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REVIEW ARTICLE

The Modern Age of POEM: the Past, Present and Future of Per-Oral Endoscopic Myotomy

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Abstract

Background Per-oral endoscopic myotomy (POEM) has gained widespread enthusiasm amongst foregut specialists since its introduction in the mid 2000s as an effective and less invasive treatment option for achalasia. As more than 6000 POEM procedures have been performed to date throughout the world, we aim to summarize the history and current state of POEM in the treatment of esophageal motility disorders.

Methods We performed a comprehensive review of the published literature focusing on the history and development of the POEM procedure, and its most current applications and outcomes.

Results Multiple favorable long-term studies have been published advocating for the use of POEM as a valid and perhaps the most valid treatment option for achalasia. The procedure is also increasingly being applied to a wider spectrum of esophageal motility disorders including type III achalasia, spastic esophageal disease or isolated lower esophageal sphincter (LES) dysfunction, as well as new endoluminal procedures such as submucosal tumor endoscopic resection (STER), endoscopic fundoplications (POEM-F) and peroral pyloromyotomy (POP or G-POEM).

Conclusions While POEM is a proved and valid procedure, its further adoption is being threatened by external factors: challenges related to teaching, institutional support (politics) and insurance reimbursement. While this technique has come an incredible distance in its relatively short lifespan, the future of POEM in the USA will depend on the support from surgical societies to validate it as a valuable tool in the esophageal specialist's armamentarium, and to encourage a commitment to training in endoluminal surgery.

Keywords POEM · Review · Heller · Esophageal myotomy

Introduction

Since its introduction in the mid-2000s, per-oral endoscopic myotomy (POEM) has become an increasingly popular treatment for the management of achalasia and other esophageal motility disorders around the world based on sound outcomes evidence. In the past decade, a multitude of publications have evaluated the safety, efficacy, and indications for POEM in the modern surgical management of esophageal disease with uniformly promising results both alone[1–4] and when compared with the standard therapy of Heller myotomy.[5–8] Furthermore, as the procedure ages, longer-term data from the USA and around the world has not shown any major deterioration in these outcomes.[9–11]

POEM's innovative and logical approach, which makes sense to patients and providers alike, has driven its rapid adoption. A simple literature review on PubMed for publications relating to POEM reveals nearly 1500 articles to date stemming from many different countries and institutions and reporting results from thousands of patients. Nevertheless, the current status of POEM in the USA is threatened by ongoing criticisms of the procedure, by limited availability of training programs for POEM, and perhaps most of all, by lack of insurance reimbursement for the procedure.

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The History of Poem

Natural Orifice Transluminal Endoscopic Surgery (NOTES) was first described in the early 2000s, and is emblematic of less invasive surgical approaches using novel endoluminal therapies.[12] While many NOTES procedures have remained largely experimental or theoretical, per-oral endoscopic myotomy (POEM) has become the first widespread, accepted and validated application of NOTES that has the potential to compliment, if not replace its traditional surgical counterpart, the Heller myotomy.

POEM was first clinically applied in Japan, where surgeons regularly employ advanced therapeutic endoscopic techniques as treatment tools due to the high prevalence of esophageal and gastric pathology in the region. As early as the 1950s, saline lift techniques and complex polypectomy were being performed endoscopically in the colon. This technology would make its way to the upper GI tract by the 1970s, and in the 1990s, advanced endoscopic mucosal resections (EMR) were considered standard of care, establishing the feasibility of endoscopic therapy for esophageal and gastric diseases. As pioneering surgeons continued to push the boundaries of endoluminal therapy, improving resection and the ability to dissect into deeper layers of the esophageal wall, progressing from a mucosal resection (EMR) to a submucosal dissection (ESD), endoscopists noted that it was difficult to control the specimen that was being removed. In 2007, as an attempted solution to this problem, the first endeavors into the "third space" were proposed with the idea of creating a submucosal tunnel to approach the lesion, allowing the endoscopists to complete the muscular dissection first and thus limit the problematic mobility of specimens being resected.[12] While this would not gain widespread popularity, it would be the key development that would allow POEM to take hold.

