirm the smooth passage of contrast media into the stomach without leakage or stasis on the second day. A liquid diet was started on the day after surgery, followed by soft diet on post-POEM day 3, with resumption of a normal diet on post-POEM day 4. On discharge, patients were prescribed a proton pump inhibitor (PPI) for one month only after which they were asked to discontinue until the postoperative evaluation. Patients on anticoagulant therapy; however, were asked to continue the PPI treatment.

Investigation after POEM

To investigate the clinical effectiveness of POEM and to evaluate gastroesophageal reflux disease (GERD) after POEM, symptoms were quantified with the Eckardt scores and the frequency scale for the symptoms of GERD (FSSG) 3 months after POEM [12]. Patients were also weighed, and endoscopy and manometry were performed simultaneously with 24-h pH monitoring. Manometry was performed using the InSIGHT G3 System (Sandhill Scientific, USA), and 24-h pH monitoring was performed with the ZepHr® Impedance/pH Reflux Monitoring System (Sandhill Scientific, USA).

Evaluation of treatment effect

An Eckerdts score of <3 3 months post-POEM was deemed as a successful outcome.

Statistical Analysis

All statistical analysis were conducted using the Statistical Package for the Social Sciences software version 22 (SPSS Inc, Chicago, IL). The data was analyzed by univariate chi-square test and student's t test. P values of <0.05 were considered as statistically significant.

RESULTS

Patient characteristics

Between September 2011 and December 2014, 108 patient were diagnosed with achalasia at our hospital, and two patients with mild symptoms were treated with medication based on their choice (Table 1). Two additional patients, one with terminal pancreatic cancer and the other an 89-year-old female in American Society of Anesthesiologists physical status (ASA-PS) class IV, were treated by balloon dilatation. Further, another 89-year-old female in ASA-PS class IV) was treated by botulinum toxin injection. Remaining 103 patients underwent POEM for achalasia and were followed up for 3 months after POEM. However, three patients did not return for follow-up appointments at their own discretion. Of the remaining 100 patients, including 42 men and 58 women with achalasia, the average age was 48.2 ± 18.8 (range, 9–91) years (Table 2). Twenty-three patients had undergone balloon dilation, and three patients had undergone the Heller–Dor operation prior to enrolment in this study.

Results of POEM

The average total length of myotomy was 12.6 ± 3.9 cm (range, 5–26 cm), and the average length of gastric myotomy was 2.5 ± 1.0 cm (range, 1–5 cm; Table 2). The

mean operation time was 150.8 ± 49.3 min. Pneumoperitoneum which affected anesthesia during the procedure occurred in 11 cases; all were treated with abdominal puncture by a long 16-gauge needle to release abdominal pressure. The mean preoperative and postoperative LES pressures were 43.6 ± 26.2 and 20.9 ± 12.7 mmHg, respectively, indicating a statistically significant decrease after POEM ($P < 0.05$). The mean preoperative and postoperative integrated relaxation pressure (IRP) were 33.5 ± 15.2 and 15.3 ± 6.5 mmHg ($P < 0.05$). Furthermore, the Eckardt score significantly decreased from 5.9 ± 2.5 preoperatively to 0.8 ± 0.9 postoperatively ($P < 0.05$). In subgroup analysis, POEM outcomes were the same regardless of age or previous treatment (Table 3). One patient was diagnosed with incomplete myotomy of LES and underwent a second POEM procedure one year later and achieved symptomatic relief.

Adverse events (Table 4)

We did not experience adverse events over Grade IIIb in the Clavien–Dindo classification (Table 4) [13]. Esophagitis due to mucosal injury occurred in six cases. Mediastinitis by late and extensive mucosal injury occurred in one case; however, as the patient's general condition was not severe, he was treated with fasting, antibiotics, and

enteral nutrition. While inflammation improved, the recovery took about 50 days. Delayed bleeding from mucosotomy due to clip dislodgement on 7 days after POEM occurred in one case. Pneumothorax occurred in one case immediately after POEM, but no special treatment was needed. All cases, including abovementioned cases with complications, were treated by conservative therapy.

Incidence of GERD after POEM

Excluding seven patients who had been treated with anticoagulants, postoperative endoscopic findings led to the classification of grade N, A, B, and C reflux esophagitis in 32% (30/93), 48% (45/93), 13% (12/93), and 7% (6/93) of patients, respectively, as per the Los Angeles (LA) classification [13]. Twenty-four-hour pH monitoring was performed in these 93 patients, which indicated that the percent of monitoring time with a pH < 4 was 3.5 (3/86) in patients not on PPIs.

