

## REVIEW ARTICLE

## Peroral endoscopic myotomy for achalasia

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## Key Messages

- Current endoscopic and surgical treatments for achalasia carry risks for potential severe complications and symptom recurrence occurs in a significant subgroup.
- Recently per-oral endoscopic myotomy (POEM) has been introduced as a promising alternative to the current treatments.
- We reviewed the currently available literature on this technique and describe our findings and experience with POEM.
- Several open label studies have been published showing excellent short term results with only few complications.
- The authors identify the need for randomized controlled trials with long term follow up comparing POEM with standard treatment.

## Abstract

**Background** Treatment of achalasia is complicated by symptom recurrence and a significant risk for severe complications. Endoscopic myotomy was developed in the search for a highly efficacious treatment with lower risks. Since its introduction in 2010, several centers have adopted the technique and published excellent short-term results of open label series. Randomized trials with long-term endpoint comparing per-oral endoscopic myotomy (POEM) with the established treatments such as balloon dilation and surgical myotomy are now warranted, before POEM can be regarded as the routine clinical care for achalasia patients. **Purpose** This review describes the development, technical aspects, efficacy, and complications of POEM.

**Keywords** endoscopy, esophagus, motility, NOTES, spasms.

## INTRODUCTION

Despite attempts to clarify the pathophysiology of achalasia, there is not much known about the cause of this disease. An initial event of unknown origin triggers inflammatory destruction of myenteric plexus ganglion cells resulting in dysrelaxation of the lower esophageal sphincter (LES) and aperistalsis of the esophageal body musculature. It has been suggested that autoimmunity, viral infections, and genetics play a role, but this far a unifying hypothesis is lacking.<sup>1–4</sup> Sometimes achalasia is secondary to another disease such as malignancy, sarcoidosis, or trypanosome cruzi infection (Chagas' disease), but these cases are fundamentally different from idiopathic achalasia and not considered in this review.<sup>5–7</sup>

Fortunately, there is consensus on how the diagnosis should be made. In case of achalasia, manometry or preferably high-resolution manometry (HRM) of the

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Received: 3 September 2013

Accepted for publication: 6 October 2013

esophagus reveals aperistalsis in the esophageal body and incomplete LES relaxation.<sup>8</sup> Usually, the upper esophageal sphincter (UES) is not involved in the disease and will relax completely. Recent studies have shown that HRM has a small but significant diagnostic advantage over traditional manometry in diagnosing achalasia, as with HRM esophageal shortening cannot result in so-called LES pseudorelaxation whereas with traditional manometry considerable shortening of the esophagus can cause it to appear as if the LES relaxes.<sup>9</sup> High-resolution manometry has also made it clear that it is possible to subclassify achalasia into three distinct subtypes, type I or classic achalasia, type II with panesophageal pressurization, and type III with a spastic component.<sup>10</sup> This classification of achalasia is important, as it has prognostic value and may be helpful to direct treatment. A special variant of achalasia is esophagogastric junction outflow obstruction, where LES dysrelaxation occurs in conjunction with preserved peristalsis.<sup>8</sup>

Additional information on the presence and degree of stasis and esophageal dilation can be obtained with a barium swallow. A special form of the barium swallow, the timed barium esophagram, is particularly useful to quantify the degree of stasis.<sup>11</sup> For a timed barium esophagram a radiograph is made at baseline, and after 1, 2, and 5 min after intake of a 200 mL barium solution. The test allows comparison before and after a procedure and helps to make a decision in case of symptom recurrence after treatment.

As the primary cause of achalasia is unknown, all treatment options are palliative and directed at reduction in the occlusion at the LES. Medical, endoscopic, and surgical options are available. The effect of pharmacological treatment with calcium channel antagonists and nitrates is only limited and these drugs do not stop the progression of esophageal dilation, therefore their use as primary treatment of achalasia has been abandoned.

Endoscopic pneumodilation is currently the most performed treatment for achalasia. With endoscopy a guidewire is inserted and a rigid balloon is passed over the wire until it is positioned at the level of the esophagogastric junction. This can be carried out under fluoroscopic guidance. The balloon is inflated and subsequently dilates the LES. Different balloon sizes can be used and the procedure can be repeated in case of limited effect or recurrence. The most feared complication is perforation, which was encountered in 4% of cases in a recent large randomized controlled trial.<sup>12</sup> Other complications are bleeding and pain. The advantage of pneumodilation is the relatively little invasive nature of the procedure, and the fact it can be

performed under conscious sedation or using propofol. Disadvantages of pneumodilation are the relatively high rate of symptom recurrence which usually makes repetitive treatment sessions required and the high prevalence of reflux after treatment.