The first reports of endoscopic myotomy itself actually predate even the early developments of EMR and ESD. In 1980, Ortega et al. in Venezuela reported on a series of 6 canines followed by 17 human patients who underwent direct transmucosal endoscopic myotomy with a specially fashioned needle knife. In this series, there were no reports of full-thickness perforation or major complications, and patients reported some improvement in dysphagia.[13] However, the procedure failed to gain traction due to obvious potential for complications. In 2007, Pasricha et al. reported on an innovative alternative approach in which a submucosal tunnel approach was employed first, followed by a directed and controlled endoscopic myotomy of the circular muscle fibers in a pig model.[14] These techniques were subsequently adopted by Haruhiro Inoue and colleagues who performed the first POEM procedure in a human in September of 2008 and published their initial series of 17 patients in the years that followed, initiating a wildfire-like spread of this new technology throughout the world.[3]

The Modern Age of Poem: Technique Evolution

By 2018, 10 years after the initial human patients were completed, it was estimated that over 6000 POEM cases had been performed worldwide.[9] It is likely that the actual number is much higher than this as several series reporting more than 1000 cases.[15]

Since its first introduction, the technical aspects of POEM have continued to be refined.[15, 16] This includes the transition from a retrograde to an antegrade myotomy, refined techniques for entry into the submucosal tunnel using caps and balloon, tailoring of where to perform the mucosotomy on the esophagus (both distance and clock face orientation), whether to perform a full-thickness (longitudinal and circular) or partial (circular only) myotomy, and how to identify an adequate myotomy length.

Further tailoring of the POEM procedure has been facilitated by the application of functional luminal imaging and endoscopic esophageal topography (Endoflip, Medtronic, USA). This technology is being utilized with increasing frequency to better assess the adequacy of a myotomy by obtaining real-time pressure and compliance readings of the esophagus before, during, and after myotomy.[17, 18] While the ideal distensibility targets are still being defined, this adjuvant technology will likely continue to shape the future of the procedure.

Successes and Failures: Outcomes of the First 10 Years

The last decade of reports based on fastidious outcome tracking and diligent reporting have given us robust and reassuring data on early outcomes relating to POEM. Today, its validity as a safe and effective treatment for achalasia is no longer in question. The procedure has been shown in multiple different institutions to be safe, with a low complication rate and extremely good initial clinical response, generally 80–90% immediate symptom improvements and good short-term durability.[1–4] A recent 5-year follow-up by Teitelbaum et al. suggests that there may be a small worsening of symptoms between 2 and 5 years, though the clinical relevance of this remains to be seen.[10] As we are only now just past 10 years past the inception of POEM, true long-term outcomes are only now starting to be reported in large patient populations, and the long-term durability of the procedure still needs to be documented.[9]

When evaluating long-term clinical outcomes, it is important to consider that up to 10–20% of patients with a surgical myotomy (endoscopic or transabdominal) will have recurrent symptoms in the years following their index operation. However, the clinical significance of this is difficult to predict, as symptoms in patients with achalasia are extremely variable

and unreliable. Furthermore, given that achalasia is a progressive disease and esophageal function is unlikely to improve significantly regardless of intervention, it may be that some of these recurrent symptoms are related more to the natural history of the disease rather than a treatment failure. Unfortunately, longitudinal reports on the rates of re-intervention after POEM are not widely published, and this remains an area for further research. The few studies that evaluate this question do suggest that the need for re-intervention after POEM is rare, possibly as low as 1%.[10] How a POEM will hold up over several decades remains to be seen.