Of those seven patients on anticoagulant therapy, postoperative endoscopic findings led to the classification of grade N, A, and B reflux esophagitis in 57% (4/7), 29% (2/7), and 14% (1/7) of patients, respectively, per the LA classification. Twenty-four-hour pH monitoring determined that the percent of monitoring time with a pH < 4 was 28.5 (2/7) in patients not on PPIs.

Nine patients were diagnosed with symptomatic GERD by FSSG¹²; however, PPI treatment in patients with simultaneous reflux esophagitis and symptomatic GERD resulted in clinical improvement.

DISCUSSION

Esophageal achalasia is an esophageal motility disorder of an unknown origin and is characterised by achalasia of the LES with impaired peristalsis of the esophageal body [1]. Patients experience persistent difficulty in swallowing and chest pain and may also exhibit regurgitation into the oral cavity accompanied by pulmonary aspiration during sleep. Therefore, many achalasia patients presenting to medical institutions have markedly decreased quality of life. Surgical reduction of pressure on the LES is often required to eliminate, or at least reduce, the aforementioned symptoms due to the limited efficacy of pharmacological therapies. Previously, interventions commonly included either endoscopic balloon dilation or surgery [^{14, 15}].

Balloon dilation is a simple and effective treatment method and is one of the widely-used endoscopic treatments [^{16, 17}]. However, it is extremely difficult to apply an appropriate amount of pressure during this procedure as the inner circular muscle cannot be visualised. Too little pressure makes the procedure ineffective, whereas too much pressure may cause esophageal perforation. Therefore, this method often provides varied and inconsistent results. Moreover, as it is impossible to reach the inner circular muscle of the esophageal body even in cases where the area around the LES can be effectively tightened, it is not suitable for Chicago classification III achalasia

cases in which strong spasms of the esophageal body also contribute to symptoms [18].

On the other hand, although surgery is a superior alternative to balloon dilation as it offers reliable and permanent results, it is only suggested for achalasia patients in whom balloon dilation has been unsuccessful. This is because achalasia is a benign disease and even for small incisions, surgery requires either laparotomy or thoracotomy.

POEM, devised by Inoue et al. in 2008, is a groundbreaking treatment method, in which the principles of endoscopic treatment are applied to Heller myotomy; thus, it can otherwise be described as 'scarless Heller myotomy' [2, 19]. POEM has been previously reported as less invasive with greater treatment efficacy than conventional treatment methods. In the near future, POEM is expected to be established as the global standard treatment for esophageal motility disorders including esophageal achalasia.

The usefulness of POEM for esophageal achalasia and related diseases has already been reported [20-29]; however, as esophageal achalasia is a rare disease, few reports involve patient series of over 100. Here, we report our experience on POEM in 100 cases[3-5].

In this study, statistically significant improvements were observed in both clinical symptoms and LES pressure. Further, short-term outcomes after POEM were

extremely good independent of age, type of achalasia, and previous therapy. In addition, sub-group analysis to determine the effect of previous therapeutic history on POEM outcomes showed that improvements in the LES pressure and Eckardt scores were independent of previous treatments (Table 3). Furthermore, there were no statistical differences in the length of myotomy, procedure time or rate of adverse events related to POEM. Thus, this subgroup analysis revealed that POEM as a safe and effective approach for achalasia regardless of previous treatment. The rate of Chicago classification type is high in those with previous treatment; thus, type III achalasia is a strong negative predictor of response to balloon dilatation and Heller–Dor operation compared to other achalasia types. Thus, the high success rate of POEM for all achalasia types lends further support to its versatility.

Posterior myotomy rate was high in patients with a history of previous therapy. This is expected as posterior myotomy was performed during rescue POEM on the opposite side of previous myotomy to avoid the fibrotic area.

Procedural complications of Grade IIIa and below, according to the Clavien–Dindo classification, were observed in 10% of the patients (Table 4); however, no procedural complications requiring surgery (Clavien–Dindo classification of Grade IIIb or higher) occurred.

Incomplete myotomy occurred in one patient.

Until 3 months after first POEM, symptom (regurgitation and dysphagia) and weight improved better than treatment. However, the symptom and weightloss recurrent gradually and became same at the time of first POEM finally.

Barium swallow examination showed the stasis in the esophagus.

Endoscopic examination showed resistance in the LES part, and no improvement of esophagitis in the esophageal body. Twenty-four-hour pH monitoring showed no reflux.