Alternative to pneumodilation is the Heller myotomy, usually performed through laparoscopy. The essence of the operation is to cut the circular muscles of the LES, which is often combined with anterior fundoplication according to Dor. Heller myotomy is a very effective treatment, with a 90–95% success rate.<sup>12</sup> A potential complication typical for this procedure is a transmural perforation not recognized during the surgery occurring in about 4%, but other complications associated with laparoscopic surgery such as lesions to spleen and intestines, bleeding and infections also occur. Disadvantage of Heller myotomy is the invasiveness of the procedure, usually requiring hospital admission.

Botulinum toxin is a neurotoxin that reduces acetylcholine release from nerve endings. It can be injected in the LES region under endoscopic vision and this results in a reduction in LES pressure and improvement of dysphagia. Botulinum toxin injections are safe and easy to perform but the downsides are high costs and the effect wears off rapidly; there is nearly always recurrence after several months. This is why this modality is usually reserved for frail patients with significant comorbidity. Botulinum toxin injections are also suitable to bridge a period in which more invasive treatments are not possible, for example during pregnancy and patients temporarily using double or triple antiplatelet therapy.

## NOTES AND DEVELOPMENT OF THE POEM TECHNIQUE

After introduction of fiber-optic gastrointestinal endoscopy as a pure diagnostic technique around 1960, endoscopic therapy slowly developed. The first therapeutic possibilities consisted of removal of colonic polyps, followed by endoscopic sphincterotomy for common bile duct stones and palliative stent placement in bile ducts and esophagus for malignant obstruction. Subsequently, more advanced therapeutic techniques were developed consisting of different mucosal resection techniques and transmural procedures to drain pancreatic fluid collections.

The continuing aspirations of therapeutic endoscopists to perform surgical procedures in a less invasive way were nicely illustrated by the introduction of the term NOTES standing for Natural Orifice Transmural Endoscopic Surgery. Many animal experiments were

carried out worldwide, mostly in centers with a close cooperation between surgeons and gastroenterologist. The first report of an experimental per-oral endoscopic myotomy (POEM as we now know it) in animals was published in 2007.<sup>13</sup> The report describes a new technique of performing endoscopic myotomy under direct endoscopic vision in four pigs after the creation of a submucosal esophageal tunnel. Its efficacy was demonstrated by a drop in LES pressure after 7 days in this survival study. The technique was later on slightly adapted and the first human study report was published by Inoue *et al.* in 2010.<sup>14</sup>

This publication was not the first report of an endoscopic myotomy in humans, as this had already been published in 1980.<sup>15</sup> In this article however the myotomy was performed in an uncontrolled fashion by blindly incising the mucosal and deeper layers in the distal esophagus with a needle knife at the site of the convergence of the folds in 17 humans. Although uncontrolled and thereby at high risk for perforation, the technique was technically successful in all patients. Postoperatively, dysphagia improved and an average weight gain of 5 kg was achieved. Only two patients complained of minimal dysphagia, but this was regarded significantly less than preoperatively. Esophageal manometry showed a reduction in resting LES pressure from 34.5 to 9.2 mmHg. Although the cardia was wide open after the procedure, there was no reporting of any newly developed reflux symptoms or esophagitis. The technique was not reported a second time in the literature, probably because of considerable risk of perforation.

## TECHNICAL ASPECTS OF THE POEM PROCEDURE

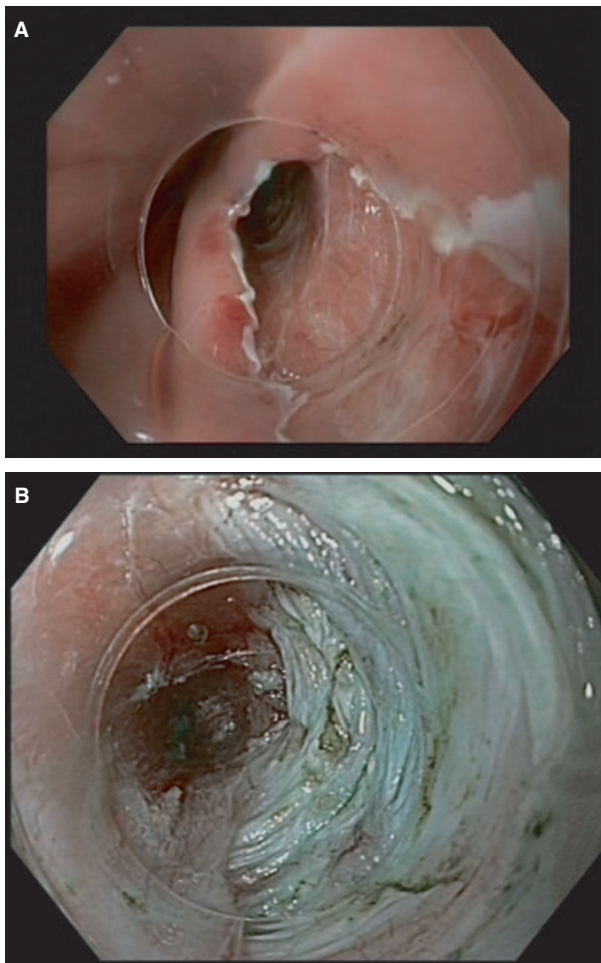
The POEM procedure can be divided into four consecutive parts, being the mucosal incision and entry in the submucosa, creation of the submucosal tunnel, the actual myotomy, and finally the closure of the mucosal incision. These four steps will be discussed separately and preprocedural and postprocedural care for patients undergoing a POEM procedure will also be discussed.