Not Just for Achalasia Anymore

While the POEM technique is most commonly associated with achalasia treatment, there exists a wider world of esophageal disorders that can present with an array of clinical symptoms and dynamic differences in esophageal function. While achalasia is the most well-defined, disorders of esophageal motility can also include esophageal outflow obstruction, major disorders of peristalsis (diffuse esophageal spasm (DES), hyper-contractile esophagus, absent contractility), and minor disorders of peristalsis (ineffective esophageal motility, fragmented peristalsis).[19, 20] As our understanding of esophageal physiology has improved over the years, thanks primarily to the introduction of high-resolution manometry and improving imaging modalities, it has become apparent that esophageal myotomy may have a broader potential benefit beyond the treatment of classic achalasia.[21]

Type III/Spastic Achalasia

POEM would appear to be the ideal treatment for longer-segment disorders of esophageal peristalsis such as type III achalasia or diffuse esophageal spasm. Medical treatments are considered ineffective for all but minor cases, and laparoscopic Heller myotomy, which only addresses the GE junction, has demonstrated only moderate efficacy. A combined laparoscopic/thoracoscopic approach for an extended myotomy can be considered, though this adds additional morbidity. For these indications, a per-oral technique starting very high on the esophagus provides an opportunity to address the disease along its entire length through a minimally invasive approach. Studies of POEM specifically for type III achalasia have shown it to be safe and effective in long-term symptom relief in more than 90% of cases.[22, 23]

Jackhammer Esophagus/Diffuse Esophageal Spasm

Jackhammer and DES differentiate themselves from achalasia though the presence of some degree of preserved peristalsis. They tend to present with the defining clinical characteristic of non-cardiac chest pain or odynophagia which can be quite debilitating to patients. Esophageal myotomy has been shown to be effective for these hyper-contractile disorders, as cutting the muscle decreases its ability to spasm. Case reports and studies have begun to show that a long POEM can be a potential treatment for these difficult cases of non-cardiac chest pain related to diffuse esophageal spasm or Jackhammer esophagus.[24] However, the effects of trading a previously hyper-peristaltic esophagus for a functionally aperistaltic one as a result of a complete myotomy is not trivial, and careful patient selection is key in these cases.

Technical Challenges to Poem

Hiatal/Paraesophageal Hernia

In the early adoption of POEM, hiatal hernias were seldom considered in the selection of patients for the procedure. Fortunately, large hernias are less common in cases of achalasia but certainly can exist concurrently with either classic or alternate esophageal motility disorders. As experience has accumulated, it has become apparent that larger hiatal hernias, while not technically impossible, are not a good indication for POEM as the incidence of severe reflux is much higher after POEM in these patients. For these patients it is usually recommended they have a Heller myotomy rather than POEM.

Sigmoid Esophagus

Similar to the issues surrounding hernias, the presence of a sigmoid esophagus increases the technical difficulty in performing a POEM procedure. The looping of the scope in the esophagus makes it easy to lose orientation and fail to access the stomach or to create inadvertent mucosotomies or full-thickness perforations. However, with increasing familiarity with the procedure, skilled endoscopists have been successful in performing POEM, even in these challenging situations.[25] In cohorts following such patients forward, reported 2-year outcomes have remained excellent with 96% having long-term symptom relief without serious complications.[26]

Re-do POEM

In cases of a recurrent or persistent dysphagia related to a previously failed myotomy, POEM is a reasonable treatment option.[27–31] POEM is particularly attractive after a failed Heller as it allows for the creation of an extended myotomy in a new plane (off anterior) more easily and with less risk than a laparoscopic revision. POEM after Heller comes with the additional benefit that most patients have had an anti-reflux procedure as part of their initial operation, thus minimizing the

risk of GERD following the POEM. Even in the setting of a previous POEM, re-do POEM in a new plane has been shown to be technically possible, though compared with first time POEM, clinical success rates are somewhat lower (around 85%), complication rates are slightly higher (around 17%)[31] and the procedure itself can take twice as long.[32]

Has the Debate Been Put to Rest? Heller vs POEM

Myotomy of the lower esophageal sphincter through an abdominal approach (Heller myotomy) has been the mainstay of treatment for achalasia for decades and has uniformly favorable results, particularly using laparoscopic approaches. Multiple studies have suggested comparably good outcomes with either a surgical or endoscopic myotomy, with an 80–90% initial clinical response rate when applied to appropriately selected patients, particularly for classic achalasia cases.[5] Across the board, surgical myotomy results have been superior to that of pneumatic dilation which only tends to achieve long-term treatment success rates in around 50–60% of patients, but certainly still plays a role for high-risk patients who may not be suitable for operative intervention.[33, 34]