Furthermore, manometry showed high pressure zone remained in the distal side of

LES. We diagnosed incomplete myotomy in the first POEM, and redo-POEM was performed 1 year after first POEM. The Patient was relieved from symptoms after redo-

POEM. First POEM of this patient is 64th cases in our institution. POEM procedure itself was stable. At the time of first POEM, the secure incision of the LES was identified by

the described points except insertion of second scope [10, 11]. Despite LES is incomplete resection anatomically, there was no resistance in the LES part during

procedure. However, two days after POEM, endoscopic examination showed the LES

part became narrow and there exist resistance. It is considered that temporary relaxation of muscles may occurred by electrical stimulation, but the details is unknown.

After this event, we routinely insert a second scope (GIF-N260) on the stomach side,

and release the LES after confirming that the main scope has reached the stomach side using the light transmitted through the mucous membrane[11]. This method allowed for the prevention of unreliable LES incision and by this method, we could subsequently prevent incomplete myotomy.

With regards to GERD onset following POEM, no intractable symptoms or ulceration were observed, and all cases were controlled with oral proton pump inhibitor administration.

Twenty-four-hour pH monitoring documented that Percent total time pH < 4 was 3.5% (3/86) of patients without PPI prescription.

These results indicate lower incidence of postoperative GER than that observed after Heller myotomy with or without fundoplication [¹⁵].

Antireflux mechanisms involve the inner circular muscles, oblique muscle, crus of diaphragm, and the phrenicoesophageal ligament[³⁰].

Simić et al. reported that preservation of the phrenicoesophageal ligament during Heller myotomy can suppress the development of GERD, regardless of whether fundoplication is performed [³¹].

Preservation of the phrenicoesophageal ligament is believed to hold the key to the development of postoperative GERD [³²].

POEM preserves the adjacent structures surrounding the distal esophagus, and the phrenoesophageal ligament remains intact.

In other words, in terms of preserving the antireflux mechanism, POEM is equally or more effective than Heller myotomy in that it preserves the phrenoesophageal ligament partially. Therefore, it is natural that the rate of GERD after POEM is low.

The reason for high rate (28.5%) of GERD occurrence in patient with PPI prescription is considered that the patient was on anti-coagulant therapy which needed PPI prescription tend to be elder.

And the two patient who diagnosed GERD by 24-h pH monitoring had round shoulders.

We performed long myotomy from the upper thoracic esophagus to the stomach side in the cases of Chicago classification type III achalasia accompanied by spasms of the esophageal body. For 12 cases of Chicago classification type III achalasia, myotomy involving lateral wall–anterior wall incision was performed. In remaining 2 cases, muscle layer incision of the posterior wall was performed.

When performing long myotomy, careful selection of the strategy used for muscular incision of the upper thoracic esophagus is required as theoretically, esophagotracheal fistula can result when the trachea and esophagus are in contact.

The first method we used involved performing myotomy on the lateral wall (3 o'clock

direction) in the upper thoracic esophagus, where the trachea and oesophagus are in contact, before shifting to the 2 o'clock direction to preserve the oblique muscles below the tracheal bifurcation. We were able to perform POEM without complications using this method but it had the disadvantage of being technically demanding and possibility of esophageal diverticulum. However, long myotomy on the posterior wall side is not technically as challenging except that the area is submerged. Anatomically, this procedure is relatively safe when the aorta can be avoided, and the risk of esophagotracheal fistula onset during anterior wall incision can be eliminated. Moreover, as the vertebral bodies are posterior to the oesophagus, this procedure could also help prevent postoperative hernia. Accordingly, when performing long myotomy from the upper thoracic oesophagus to the stomach side, we believe that posterior wall myotomy is particularly useful.

We were able to perform three cases of POEM for failed surgical myotomy.

Symptoms remained after previous surgery because of insufficient myotomy in all cases. (Two cases: LES part, one case: esophageal body).

Scar of previous myotomy exist in anterior wall in all cases.

Therefore, we make a new submucosal tunnel on posterior wall to avoid the fibrosis and perform redo myotomy including responsible part.

In all cases, symptoms were improved.

Redo Heller myotomy is more technically demanding because of the presence of adhesions, fibrosis, and scars resulting from the previous surgery.

However, in rescue POEM (POEM after previous surgery for achalasia), we are able to make a new submucosal tunnel on opposite side of previous myotomy to avoid the fibrosis.

There is no adhesion and easy access to the responsible part. Rescue POEM is also an effective method for failed surgical myotomy instead of redo surgical Heller myotomy in this study.

The following are the limitations of this study: it was conducted at a single centre, only one surgeon performed all procedures and long-term outcomes were not evaluated.

Further research works, including long-term results of multiple centers, are awaited.

