



Is Peroral Endoscopic Myotomy for Achalasia Safe in a Small-Volume Center?

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Abstract

Background and Aims: Peroral endoscopic myotomy (POEM) is a minimally invasive procedure for the surgical treatment of achalasia and an endoscopic alternative to open or laparoscopic Heller myotomy (HM). POEM was initially developed in Japan, was first published in 2010, and has since been increasingly adopted in Western countries. The aim of this study is to present preliminary data from the introductory phase of POEM in a small-volume center.

Material and Methods: The first 14 patients operated with POEM for achalasia at the University Hospital of North Norway were registered in a prospective database and retrospectively evaluated, as a quality assurance study. Indications for the procedures were manometric diagnosis of achalasia and a significant Eckardt symptom score (≥ 7 points).

Results: A total of fourteen patients, 6 female, median age 47 years (19-77 years), were operated in a day care unit and observed in the hospital ward for a median of 1 day (1-17 days). The preoperative and three month postoperative follow-up median Eckardt symptom scores were 8 (7-12) and 0 (0-9), respectively. One complication was encountered, which resulted in an intraoperative mucosal perforation, and was subsequently treated with an endoscopically implanted stent. Four patients reported acquiring occasional gastro esophageal reflux disease (GERD), which did not necessitate regular antacid medication.

Conclusion: Preliminary results from the introductory phase of POEM for achalasia in a small volume center demonstrate that the procedure was performed safely and with satisfactory short term results.

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Keywords: Per oral endoscopic myotomy; POEM; Achalasia

Introduction

Achalasia is a severe neuro-inflammatory disease of the esophagus causing dysfunction of the esophagus that, if not treated, results in weight loss and malnutrition [1]. A disturbance or weakening of the esophageal peristalsis combined with a lack of relaxation of the Lower Esophageal Sphincter (LES) when swallowing causes dysphagia with chest pain and regurgitation as concurrent symptoms. The condition is commonly misdiagnosed as GERD [2].

Traditional treatments of achalasia include botulinum toxin injection to relax the LES, PBD (pneumatic balloon dilation) to stretch the circular muscle fibers and finally surgical division (myotomy) of the LES in order to assist the passage of food and liquid into the stomach. Botulinum toxin injection and PBD are considered to give only temporary symptomatic relief, whereas myotomy results in a permanent solution for most patients [3].

Until quite recently an open or laparoscopic HM was the only surgical procedure in the treatment of achalasia. Fundoplication most often accompanies HM in order to prevent GERD after opening of the gastroesophageal junction (GE-junction) [4]. In 2010, the Japanese doctor Inoue H et al. published a new and revolutionary method for dividing the LES by an endoscopic technique based on a series of 17 patients [5]. This procedure quickly grew in popularity and became widespread in the course of few years because of its minimally invasive nature [6,7]. Inoue's novel endoscopic procedure spares patients open or laparoscopic surgery and has minimal impact on the patient, entailing only a small incision in the mucosa and myotomy of the circular muscle layer including the LES. It is debated whether there is more reflux following POEM than HM combined with fundoplication but this question is not yet fully answered.

Table 1: Patient and procedure data.

Number of patients (n)	14
Age, year, median; (range)	47 (19-77)
Female/male, n	8-Jun
Type I/type II/type III achalasia, n	3/10/2001
Resting LES pressure, mmHg, median; (range)	39 (26-68)
Barium esophagography diagnostic for achalasia, n	12
Previous pneumatic balloon dilation, n	5
POEM procedure time, min., median;(range)	167 (110-219)
Hospitalization after POEM, nights, median; (range)	1 (1-17)
CRP post-op. day 1, mg/L, median; (range)	37 (5-73)
Complications (intraoperative mucosal perforation)	1
Pre-op.Eckardt symptom score median; (range)	8 (7-12)
Post-op.Eckardt symptom score median; (range)	0 (0-9)
Post-procedure GERD, n	4



Figure 1: A) Primary mucosal incision, B) developing the submucosal tunnel with inner circular muscle (CM) to the right, C) tunnel entrance with mucosa (MC) flap, D) outer longitudinal muscle (LM) exposed after myotomy of the circular muscle, E) pericard (PC) is visible after spontaneous cleavage of longitudinal muscle layer, F) clip-suturing of primary mucosa incision.