Preprocedural preparation for POEM should include assessment of comorbidities and anesthesiological risk. Fortunately, most achalasia patients are otherwise healthy and fit to undergo an invasive endoscopic procedure under general anesthesia. In case of use of anticoagulant or antiplatelet therapy, these medications should be stopped with the exception of acetyl salicylic acid when prescribed as secondary prophylaxis. Patients are on nil by mouth for at least 6 h prior to the procedure and in some centers they are put on a

clear liquid diet for 24–48 h before that. In case of severe stasis, these periods can be extended. Prophylactic antibiotics are generally prescribed, either as a single dose or as a short course of maximally 72 h. For the actual POEM procedure patients are placed in supine position and receive general anesthesia with endotracheal intubation.

After introduction of a normal caliber gastroscope with a transparent cap attached to its tip, the esophagus is carefully inspected and all residual food and fluid is removed. The level of the esophagogastric junction is determined and 10–15 cm proximal from this the site for the mucosal incision is determined. It is argued that for type III achalasia with proximal esophageal spasms, the mucosal entry should be made more proximal in order to allow a longer myotomy. Usually, the incision is made at the right lateral side (3 o'clock in supine position). The best way to keep a good right lateral orientation is by repeatedly checking the position of the lesser gastric curve relatively to the incision and tunnel. After injection of 10mls blue stained saline in the submucosa, a longitudinal incision in the mucosa can be made with an endoscopic electro-cautery knife such as the triangle-tip knife (Olympus Medical Systems, Hamburg, Germany). The incision should be superficial and around 25 mm long, allowing the cap on the tip of the endoscope to enter the blue stained submucosa. In case of difficulty of entering in the submucosa, additional fluid can be injected and/or the incision extended.

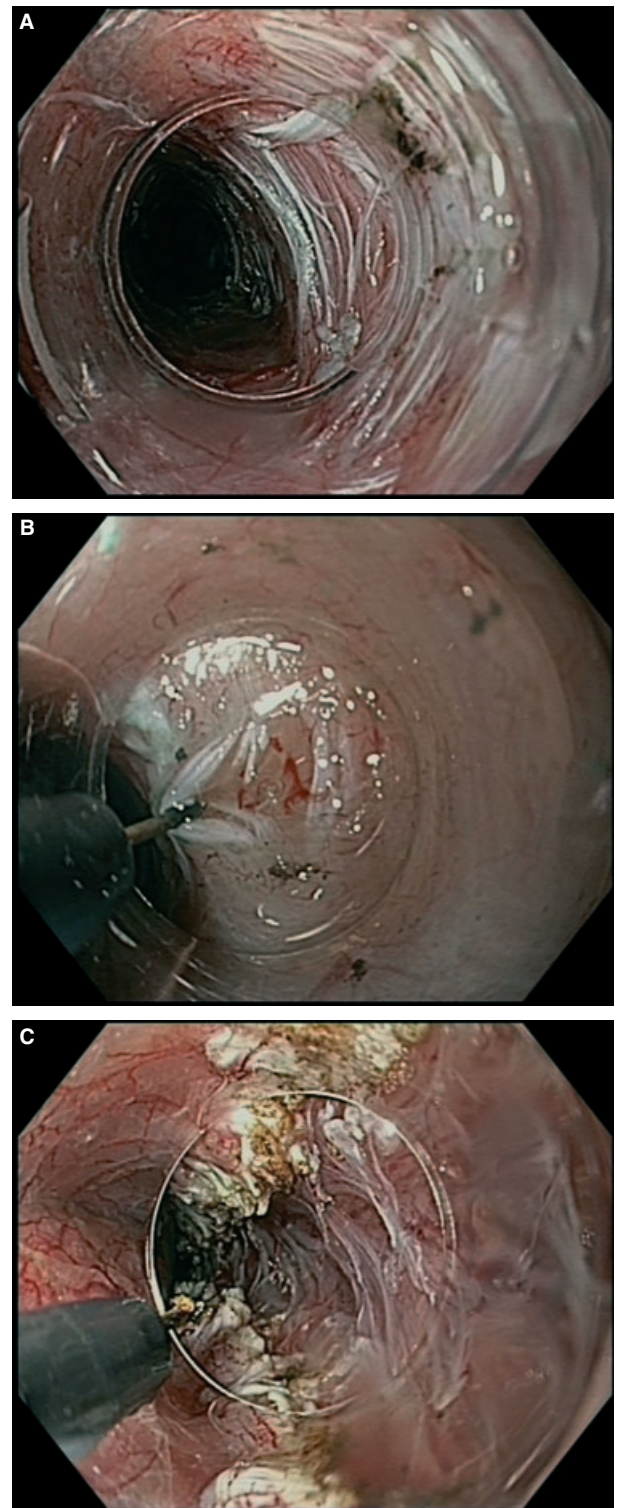
Once the scope has entered the submucosa, injection is repeated but from now on always with blunt catheters such as closed needles or spray catheters that are commonly used for chromoendoscopy. Creation of the tunnel consists of injections alternated with separating the submucosal tissue by coagulation (Fig. 1). For the tunnel formation spray-coagulation is typically used, a technique consisting of contact-free surface coagulation with low penetration depth that seems to be perfectly fitted to this part of procedure. As an alternative to the repeated exchange of instruments a so-called hybrid knife (Erbe, Tuebingen, Germany) can be used which allows for both injection and electro-cautery. During the tunneling, depth and correct orientation of the tunnel are repeatedly checked by pulling the scope out of the tunnel and advancing it into the esophageal lumen and the stomach. The required maximal depth of the tunnel should be at least 2 cm below the level of the LES to assure complete exposure of the LES area for myotomy in the next stage. Creating the most distal 5 cm of the tunnel can be quite challenging as the accessibility of the submucosa is reduced by the hypertensive