In conclusion, our results confirm the efficacy of POEM in a large series of patients.

POEM will become one of the first-line therapies of achalasia in the near future.

ACKNOWLEDGMENTS

The authors thank all patients and clinical staff for their participation and contribution to this study.

Tables

Table 1 Recruitment of patients

Table2. Patient Demographics and Perioperative Characteristics

Table 3 Comparison of the therapeutic effect due to the presence or absence of previous treatment history

Table 4 Adverse events (Clavian–Dindo classification)

Figure legends

Figure 1

POEM procedure (anterior myotomy)

a: Mucosal entry

b: Creating submucosal tunnel

c: After creating submucosal tunnel

d: Myotomy

e: After myotomy

f: Closure of mucosal entry

Figure 2

Barium swallow examination before and after POEM

Figure 3

High resolution manometry before and after POEM

References

1. Richter JE. Oesophageal motility disorders. *Lancet* 2001;358:823-8.
2. Inoue H, Minami H, Kobayashi Y, et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia*. *Endoscopy* 2010;42:265-71.
3. Sharata AM, Dunst CM, Pescarus R, et al. Peroral endoscopic myotomy (POEM) for esophageal primary motility disorders: analysis of 100 consecutive patients. *J Gastrointest Surg* 2015;19:161-70; discussion 70.
4. Inoue H, Sato H, Ikeda H, et al. Per-Oral Endoscopic Myotomy: A Series of 500 Patients. *J Am Coll Surg* 2015;221:256-64.
5. Familiari P, Gigante G, Marchese M, et al. Peroral Endoscopic Myotomy for Esophageal Achalasia: Outcomes of the First 100 Patients With Short-term Follow-up. *Ann Surg* 2014.
6. Eckardt VF. Clinical presentations and complications of achalasia. *Gastrointest Endosc Clin N Am* 2001;11:281-92, vi.
7. Onimaru M, Inoue H, Ikeda H, et al. Greater curvature myotomy is a safe and effective modified technique in per-oral endoscopic myotomy (with videos). *Gastrointest Endosc* 2015;81:1370-7.
8. Onimaru M, Inoue H, Ikeda H, et al. Peroral endoscopic myotomy is a viable option for failed surgical esophagocardiomyotomy instead of redo surgical Heller myotomy: a single center prospective study. *J Am Coll Surg* 2013;217:598-605.
9. Zhou PH, Li QL, Yao LQ, et al. Peroral endoscopic remyotomy for failed Heller myotomy: a prospective single-center study. *Endoscopy* 2013;45:161-6.
10. Phalanusitthepha C, Inoue H, Ikeda H, Sato H, Sato C, Hokierti C. Peroral endoscopic myotomy for esophageal achalasia. *Ann Transl Med* 2014;2:31.
11. Baldaque-Silva F, Marques M, Vilas-Boas F, Maia JD, Sa F, Macedo G. New transillumination auxiliary technique for peroral endoscopic myotomy. *Gastrointest Endosc* 2014;79:544-5.
12. Kusano M, Shimoyama Y, Sugimoto S, et al. Development and evaluation of FSSG: frequency scale for the symptoms of GERD. *J Gastroenterol* 2004;39:888-91.
13. Armstrong D, Bennett JR, Blum AL, et al. The endoscopic assessment of esophagitis: a progress report on observer agreement. *Gastroenterology* 1996;111:85-92.
14. Boeckxstaens GE, Annese V, des Varannes SB, et al. Pneumatic dilation versus laparoscopic Heller's myotomy for idiopathic achalasia. *N Engl J Med* 2011;364:1807-16.
15. Campos GM, Vittinghoff E, Rabl C, et al. Endoscopic and surgical treatments for achalasia: a systematic review and meta-analysis. *Ann Surg* 2009;249:45-57.