The relatively small population of 0.5 million people in the region served by the University Hospital of North Norway, combined with a low incidence of achalasia ranging from 1-2/100.000 implies few cases per year [8]. In a small volume center it is crucial to demonstrate a sufficient level of quality and safety in order to provide a given surgical procedure.

Methods

From June 2016 to February 2018, 14 patients with achalasia were operated with POEM at the University Hospital of North-Norway and prospectively registered in a database, which was analyzed retrospectively. The selection of patients suitable for POEM was based on a clinical scoring system for achalasia (Eckardt score) [9], esophageal High Resolution Manometry (HRM) according to the Chicago classification [10], gastroscopy-findings and an esophageal X-ray after oral ingestion of barium contrast. Patients with an Eckardt score of ≥ 7 out of a maximum of 12 points and manometric findings consistent with achalasia were selected for POEM if gastroscopy and barium esophagography excluded other esophageal diseases. Patients received written and oral information regarding the procedure with an emphasis on potential complications and the risk of GERD following the division of the LES. The evaluation of

the implementation of POEM, as a procedure already in use in many other countries, is categorized as a quality assurance project with no requirement for disclosure or consent according to the rules of the Norwegian ethical committee. Due to its recent introduction as a surgical operative technique, POEM is registered in the National Norwegian database for evaluation of new methods in hospitals at The Norwegian Institute of Public Health.

All patients were operated in a day care unit under general anesthesia. Patients received prophylactic antibiotics intravenously as well as Proton Pump Inhibitor (PPI) intraoperative. The esophagus was washed with an antiseptic chlorhexidine solution 1 mg/ml (Fresenius Kabi, Halden, Norway). The operations were conducted with a gastro scope (Olympus GIF-HQ190, Olympus, Hamburg, Germany) with an oval, transparent cap on the tip (Fujifilm DH-29CR, Tokyo, Japan) and with CO₂ gas for insufflation. An Erbe VIO 300 (ErbeElectromedicin GmbH, Tübingen, Germany) was used for diathermy. The POEM procedure used, as initially described by Inoue [5], is outlined below.

A submucosal bubble was first created by injecting a solution of saline with 2% Indigo Carmine (Amino AG, Gebenstorf, Switzerland) approximately 14 cm cranial to the GE-junction between the 1 and 3 o'clock position using an endoscopic needle (Needle master NM-610U-0426, Olympus). A 2 cm longitudinal incision was made in the lifted mucosa (Figure 1A) with a Triangle Tip knife (KD645-L, Olympus). This mucosal incision was used to create a 15 cm submucosal tunnel, which exposed the circular muscle layer. The submucosal tunnel was extended caudally and ended 3 cm caudal to the GE-junction (Figure 1B and 1C). The tunnel was washed with a gentamicin solution 80 mg/20 ml NaCl (Sanofi-Aventis, Paris, France). A 13 cm myotomy of the circular muscle was then performed. This myotomy, which included the LES, was made in a caudal direction from 2 cm below the lower edge of the mucosal incision to 3 cm below the GE-junction (Figure 1D and 1E). Finally the mucosal incision was closed with small clips (N1085930, Olympus) (Figure 1F). Free gas in the abdomen was drained intra operatively with a left sub costal venflon if needed.

Patients were allowed to drink water immediately following the operation and received analgesics as required. Patients stayed overnight in the ward and were discharged on the first postoperative day if the clinical condition was satisfactory. No routine X-ray was performed before discharge. They were allowed liquid nutrition from day one with a gradual transition to solid food during the first week. Patients were given an extended antibiotic prophylaxis for five days (doxycycline 100 mg \times 1, metronidazole 400 mg \times 3) and PPI (pantoprazole 40 mg \times 1) for one month.

A follow-up telephone interview was performed after three months with an Eckardt symptom score. In addition, patients were asked if they experienced symptoms of GERD and if they still required the use of PPI medication.