**Figure 1** The mucosal entrance to the submucosal tunnel and the lumen of the esophagus. (B) Inside the submucosal tunnel, delineated by the mucosa of the esophagus on the left and the circular muscle fibers on the right.

LES. Apart from using saline or more viscous fluids, special gels are under development, which create an immediate tunnel by pushing the submucosal tissue aside instead of diffusely penetrating it.<sup>16</sup> After the tunnel has been completed, the mucosal integrity in the esophageal lumen and proximal stomach is checked for injury. In case of severe injury, it is contraindicated to continue with the myotomy because of the risk of full-thickness perforation after completion of the myotomy.

The third stage of the procedure is the actual myotomy. The start of the myotomy should be at least 2 cm below the distal end of the incision in order to have a section where both mucosa and muscle layer are intact. This is considered essential as in this area the two layers will probably quickly fuse again after the procedure, thereby creating a second closure area just



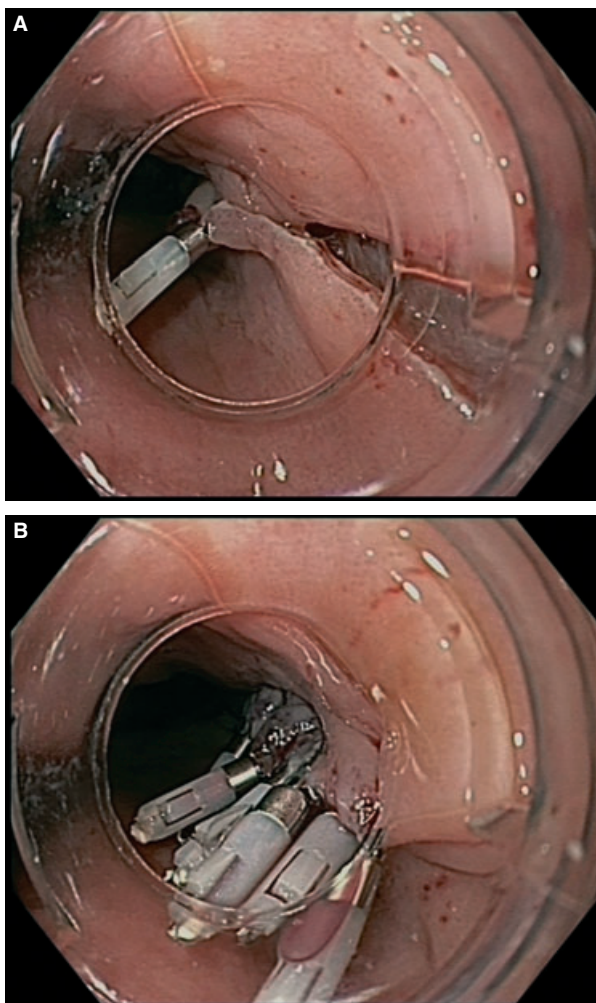
**Figure 2** The circular muscle fibers are clearly visible in the submucosal tunnel (A), myotomy of circular muscle is started by pulled up and cutting the muscle fiber bundles (B). After the myotomy the muscle layers open and the longitudinal muscle layers become visible (C).

below the closed mucosal incision. Myotomy of the circular muscle layer is performed with an angulated tip of an electro-cautery device such as the TT-knife or hybrid knife. Individual fiber bundles of the circular muscle layer are pulled up and cut from proximal to distal (Fig. 2). This is an adaptation to the original description in 2007 where the myotomy was performed from distal to proximal. The myotomy is usually not the most difficult part of the procedure although it has to be carried out very carefully in order to make sure all fibers are separated and no blood vessels are accidentally damaged. In the gastric part of the tunnel, the risk of bleeding is higher and bleeding in this area can be difficult to control.