16. Gelfand MD, Kozarek RA. An experience with polyethylene balloons for pneumatic dilation in achalasia. *Am J Gastroenterol* 1989;84:924-7.
17. Tanaka Y, Iwakiri K, Kawami N, et al. Predictors of a better outcome of pneumatic dilatation in patients with primary achalasia. *J Gastroenterol* 2010;45:153-8.
18. Pandolfino JE, Kwiatak MA, Nealis T, Bulsiewicz W, Post J, Kahrilas PJ. Achalasia: a new clinically relevant classification by high-resolution manometry. *Gastroenterology* 2008;135:1526-33.
19. Heller E. Extramuköse Kardioplastik beim chronischen Kardiospasmus mit Dilatation des Oesophagus. *Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie* 1914;27:141.
20. Khashab MA, Messallam AA, Onimaru M, et al. International multicenter experience with peroral endoscopic myotomy for the treatment of spastic esophageal disorders refractory to medical therapy (with video). *Gastrointest Endosc* 2015.
21. Khashab MA, Saxena P, Kumbhari V, et al. Peroral endoscopic myotomy as a platform for the treatment of spastic esophageal disorders refractory to medical therapy (with video). *Gastrointest Endosc* 2014;79:136-9.
22. Stavropoulos SN, Desilets DJ, Fuchs KH, et al. Per-oral endoscopic myotomy white paper summary. *Gastrointest Endosc* 2014;80:1-15.
23. Minami H, Isomoto H, Yamaguchi N, et al. Peroral endoscopic myotomy for esophageal achalasia: clinical impact of 28 cases. *Dig Endosc* 2014;26:43-51.
24. Stavropoulos SN, Modayil RJ, Friedel D, Savides T. The International Per Oral Endoscopic Myotomy Survey (IPOEMS): a snapshot of the global POEM experience. *Surg Endosc* 2013.
25. Chiu PW, Wu JC, Teoh AY, et al. Peroral endoscopic myotomy for treatment of achalasia: from bench to bedside (with video). *Gastrointest Endosc* 2013;77:29-38.
26. Swanstrom LL, Kurian A, Dunst CM, Sharata A, Bhayani N, Rieder E. Long-Term Outcomes of an Endoscopic Myotomy for Achalasia: The POEM Procedure. *Ann Surg* 2012;256:659-67.
27. von Renteln D, Inoue H, Minami H, et al. Peroral endoscopic myotomy for the treatment of achalasia: a prospective single center study. *Am J Gastroenterol* 2012;107:411-7.
28. Shiwaoku H, Inoue H, Beppu R, et al. Successful treatment of diffuse esophageal spasm by peroral endoscopic myotomy. *Gastrointest Endosc* 2013;77:149-50.
29. Maselli R, Inoue H, Misawa M, et al. Peroral endoscopic myotomy (POEM) in a 3-year-old girl with severe growth retardation, achalasia, and Down syndrome. *Endoscopy*

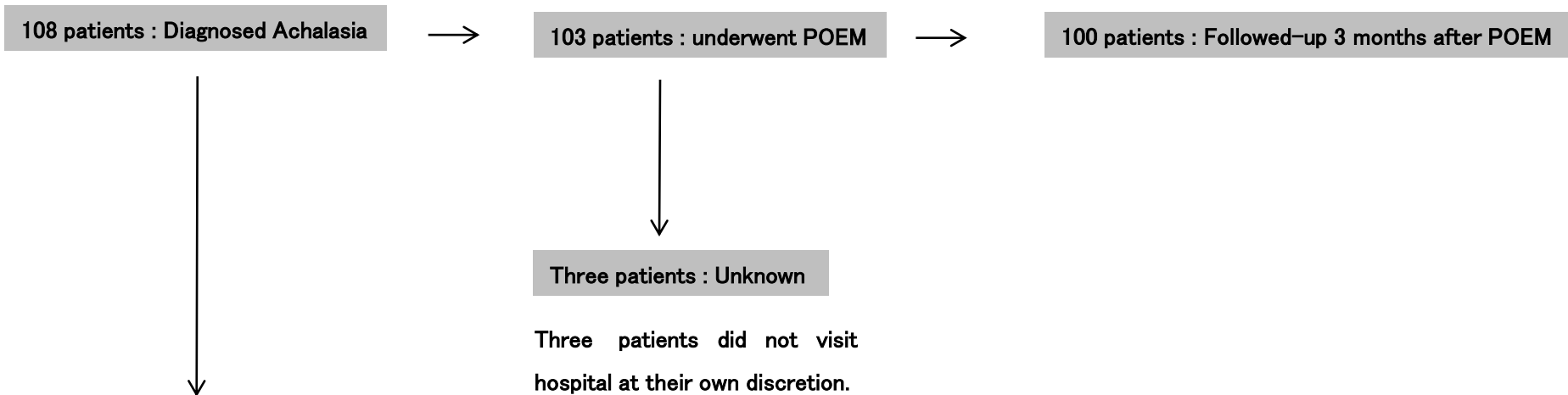
2012;44 Suppl 2 UCTN:E285-7.

30. Mittal RK, Balaban DH. The esophagogastric junction. *N Engl J Med* 1997;336:924-32.

31. Simic AP, Radovanovic NS, Skrobic OM, Raznatovic ZJ, Pesko PM. Significance of limited hiatal dissection in surgery for achalasia. *J Gastrointest Surg* 2010;14:587-93.