Results

In all, 14 patients, 6 female and 8 male, were included in the study. All patients with achalasia referred to The University Hospital of North-Norway during the study period fulfilled the criteria for POEM operation with a significant Eckardt score (≥ 7) and a diagnostic manometry. Patient and procedural data are listed in Table 1. Median age 47 years (19-77 years). Type II achalasia was most frequent with 11 patients, followed by type I and type III with two and one patients,

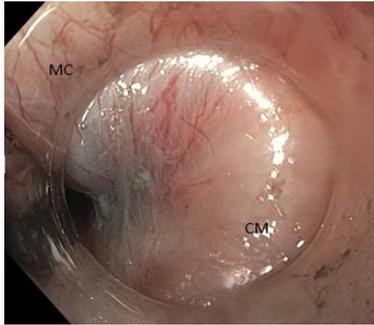


Figure 2: Severe submucosal fibrosis in the LES with no visible or dissectible layer between the mucosa (MC) and the circular muscle (CM).



Figure 3A: Intraoperative mucosal perforation at the GE-junction.



Figure 3B: Free air under the right hemidiaphragm due to insufficient clipping of the perforation.



Figure 3C: X-ray of the esophagus with barium contrast showed no leak after stenting. The stent is fixed with two clips to prevent migration.

respectively. Median integrated relaxation LES pressure (IRP4s) was 38.38 mmHg (26-68 mmHg). Five patients had previously been treated with 1 to 3 PBDs and one patient with botulinum toxin injection in the LES. A barium esophagography was diagnostic for achalasia in 12 of the 14 patients. Median procedure time in the operating theatre was 167 mins (110-219 mins) with the shortest procedure being the last. Four of the first seven patients required intra operative drainage of free gas from the abdomen. The median number of nights in the

ward after POEM was 1 day (1-17 days).

One patient presented with severe submucosal fibrosis around the LES (Figure 2), did not profit from the POEM, and was admitted for a total of 17 days. This patient had suffered weight loss due to achalasia and was therefore admitted to receive intravenous nutrition therapy after the failed POEM procedure. This fibrotic LES was later treated with several PBDs and stented with no permanent symptomatic relief. After a second POEM, still without effect, an intraluminal endoscopic incision through the hard fibrotic stricture was undertaken, and the patient was finally able to eat slowly.

The blood test C-reactive protein (CRP) was slightly elevated to a median value of 37 mg/l when measured the day after the operation, but with a great variation (5-73 mg/L). One complication occurred, which was treated endoscopically. A 2 mm hole in the mucosa resulted from application of diathermia to cauterize a bleeding artery in the mucosa at the GE-junction (Figure 3A). Ligation with intraluminal clips proved to be insufficient, due to the defect's difficult position, and therefore a covered stent was inserted when free intra-abdominal gas under the right hemi diaphragm presented on x-ray the day after the procedure (Figure 3B and 3C). The stent proved patent upon barium X-ray (Figure 3C).

Patients were scored for achalasia symptoms with the Eckardt score before and three months after the operation with the exception of the last patient operated, who was scored just under two months postoperatively. Median preoperative Eckardt score was 8 (7-12) while median postoperative score was 0 (0-9). Four patients reported mild and occasional GERD symptoms and two of these used PPI medication occasionally.

Discussion

This study reports a satisfactory level of treatment effect and safety following the introduction of a new endoscopic technique for the treatment of achalasia, which will replace the laparoscopic HM in our department. A meta-analysis of four nonrandomized studies comparing laparoscopic HM with POEM demonstrated lower Eckardt symptom score after surgery in the POEM group and no difference in the rate of complication or length of hospital admission [11]. Thus far there is no meta-analysis reporting an inferior outcome of POEM compared to HM [6,7,11-13].

Studies comparing post-procedural GERD in POEM vs. laparoscopic HM show that patients undergoing POEM were more likely to develop GERD symptoms in some meta-analysis [6,12,13] while in another meta-analysis no difference in symptomatic GERD was found [7]. In this study four patients (27%) reported occasional and mild GERD with no need for regular PPI-medication. Due to great variability regarding post-POEM GERD in different studies [7], a 2-year follow-up study of patients operated with POEM at the University Hospital of North-Norway is planned in order to elucidate the risk of developing GERD following POEM with greater certainty.