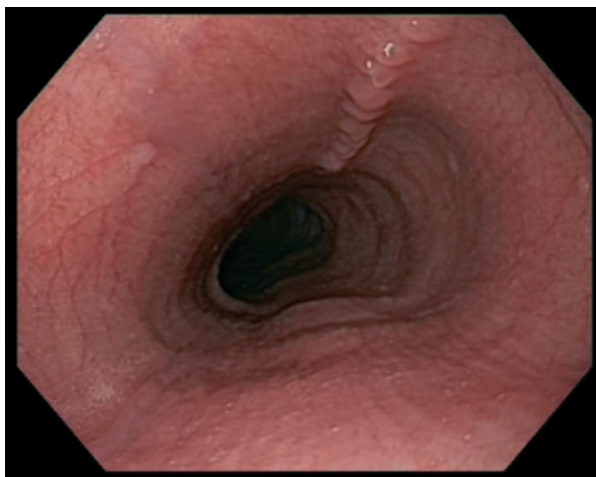
Distally in the tunnel, some of the muscle fibers sometimes run obliquely and should also be cut to assure a complete myotomy. The longitudinal muscle fibers are exposed readily once the circular fibers are cut and sometimes separate spontaneously allowing a clear view of the mediastinal structures. Once the myotomy is completed, passing through the esophageal sphincter area into the stomach should have become easy and again measurements are taken to ensure that the tunnel and myotomy have included the entire LES. Some endoscopists administer antibiotics locally after completion of the myotomy. As POEM is a young procedure, there is absolutely no evidence base for these small additional steps in the procedure and these are left to the individual preference of the local institution.

The final and a critical part of the procedure is the closure of the mucosal entry. This is usually performed with multiple endoscopic clips. Placing the first distal clips can be challenging as the repeated movements of the endoscope during the entire procedure have sometimes stretched the distal end of the incision. It is important to place the first clip a few millimeters below the incision to approximate the edges thereby facilitate further closure (Fig. 3). Between 8 and 12 clips are generally required and closure takes usually between 10 and 20 min with exceptions of up to an hour. Several alternatives to facilitate closure have been reported in literature. Examples are the addition of surgical glue to the clips, using a large over the scope clip (OTSC, Ovesco Tuebingen, Germany), and closure of the incision with an endoscopic suturing device and a running suture (Overstitch; Apollo Endosurgery, Austin, TX, USA).<sup>17,18</sup>

Pneumoperitoneum is an event that occurs during POEM in at least 30% of cases and is caused by the non-pressure controlled insufflation of carbon dioxide while working in the submucosal tunnel. Pneumoperitoneum does not usually interfere with the procedure



**Figure 3** The mucosal entrance is closed by placement of clips, and the first clip is placed just proximal of the proximal start of the incision.



**Figure 4** After 3 months, only a scar is visible at the site of the mucosal entrance.

but can become apparent when ventilation pressures rises. Desufflation of the pneumoperitoneum is easy and this should not be considered an adverse event as it will not influence further management of the patient.

Postprocedural care minimally consists of admission for one night, and a water soluble contrast X-ray the next morning to assure the absence of leakage of contrast into the mediastinum. Patients are generally kept on a semi-solid diet for 14 days after the procedure. Routine upper endoscopy 1 or 2 days after the procedure is sometimes performed but does not seem to influence management. The clips fall off and the mucosal entrance heals within a few weeks (Fig. 4). In order to prevent any possible damage by gastric acid to the vulnerable mucosa above the tunnel and at the level of the mucosal opening, we prescribe our patients acid suppression for 2 weeks postoperatively.

## EFFICACY OF POEM

All reports on POEM show that the technique is highly efficacious in the short-term, as summarized in Table 1. In most studies, treatment success was defined as postoperative Eckardt score  $\leq 3$ , and this was achieved in 89–100% of cases.<sup>14,19–24</sup> However, all data are derived from uncontrolled setting in open label studies and follow-up is short and often not standardized. One should also realize that with an Eckardt score of 3, a patient can still have daily symptoms at each meal (Table 2).

In the first report on POEM in humans, Inoue *et al.* reported the results of the procedure in 17 patients in which the procedure was performed technically successful in all subjects.<sup>14</sup> After a mean follow-up of 5 months, a dysphagia symptom score (ranging from 10, most severe, to 0, none) was reduced from 10 to 1.3 and the resting LES pressure from 54.4 to 19.9 mmHg. One patient developed reflux esophagitis grade B which responded well to antisecretory treatment with PPI.