32. Shiwaku H, Inoue H, Sasaki T, et al. A prospective analysis of GERD after POEM on anterior myotomy. *Surg Endosc* 2015.

Table1. Recruitment of patients



2 patients : Observation

Male aged 59 and Female aged 53 : symptoms were mild and treated with medication based on patient's choice

2 patients : Balloon dilatation:

**Male aged 59 : pancreatic cancer Stage IV
Female aged 89 : ASA classification IV**

1 patient : Botox injection:

Female aged 89 : ASA classification IV

Table2. Patient Demographics and Perioperative Characteristics

Age, years, mean \pm SD (range)	48.2 \pm 18.8 (9 -91)
Sex	58 women, 42 men
Type of achalasia	
Straight type	90
Sigmoid type	10
Chicago classification	
Type I	12
Type II	74
Type III	14
Primary procedure, n	
Balloon dilatation	23
Heller-Dor operation	4
Botox injection	1
Length of procedure (range), minutes	150.8 \pm 49.3 (75-370)
Myotomy length, mean (range), cm	
Total	12.6 \pm 3.9 (5-26)
Esophageal	10.2 \pm 3,7 (3-23)
Gastric	2.5 \pm 1.0 (1-5)
Direction of myotomy	Anterior: 92 Posterior:8
Postoperative stay, mean \pm SD (range), days	7.4 \pm 2.4 (3-23)

SD, standard deviation

Table3. Comparison of the therapeutic effect due to the presence or absence of previous treatment history

	Without primary procedure (n=72)	With primary procedure (n=28)	p value
Balloon dilatation	0	23	
Heller-Dor operation	0	4	
Botox injection	0	1	
Sex (men/women)	25/47	18/10	0.013
Age	48.0±19.0	49.1±18.6	0.411
Disease duration, month	90.6±108.6	129.2±121.9	0.599
Type of achalasia			0.263
Straight type	67	23	
Sigmoid type	5	5	
Chicago classification			
I	4	4	0.022
II	50	16	
III	6	4	
ASA-PS			
I	57	20	0.287
II	20	8	
Adverse event, n	5	5	0.13
Pneumoperitoneum, n	7	4	0.485
Direction of submucosal tunnel, n			0.000
Anterior	71	21	
Posterior	1	7	
Eckardt score : Preoperative	5.9±2.5	5.7±2.4	0.964
Eckardt score : Postoperative	0.8±0.9	1.0±1.1	0.678
Eckardt score: (Preoperative)-(Postoperative)	5.2±2.5	4.7±2.8	0.357
Postoperative Eckardt score: improvement 3 points and more	59	18	0.345
Postoperative Eckardt score 3 or 3>	69	25	0.274
GERD			0.15
N/A	61	19	
B/C	11	8	
Operation time, min	146.3±42.5	164.0±62.5	0.126
Length of submucosal tunnel, cm	14.8±3.8	14.3±4.2	0.917
Length of myotomy, cm	12.9±3.7	12.0±4.4	0.869
Esophageal	10.4±3.5	9.7±4.1	0.866
Gastric	2.5±1.0	2.3±1.0	0.569
Postoperative stay, day	7.1±1.9	8.1±3.4	0.026
LES residual pressure : preoperative, mmHg	24.2±13.3	18.5±8.8	0.028
LES residual pressure : postoperative, mmHg	10.8±6.1	11.4±5.9	0.999
IRP: preoperative, mmHg	36.5±15.3	25.1±12.2	0.161
IRP: postoperative, mmHg	15.4±6.4	14.7±7.3	0.508

ASA-PS: American Society of Anesthesiologists physical status GERD : gastroesophageal reflux disease

LES : lower esophageal sphincter

IRP : integrated relaxation pressure

Table4. Adverse Events (Clavian–Dindo classification)

Grade I

Submucosal hematoma	1
---------------------	---

Pneumothrax	1
-------------	---

Grade II

Esophagitis due to mucosal injury	6
-----------------------------------	---

Mediastinitis due to mucosal injury	1
-------------------------------------	---

Grade IIIa

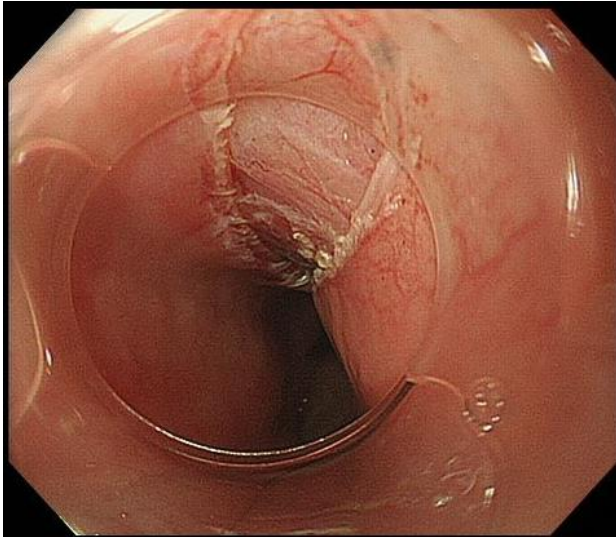
Bleeding from mucostomy due to clip dislodgement	1
--	---