HRM is the gold standard for providing the diagnosis of achalasia. Elevated resting pressure in the LES is found in all three subtypes of achalasia. Specific deviations from normal peristalsis determines subtypes I - III. In subtype III, characterized by spastic esophageal contractions, the myotomy may be extended in the oral direction if needed to include proximal spastic parts of the esophagus [14]. Types I and II are treated with the standard length myotomy. In this study the only patient diagnosed with type III achalasia did not need an

extended myotomy to be cured. In addition to patients with achalasia, POEM was applied to treat a patient with a related diagnosis of severe esophageal gastric junction obstruction, but was not included in this study. Barium contrast X-ray of the esophagus is not a sensitive test for achalasia and is reported to be diagnostic in about two thirds of achalasia patients [15]. In this study 86% obtained a positive esophagram.

The operative technique used was essentially in accordance with the original method described [5], except that the length of the myotomy above the GE-junction was somewhat longer in this study. The longitudinal muscle layer was found to divide itself after making a thorough myotomy of the circular muscle layer. Intraoperative hemorrhages occurred mainly in the muscle layer of the cardia and was avoided by coagulation prior to incision. Free CO₂ gas in the abdomen was detected and intraoperatively drained with a venflon inserted below the left costal arch in four of the first seven patients. Also, subcutaneous emphysema of the upper chest and throat was detected in the first half of the patients, suggesting a decreased use of insufflation gas with increasing experience.

Five of the study patients were previously treated with PBD and one with botulinum toxin injection in the LES. These procedures resulted in temporary symptom relief as shown in other studies [16,17]. In this study, the POEM procedure was the primary treatment if Eckardt score was significantly elevated and manometric findings were diagnostic for achalasia. It is debated whether botulinum toxin injections and/or PBD lead to submucosal fibrosis in the LES, reducing or preventing the circumferential relaxation of the LES after myotomy. One patient presented with severe sub mucosal fibrosis with no prior achalasia treatment (Figure 2). This patient did not receive symptomatic relief following POEM. In a review of 1693 patients operated with POEM, 0.77% procedures were aborted and of these 92.3% were due to severe sub mucosal fibrosis [18].

In an international multicenter case control study the prevalence of adverse events with POEM was 7.5% of which 0.5% was severe [19]. Mucosal perforations occurred at a rate of 2.8%. In this sample one inadvertent mucosal perforation occurred. This perforation was first repaired with intraoperative endoscopic clipping, which proved insufficient, and thereafter definitively with a covered stent for two weeks (Figure 3). Despite the POEM procedure's proximity to vital structures in the mediastinum, such as the heart (Figure 1), severe complications are rare [19-21].

The POEM procedure's efficacy at reducing achalasia symptoms was striking, with a median Eckardt symptom score of 0 (0-9), three months postoperatively. This means a majority of the patients (9 out of 14) had no dysphagia, chest pain, regurgitation or further weight loss at follow-up. The observation period of three months in this study is short and recurrences may occur in the long term. However, the largest long term study after POEM for a series of 500 Japanese patients shows a median Eckardt score of 1.0 (\pm 2.0) after two months, which persisted at the three year follow-up [20]. In a long term study from the USA including 115 patients a 92% success rate was observed after 2.4 years [21].

One gastrointestinal surgeon (C.R.) performed all the POEM procedures after participating in several at Haukeland University Hospital, Bergen, Norway. The first two procedures at the University Hospital of Northern Norway were performed under the supervision of an experienced POEM surgeon - Dr. Bengt Håkansson, Ersta

hospital, Sweden. Some authors suggest that preclinical POEM procedures should be performed in animal models in order to learn the procedure [22], however this option was not available. Moreover, the surgeon C.R has extensive experience from more than 400 endoscopic mucosal resections and sub mucosal dissections before starting with POEM [23]. Whereas some endoscopic resections are performed with the endoscope in difficult angulations, or even inverted, the POEM procedure is performed with the gastroscope straight forward and is therefore technically not very difficult. However, even if reported serious complications are few, the potential for serious complications is significant and requires that the operator possesses endoscopic skills from other advanced endoscopic procedures before learning POEM.

In conclusion POEM in the treatment of achalasia can be performed safely and with good short term results in a small-volume center based on a thorough preoperative investigation including HRM, and performed by an operator experienced in endoscopic resections and interventions. In this study mild symptomatic post-POEM GERD was reported in a quarter of the patients. More studies of long term efficacy and post-POEM GERD are needed.

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