Von Renteln published the results of POEM in 16 achalasia patients.<sup>19</sup> In all but one patient (94%) the

treatment was successful, with a 3-month Eckardt score  $\leq 3$ . The patient that was considered a failure required additional endoscopic balloon dilations after which his Eckardt dropped to 2. Mean LES resting pressure decreased from 27.2 to 11.8 mmHg. Reflux symptoms were not reported but in one patient grade A esophagitis was seen on follow-up gastroscopy.<sup>19</sup>

From the same authors, recently the follow-up results became available of a cohort of 70 achalasia patients treated with POEM.<sup>24</sup> The 3-month results show a treatment success (decrease in Eckardt score  $\leq 3$ ) in 97% of patients. LES pressure decreased from 28 to 9 mmHg. At 6 and 12 months, treatment success persisted in 89 and 82% of patients, respectively, suggesting a decrease in efficacy over time.

The results of the largest published series this far mention 205 patients treated in China, and treatment was not possible in three because severe submucosal fibrosis requiring preoperative abortion of the technique. In all 199 treated patients dysphagia was effectively relieved.<sup>20</sup>

Results from Italy are rather similar to the above described reports.<sup>22</sup> Endoscopic myotomy was technically feasible in 10 out of 11 patients, and clinical success defined as Eckardt  $\leq 3$  at 1 month was obtained in all 10 treated patients. Resting LES pressure decreased from 45.1 to 16.9 mmHg. Esophagitis was not seen in any of these patients during endoscopy 3 months later.

Another Japanese study in 28 achalasia patients showed large reductions in Eckardt score, LES pressure, and barium column height.<sup>25</sup> Symptomatic reflux was present in six patients (21%).

**Table 2** Eckardt score

Score	0	1	2	3
Dysphagia	No	Occasionally	Daily	At each meal
Regurgitation	No	Occasionally	Daily	At each meal
Chest pain	No	Occasionally	Daily	At each meal
Weight loss	0 kg	0–5 kg	5–10 kg	>10 kg

**Table 1** Efficacy of POEM

Study	N	Outcome measure	Reported efficacy	Follow-up
Inoue, 2010	17	Dysphagia score (0–10)	1.3	5 months average
Von Renteln, 2012	16	Eckardt score $\leq 3$	94%	3 months
Von Renteln, 2013	70	Eckardt score $\leq 3$	97%, 89% and 82%	3, 6 and 12 months
Zhou, 2012	205	Dysphagia relief	97%	8.5 months average
Costamagna, 2012	11	Eckardt score $\leq 3$	91%	1 month
Minami, 2013	28	Eckardt score $\leq 3$	100%	3 months
Swanstrom, 2012	18	Eckardt score $\leq 3$	94 and 100%	1 and 6 months
Hungness, 2013	18	Eckardt score $\leq 3$	89%	6 months average
Lee, 2013	13	Eckardt score $\leq 3$	100%	3 months

Swanstrom *et al.* report on the results of POEM in 18 patients with achalasia.<sup>26</sup> All patients responded to the treatment, and only one patient had an Eckardt score above 1 at 6 months follow-up. Six patients reported heartburn, 14 patients underwent upper endoscopy after treatment, and esophagitis is found in four (28%). Thirteen patients underwent pH monitoring, and six (46%) had a pathological acid exposure. Esophageal manometry was performed in 12 patients and showed a reduction in resting LES pressure from 45.0 to 16.8 mmHg.

Hungness *et al.* reported similar results in 18 patients undergoing POEM with 16 (89%) having treatment success with Eckardt scores  $\leq 3$  and significant reductions in LES pressure and barium column height.<sup>27</sup> Reflux symptoms were present in 22% and esophagitis in 33% of the treated patients. A Korean report mentions that 13 out of 13 patients were successfully treated with POEM in complete absence of GERD symptoms, whereas a large reduction in LES pressure was obtained.<sup>23</sup>

From all studies it appears that there is no evidence to suggest that prior botulinum toxin injections or balloon dilations affect the efficacy or complication risk of a subsequent POEM procedure.<sup>28</sup> There are reports showing that POEM is even feasible and effective after recurrent symptoms after Heller myotomy. The first report mentions that 12 patients with failed Heller myotomy underwent POEM without serious complications.<sup>29</sup> Treatment success was achieved in 11/12 patients with a large reduction in both symptom score from 9.2 to 1.3 and mean LES pressure from 29.4 to 13.5 mmHg measured 5–14 months after treatment. These results were confirmed by Onimaru *et al.* who describe that so-called rescue POEM after failed pneumodilation and Heller myotomy was effective in reducing LES pressure and Eckardt score in all 10 patients treated as such after failed Heller myotomy.<sup>30</sup>

In the previously mentioned large case series from Zhou, it is mentioned however that POEM was not feasible in three out of 202 patients because of severe submucosal fibrosis; the authors suggest that this is possibly due to previous treatment but the nature of the previous treatments was not mentioned. We also experienced severe submucosal fibrosis in one patient, preventing us from creating a submucosal tunnel and thus making it impossible to perform a myotomy. This patient was never treated before, however, and the fibrosis was present in the entire esophagus, making us believe that this is a primary characteristic of a specific achalasia variant.

