

Per-oral endoscopic myotomy for achalasia

Steven R. DeMeester

Thoracic, Foregut and Minimally Invasive Surgery, The Oregon Clinic, Portland, USA

Correspondence to: Steven R. DeMeester, MD. The Oregon Clinic, 4805 NE Glisan St, Suite 6N60, Portland, OR 97213, USA.

Email: stevenrdemeester@gmail.com.

Abstract: Symptoms in patients with achalasia are produced by outflow obstruction at the level of the lower esophageal sphincter (LES). As a consequence of neural destruction the LES does not undergo normal swallow-induced relaxation. In addition, the esophageal body loses normal peristaltic function and esophageal emptying is on the basis of gravity. All therapies for achalasia are palliative in that normal LES or esophageal body function cannot be restored. The efficacy of any therapy for achalasia is directly related to its ability to reduce the outflow obstruction at the LES. The three main treatment options are pneumatic dilatation, laparoscopic myotomy and partial fundoplication and per-oral endoscopic myotomy or per-oral esophageal myotomy (POEM). Details of the procedures and outcomes will be discussed.

Keywords: Achalasia; laparoscopic myotomy; Heller myotomy; per-oral endoscopic myotomy (POEM); Botox; pneumatic dilatation

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Symptoms in patients with achalasia are produced by outflow obstruction at the level of the lower esophageal sphincter (LES). As a consequence of neural destruction the LES does not undergo normal swallow-induced relaxation and the esophageal body loses normal peristaltic function. Consequently, esophageal emptying is on the basis of gravity. All therapies for achalasia are palliative and the efficacy of any therapy is directly related to its ability to reduce the outflow obstruction at the LES. In its untreated form achalasia is at the opposite end of the spectrum from gastroesophageal reflux disease (GERD). Treatment for GERD is augmentation of the defective LES while treatment for achalasia is to render the LES less competent. Overzealous augmentation of the LES for GERD can lead to an achalasia-like condition, and all treatments for achalasia risk inducing significant GERD.

Recently the role of manometry has taken on importance beyond confirming the diagnosis of achalasia. On high resolution manometry (HRM) three achalasia types have been defined, and the outcome with achalasia treatment has been linked with the specific subtype. Type I or “classic” achalasia has incomplete LES opening and an aperistaltic, flaccid esophageal body. Type II has panesophageal

pressurization, and type III has no normal peristalsis, but evidence of distal esophageal spasm. Characteristic of all three types is an elevated integration relaxation pressure (IRP) above 15 mmHg (1). The highest success rates with treatment for achalasia appear to be in patients with Type II achalasia (2,3). Laparoscopic myotomy and per-oral endoscopic myotomy (POEM) are effective in all subtypes of achalasia, but the outcome with pneumatic dilatation has been shown to be poor in patients with type III achalasia (2). In these patients alternative therapies are recommended.

Until recently the treatment of achalasia involved trade-offs between efficacy and invasiveness. On the low efficacy and low invasiveness side are Botox injection and a single pneumatic dilatation. While these can be efficacious they tend to less reliably produce good long-term outcomes than therapies on the more invasive end of the spectrum. Moving toward more invasive and better efficacy are multiple pneumatic dilatations and Heller myotomy. The introduction of laparoscopic techniques for a Heller myotomy has reduced the invasiveness without compromising efficacy. Now, with the introduction of POEM a paradigm shift has occurred where patients can have the efficacy of the laparoscopic Heller myotomy with

essentially the invasiveness of a single pneumatic dilatation.

Injection of botulinum toxin is an attractive option for patients with achalasia given the simplicity of the procedure. During endoscopy 100 units of botulinum toxin A is injected in equal aliquots around the gastroesophageal junction, typically in four or eight locations. Efficacy with botulinum toxin is typically the lowest of the achalasia treatment alternatives and its effects are temporary (4). Consequently, botulinum toxin is typically reserved for patients who are poor candidates for other more definitive therapies, or as a temporizing measure until a more definitive therapy can be arranged. A drawback to botulinum toxin injection is that it can induce submucosal scarring which can make a laparoscopic myotomy or POEM procedure more difficult. Further, although very safe, excessively deep injection in the area of the LES can lead to aortic injury and must be avoided.