Grade IIIb or more

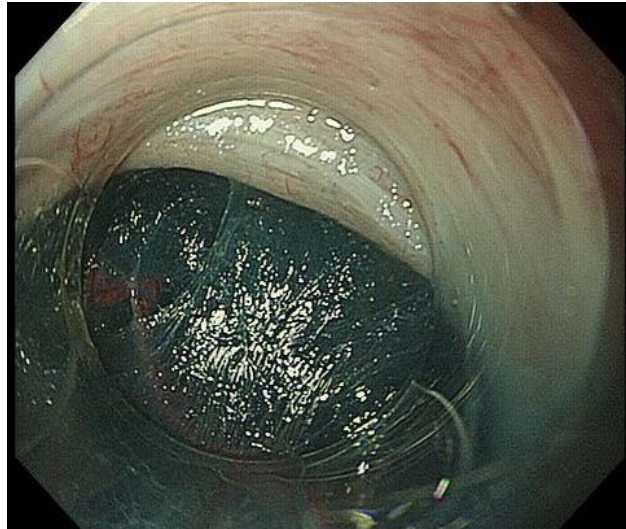
0

Figure1 : POEM procedure (anterior myotomy)

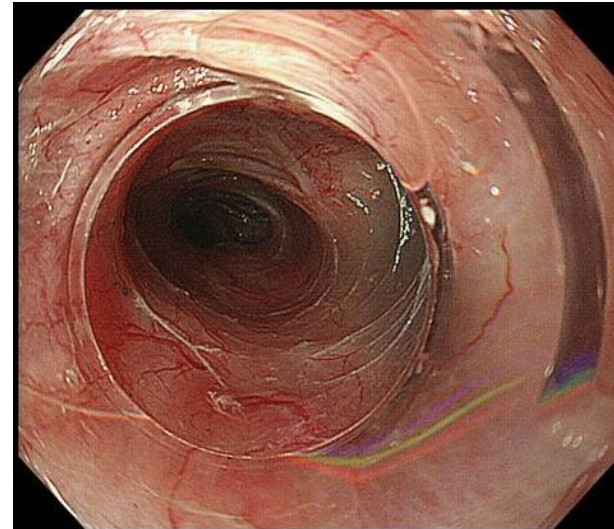
(a)



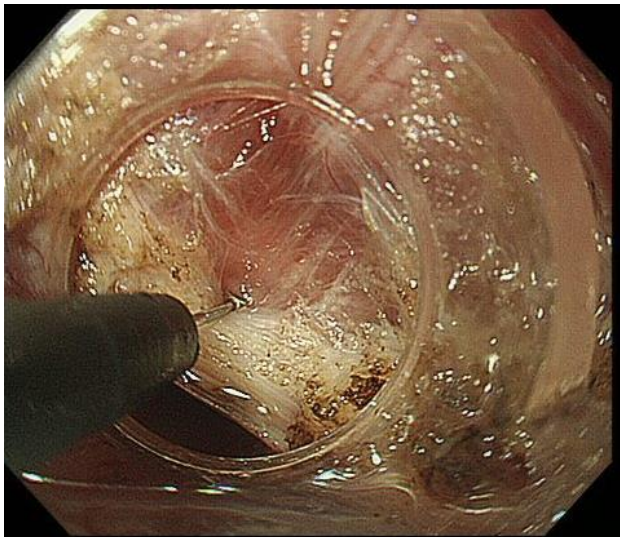
(b)