Familiari *et al.* describe the effective and safe treatment of three children with achalasia using the POEM

technique.<sup>31</sup> There is also a report that POEM was performed in 3-year-old girl with Down syndrome after failed balloon dilation, demonstrating that this treatment is feasible in small children as well.<sup>32</sup> In both reports the equipment and treatment protocol were similar to that used in adults and after 1-year follow-up the patient was still asymptomatic.

All published case series thus provide similar results, reporting a significant reduction in dysphagia and LES resting pressure, but also a relatively high prevalence of reflux. A mechanistic study showed that besides the expected reduction in LES pressure, also esophagogastric junction distensibility as measured with endoflip was increased significantly.<sup>33</sup> This explains the observation that the patients are much more susceptible to development of reflux disease after POEM treatment.

## COMPLICATIONS

Surprisingly few severe complications have been reported with POEM, considering that this is a complex procedure with a considerable learning curve (Table 3).

Reflux symptoms and reflux esophagitis occur frequently and are a logical consequence of the treatment, although the development of GERD is unwanted, it can be easily treated with PPI and are not considered a complication. Pain after the procedure is also common, and a careful perioperative pain management protocol should be present.

Rather frequently pneumoperitoneum and cervical emphysema are experienced during the procedure, and pneumomediastinum is often seen on radiological imaging. This is however relatively harmless and caused by leakage of infused carbon dioxide through the muscle layers of the esophagus to the mediastinum, neck and peritoneum, and not considered a complication either if it has no serious consequences and easy to cope with during the procedure. Pneumoperitoneum during the procedure can easily be man-

**Table 3** Potential peri-operative complications

Bleeding	
Infectious	Pneumonia
	Peritonitis
Transmural perforation	
Dehiscence of mucosal entry	
Mucosal ulcer	
Pneumothorax requiring treatment	
Atelectasis	
Thoracic effusion	

POEM, per-oral endoscopic myotomy.

aged by placing a desufflation needle through the abdominal wall into the peritoneum. Emphysema will disappear spontaneously over the next few days. Pneumothorax is rather frequently encountered when a CT is made, but it is usually discrete and does not require treatment as the infused carbon dioxide is rapidly absorbed. Only in extreme cases with respiratory consequences, placement of evacuating thoracic drains is advised.

Both refluxesophagitis, postoperative pain and air in mediastinum and peritoneum, are easy logical consequences of the procedure and easy to manage and are not considered complications.

Perforation, however, is a feared and severe true potential complication of POEM. During the cutting of the circular muscle, the mediastinum is usually seen through the muscle fibers, and this is not considered a complication. A perforation during POEM occurs when there is an opening of all wall layers at the same level in the esophagus. Because the submucosa and muscle layers are already open, minor mucosal damage is enough to have a full thickness perforation. Most perforations occur at the level of the cardia, because creation of the submucosal is more difficult at that level as the hypercontractile LES restricts movement and space and because of the natural corner at the transition from esophagus to cardia. Perforations of the mucosa result from direct damage from endoscope manipulations or from coag-

ulation damage and occur in 0–7%.<sup>22,24</sup> If such a perforation is recognized during the procedure, it can simply be treated by closing the mucosal lesion with clips. It has also been reported that a larger perforation was closed with an endoluminal suturing device.<sup>17</sup> However, when the perforation is not recognized and treated during the procedure, leakage of luminal contents can lead to mediastinitis. Therefore, it is recommended to start oral feeding only after a water-soluble contrast study has excluded a perforation (Fig. 5).

Superficial ulcers in the distal esophagus occur occasionally along the dissection route, and these are probably the result of local ischemia, endoscope manipulation or cauterization damage, and usually are no reason for concern. If required, a clip can be placed to cover the ulcer and prevent perforation; however, perforations secondary to ulcers or ischaemia have never been reported this far.<sup>24</sup>

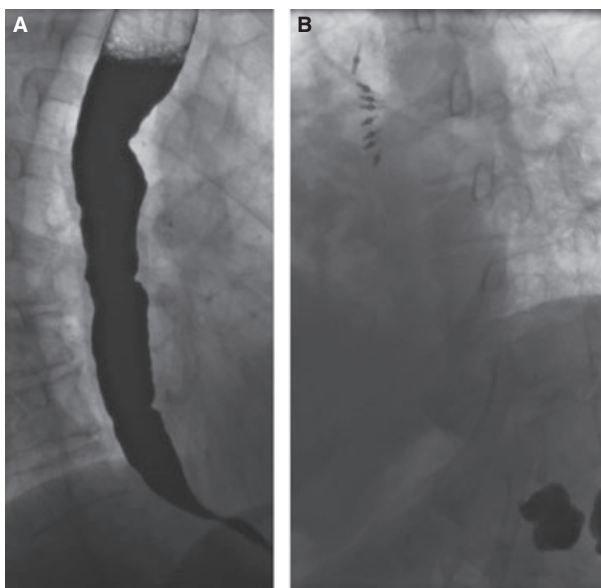
Major bleeding occurs infrequently during the procedure, probably because only few vessels are encountered in the submucosal tunnel and the view on the vasculature around the muscle fibers is excellent during the procedure. Delayed bleeding was reported in three patients in a large series of 428 patients (0.7%) and occurred without warning or preceding difficulty during treatment.<sup>20</sup> Acute hematemesis required emergency endoscopy and removal of the clips in order to evaluate the submucosal tunnel and muscle. In two out of the three patients the bleeding spot was identified and treated but in the third case no focus was found and the patient was treated with placement of a Sengstaken-Blakemore tube. Both peroperative and delayed bleedings are almost always the result of bleeding from around the muscular edges.