Pneumatic dilatation is done with an achalasia balloon that is at least 150% the normal size of the esophagus (30 mm) in an effort to disrupt the dysfunctional LES musculature. A single dilatation is unlikely to provide permanent relief of symptoms, but repeated dilatations and use of larger (35 and 40 mm) balloons for recurrent symptoms leads to improved results. In a randomized trial from Europe, an aggressive pneumatic dilatation protocol led to success rates similar to that observed with a laparoscopic Heller myotomy, but with a 4% risk of esophageal perforation (5). Success, defined as a reduction of the Eckardt symptom score to 3 or less at two years, occurred in 90% of patients after laparoscopic myotomy compared to 86% of patients after pneumatic dilatation. The frequency of an abnormal pH test and endoscopic esophagitis was similar for the two treatments (15% and 19% respectively for pneumatic dilatation and 23% and 21% respectively for laparoscopic myotomy with partial fundoplication). Risk factors for the need for re-dilatation included pre-existing daily chest pain, age younger than 40 years, and a >10 cm column of retained barium five minutes after contrast ingestion on a timed barium esophagram 3 months after dilatation (5). Long-term results after pneumatic dilatation either as a single dilatation or after multiple dilatations show a success rate of 78% at 5 years, 61% at 10 years and 58% at 15 years (6). Recently, the outcome with pneumatic dilatation has been shown to be poor in patients with type III achalasia (2). Consequently, patients with type III achalasia are considered to have a relative contraindication to pneumatic dilatation and alternative therapies are preferred.

The Heller myotomy dates back over 100 years and

is named after the German surgeon Ernest Heller. This procedure, with three important modifications, has become the gold standard therapy in the US and most centers worldwide for the treatment of achalasia. The three modifications consist of the introduction of a minimally invasive laparoscopic approach, the addition of a partial fundoplication and extension of the myotomy 2–3 cm down onto the stomach. The initial foray into minimally invasive surgery for achalasia was a thoracoscopic myotomy described by Pellegrini and colleagues in 1992 (7). However, the laparoscopic approach has been proven superior and is now the standard of care for a minimally invasive myotomy for achalasia (8). Further, following publication of a randomized trial that showed that the addition of a partial fundoplication to a Heller myotomy reduced gastroesophageal reflux compared to myotomy alone, a partial fundoplication should be added to a Heller myotomy (9). Lastly, an analysis of outcomes after myotomy showed that an extended gastric myotomy was associated with improved results. Consequently, extension of the myotomy 2 to 3 cm down onto the stomach is now accepted as the appropriate technique during laparoscopic myotomy (10).

A laparoscopic Heller myotomy with these modifications has been shown to produce excellent, durable results at centers around the world (11–13). In a series of 400 laparoscopic myotomies from Italy 82% of patients were free of symptoms 10 years after the operation (14). Further, a laparoscopic Heller myotomy and Dor has been shown to have a lower rate of re-intervention compared to pneumatic dilatation and to be effective for all subtypes of achalasia (15).

Complications can occur with a laparoscopic myotomy but mortality should be extremely rare. In an analysis of the American College of Surgeons National Surgical Quality Improvement Program database Niebisch *et al.* showed that the overall 30-day mortality after a laparoscopic fundoplication was 0.19%, and was only 0.05% for patients under the age of 70 years (16). Further, the most common complications following fundoplication were pulmonary (1.3%) and urinary tract infections (1.1%). These low mortality and complication rates for fundoplication should hold for myotomy and partial fundoplication as well (17). There are three potential complications with a laparoscopic myotomy and fundoplication that deserve focused attention. The first is mucosal perforation during the myotomy. The literature and personal experience would suggest that perforation occurs more frequently in patients previously treated for achalasia, particularly with botulinum toxin injection (18). Most perforations occur during the

myotomy on the stomach since the mucosa below the gastroesophageal junction is very thin. Repair with fine absorbable sutures and covering the site with the partial fundoplication leads to successful healing in nearly all cases.

The second complication to focus on is a leak from the myotomy site. The possibility of a leak should be considered in any patient who has fever, chest pain, or clinical signs consistent with sepsis post-operatively. The work-up should include a water-soluble contrast swallow and/or upper endoscopy. Contrast radiographic studies are known to miss small leaks, and in the clinical setting of sepsis they should not be relied upon to rule out a leak definitively. A CT scan can be useful and may show evidence of an abscess or air/fluid level near the hiatus or small air bubbles in the mediastinum. Endoscopy is a sensitive test and should be used to evaluate the esophagus if a leak is suspected or confirmed. Most small leaks can be managed with intravenous antibiotics and no oral intake, and in some cases can be treated endoscopically with clips or endoscopic suturing. Larger leaks may require CT-guided drainage, a stent or, rarely, reoperation.

The third focused complication is recurrent dysphagia. Causes include an inadequate myotomy, typically related to insufficient extension onto the stomach, scarring and closure of the myotomy, excessive fundoplication, typically from a Nissen fundoplication, or a GERD-related complication such as erosive esophagitis or a stricture. Determining the etiology usually requires upper endoscopy and a repeat manometry. In some patients a timed barium swallow or a pH test can also be useful. Treatment is based on the etiology.

Recently, a new procedure for achalasia has been introduced, the per-oral endoscopic myotomy, or POEM. It may be the best of both worlds, allowing a precise myotomy with the recovery benefits of no external incisions and no physical restrictions. The POEM procedure was first used to treat achalasia in a human by Inoue in 2008, and his initial experience was reported in 2010 (19). Since Inoue's first procedure there has now been thousands of POEM procedures performed worldwide. The POEM procedure begins with an incision in the mucosa followed by creation of a submucosal tunnel that is carried 2–3 cm below the gastroesophageal junction. A myotomy of the circular fibers of the muscularis propria down through the LES is then performed. The procedure is completed by closing the mucosal defect either with clips or sutures. There are numerous publications on the early results of POEM for achalasia. From these, a number of conclusions can be

drawn.