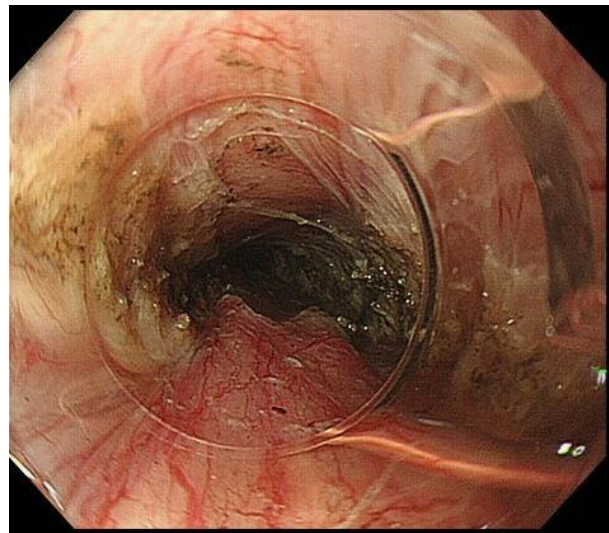
(c)



(d)



(e)



(f)

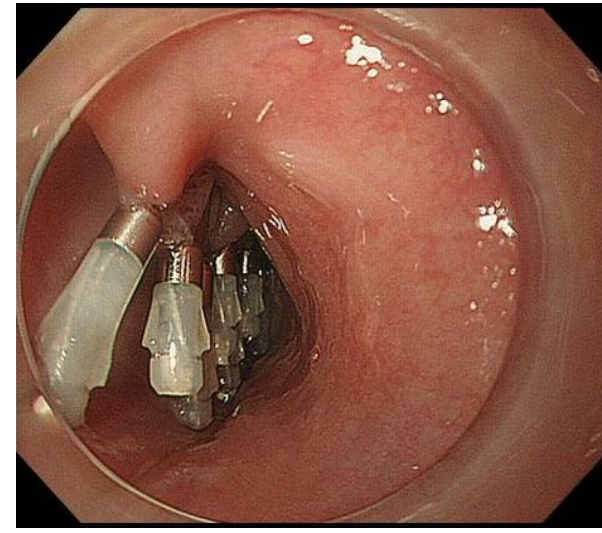


Figure2 :Barium swallow examination before and after POEM

(a)



Before POEM

(b)



After POEM

Figure3 : High resolution manometry before and after POEM

High-resolution manometry (Before POEM)

pharynx

LES

stomach

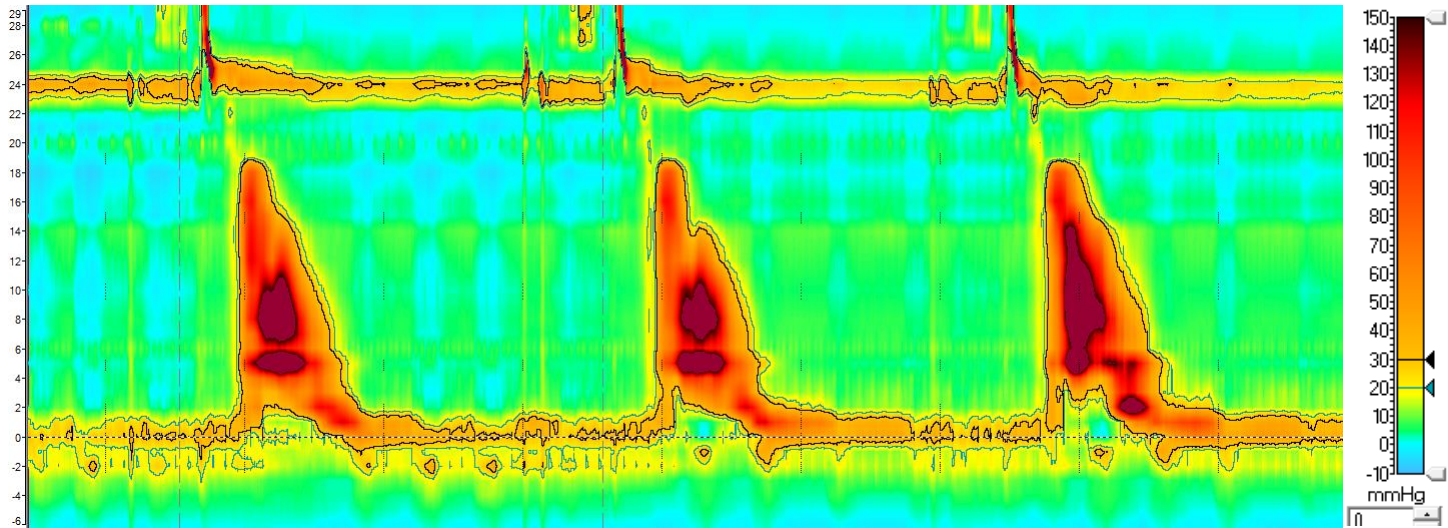


Figure3 : High resolution manometry before and after POEM

High-resolution manometry (After POEM)