Infectious complications are rare, but extensive antibiotic prophylaxis is standard in most centers. Aspiration pneumonia is mentioned once.<sup>21</sup>

Dehiscence of the entry of the tunnel 1 week postoperatively is reported, leading to creation of a pocket filled with food.<sup>27</sup> The authors described that after a conservative approach with fasting, tube feeding, and PPI the patient recovered well. We believe that this may be another argument for semi solid food for at least 2 weeks postoperatively, until we expect healing of the mucosal entry wound.

## POEM FOR TREATMENT OF OTHER DISORDERS

Currently all types of achalasia patients are treated successfully with POEM, including patients with so-



**Figure 5** Radiographs before and after the per-oral endoscopic myotomy procedure showing stasis and before the procedure. After the procedure the contrast easily moves to the stomach, and the array of clips at the site of the mucosal entrance is seen.



called type III or spastic achalasia. In some centers even patients with achalasia and a sigmoid shape esophagus are now considered candidates to undergo POEM. Patients with clear esophagogastric junction outflow obstruction on manometry and dysphagia can be regarded as having a variant of achalasia and can also be considered for POEM.

The successful treatment of all variants of achalasia led to the belief that also patients with other diseases of the oesophageal circular muscles could be treated. Recently, two case reports appeared in which POEM was successfully performed in patients with diffuse esophageal spasms.<sup>34,35</sup> Per-oral endoscopic myotomy offers the advantage above laparoscopic myotomy that cutting of muscle fibers is possible up to the proximal esophagus. When spasms are seen on manometry throughout the entire esophagus, myotomy should be started as proximal as possible.

## CONCLUSIONS AND FUTURE PROSPECTS

Per-oral endoscopic myotomy is an elegant treatment with excellent short-term results and the alternatives for achalasia, pneumodilation, and Heller myotomy, both have shortcomings suggesting a demand for a better treatment option. Within 2 years after pneumodilation, half the patients require retreatment.<sup>12,36</sup> The effect of Heller myotomy seems more durable than pneumodilation, but also decreases over time as long-term studies have shown.<sup>37,38</sup> The experience with POEM is limited however, and all available data come from uncontrolled open label studies and case series with short follow-up. When taking into account that achalasia is a chronic disorder and that an invasive treatment alternative should be effective for years, one needs to realize that there is really no sufficient data on the effectiveness of POEM. Some reports mention excellent 'long-term outcome' with beneficial 6–12-month results, however we do not consider this follow-up period convincingly long given the chronicity of the disease and given the observation that differences between Heller myotomy and balloon dilation only seem to become clear after at least 1–2 years follow-up. Studies comparing POEM with the current routine treatments pneumodilation

and Heller myotomy have been started and are including patients at the moment, but it will take years before long-term follow-up data of these trials will become available. Solid conclusions with regard to treatment policy of achalasia and position of POEM can therefore not be made at the moment.

This paucity of data has not withheld centers from starting POEM, and more and more endoscopists are treating achalasia patients now with endoscopic myotomy. Before starting with POEM treatments, it is important to realize that the currently available and sometimes overenthusiastic reports with success rates ~100% and 0% complications are written by early adopters with extensive endoscopic experience. In contrast to pneumodilation, the technique of POEM is difficult and requires extensive experience in therapeutic endoscopy. Based on this, we recommend centralization of POEM treatment, further supported by the notion that achalasia is a rare disease with an incidence of 1 per 100 000 per year. Indication for treatment should be discussed with an expert in esophageal motility and centers need esophageal manometry equipment to diagnose and follow-up cases. The authors believe that there is currently insufficient evidence to perform POEM as routine achalasia treatment. Until the long-term efficacy data from randomized controlled trials are available, POEM should be restricted to centers participating in these trials.

## ACKNOWLEDGEMENT

AJ Bredenoord is supported by The Netherlands Organisation for Scientific Research (NWO).

## FUNDING

No funding declared.

## DISCLOSURE

AB received research funding from AstraZeneca, Endostim, MMS, Shire and received speaker and/or consulting fees from MMS, Shire, and Almirall. TR received research funding from Olympus, Erbe, and Storz. PF received research funding from Olympus and consultancy fees from Olympus, Fujifilm, Cook, and Boston Scientific.

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