First, POEM is very safe, even during the learning curve (20,21). Some complications including subcutaneous emphysema, pneumothorax, and pneumoperitoneum are much more common with the use of air rather than carbon dioxide for insufflation. The use of carbon dioxide and general anesthesia is recommended (22). Bleeding from large submucosal vessels can be problematic but typically is readily controlled with the use of coagulating forceps, and with experience is easier to avoid than to treat during creation of the submucosal tunnel. Delayed bleeding occurs rarely, although in some cases has required re-exploration of the tunnel (23). Another occasional source of morbidity is the mucosal closure. Typically a barium swallow is done later that day or the day after the procedure to verify the integrity of the closure. A leak into the submucosal tunnel should prompt re-exploration. In a recent series of 500 patients published by Inoue there were 16 adverse events (3.2%). Most of these were minor and none resulted in abandonment of the POEM procedure. There were no deaths (24). Overall, for a novel procedure there has been remarkably little morbidity, although most reports are from centers with significant experience in the management of patients with esophageal disorders.

Second, POEM results in significant improvement in dysphagia and regurgitation symptoms. In a series by Swanson *et al.*, the median Eckardt score in 20 patients at 1 month after POEM was 1, down from 6 pre-POEM, and over half of the patients had complete resolution of dysphagia (25). At 18 months the median Eckardt score was 0; most patients had no dysphagia symptoms, and all were satisfied with the results of the procedure. On objective evaluation, the median emptying at 5 min by timed barium swallow had improved from 48% to 100% at 6 months post-POEM. Similarly, in an international, multi-institution series of 70 patients, the median Eckardt score dropped from 7 to 1 at 3 months after POEM, and treatment success was achieved in 97% of patients (26). The mean LES pressure decreased from 28 to 9 mmHg. At 12 months after POEM, sustained treatment success was present in 82 % of patients, and the mean Eckardt score was 1.7 in the 51 patients available for follow-up. In the recent series of 500 patients published by Inoue, 3-year or longer follow-up was available in 61 patients. Overall success rate was excellent at 88.5% and similar to the results at 1 to 2 years (24). In addition, similar to laparoscopic myotomy, POEM is effective in all HRM types of achalasia, and in fact may have an advantage in type III achalasia since a long myotomy can readily be

achieved with POEM (27).

Third, POEM by virtue of its excellent myotomy without a partial fundoplication appears to be more likely to lead to reflux than other achalasia therapies. In the series by Swanstrom *et al.*, 33% of patients reported heartburn at 6 months after POEM. On upper endoscopy, erosive esophagitis was seen in 28% of patients, and when combined with pH monitoring objective evidence of GERD was present in 50% of patients (25). In the international series 37% of patients had reflux symptoms and erosive esophagitis was present in 42% of patients at 12 months post-POEM (26). Initially it appeared that the frequency of reflux after POEM was less in the Asian population compared to that from Western countries. However, in the series of 500 patients by Inoue from Japan upper endoscopy showed reflux esophagitis in 65% of patients in the short term, and 59% at 1 to 2 years after POEM (24).

Fourth, compared to a laparoscopic Heller myotomy with partial fundoplication, POEM has been shown to lead to a similar good outcome in two series comparing these procedures. The first, by Hungness *et al.*, showed that operative times were shorter with POEM but complications and the median length of hospital stay were similar for the two procedures (28). The second, by Bhayani *et al.*, showed that post-operative Eckardt scores were lower after POEM and 100% of patients had relief of dysphagia after POEM compared to 97% after laparoscopic Heller myotomy and partial fundoplication (29). Symptoms of heartburn, reflux, and chest pain were similar for the two procedures. On objective testing the absolute and relative decreases in LES resting pressures were similar, but the resting pressure was higher after POEM. On 24-h pH monitoring, the frequency of increased esophageal acid exposure was similar at about 35% after each procedure. A meta-analysis of non-randomized studies show that compared to laparoscopic myotomy there is no significant difference in operation time, length of hospital stay, or complication rates with POEM (30). However, Eckardt scores were significantly lower after POEM compared to laparoscopic Heller myotomy.

While most POEM procedures are done for achalasia, the indications have expanded to diffuse esophageal spasm, hypertensive LES and as a technique to remove smooth muscle tumors in the muscularis propria of the esophagus and gastroesophageal junction. The concepts have also been applied to performing an endoscopic myotomy of the pylorus for delayed gastric emptying and of the cricopharyngeal for Zenker's diverticulum or

cricopharyngeal dysfunction. It is likely that endoscopic procedures employing submucosal tunneling techniques will increasingly play a role in modern therapy for a variety of gastrointestinal disorders.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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