In terms of perioperative outcomes, multiple studies have shown that POEM and Heller have similarly low rates of perioperative complications and morbidity.[5, 35] While the POEM approach does portend the possibility of specific rare complications such as mucosal perforation, submucosal tunnel leaks, or air extravasation (pneumoperitoneum, pneumopericardium, or pneumothorax), these complications can almost uniformly be managed with conservative or endoscopic techniques.[4]

The evolution of the approach to achalasia from transabdominal (Heller) to endoluminal (POEM) is perhaps simply the natural progression of the surgical technique. Multiple publications have demonstrated POEM to be at least as effective as Heller myotomy in terms of primary endpoints for achalasia including dysphagia and quality of life.[5–8] These studies have shown comparably good clinical outcomes with either a surgical or endoscopic myotomy, typically with an 80–90% initial clinical response rate when applied to appropriately selected patients, particularly in the treatment of classic achalasia.[5] A recent systematic review and meta-analysis by Schlottmann et al. evaluating more than 70 publications on these techniques has suggested that POEM may actually be superior to Heller myotomy in terms of both short- and long-term dysphagia.[8] While these data are promising, it is important to note that there are few definitive prospective trials between the two techniques to answer the question of procedure superiority. The first randomized controlled trial (RCT) between POEM and LHM recently published in the New England Journal of Medicine concluded non-inferiority of POEM in terms of symptom control for achalasia at 2 years. Though the study was somewhat underpowered, it also demonstrated better outcomes regarding dysphagia, shorter procedure times, and lower rates of adverse events in the POEM group.[36]

But What About Reflux?

The primary criticism of the POEM procedure in its current form is concern for the development of pathologic reflux disease resulting from destruction of the lower esophageal sphincter. Skeptics assert that Heller myotomy, combined with an anti-reflux fundoplication, negates this risk and thus should remain the treatment of choice for achalasia.

Review of the literature reveals a slightly more complicated story. It is absolutely true that disruption of the LES via surgical myotomy increases the risk of reflux. POEM patients are more likely to develop GERD symptoms (OR 1.69), erosive esophagitis (OR 9.3), and abnormal pH testing (OR 4.3) compared with patients treated with LHM with fundoplication, at least in the short term.[8] It is important, however, to understand that reflux is not completely prevented by partial fundoplications and tends to increase with time. While the rates of increased acid exposure in the distal esophagus after POEM are consistently around 30% on objective testing, LHM carries with it between 15 and 25% risk of reflux despite the presence of a fundoplication in intermediate follow-up.[7, 12] Furthermore, in the only currently published RCT comparing 2-year POEM versus LHM, despite a trend towards higher rates of esophagitis on endoscopy and increased return to PPI utilization, there were statistically equivalent outcomes for rates of increased acid exposure based on pH testing in POEM and LHM.[36]

In spite of the increased incidence of GERD in POEM patients compared with that in Heller patients, the quality of life scores are fairly similar between the two groups.[6] In reality, most patients with post-myotomy GERD (either from POEM or LHM) are easily managed with medications alone.[6] So although GERD rates are somewhat increased after POEM, there seems to be less effect on clinical outcomes than might be expected and therefore should not exclude POEM as a valid treatment option for this disease.

It may be that the reflux that develops after POEM is relatively mild because the actual lower esophageal sphincter (LES) complex (apart from the circular muscle fibers themselves) is left more intact with a POEM than with a LHM. In a POEM, only the circular muscle fibers are divided, sparing the longitudinal and the hiatus itself is left intact, while in a traditional LHM, the phrenoesophageal ligament and

diaphragmatic attachments are frequently taken down to allow for adequate dissection and visualization to perform the myotomy. This destruction of the extra-esophageal components of the LES may actually be detrimental for long-term reflux control.

Novel procedures to address post-myotomy reflux endoluminally may be able to offer additional adjuvant treatment options going forward for the few patients who develop troublesome reflux after POEM. Trans-oral incisionless fundoplication (TIF), which has been well-studied and applied in more than 1000 cases as a primary GERD treatment in well-selected patients, is now also being applied in post-POEM patients with good initial results.[37, 38] Alternate modalities such as POEM fundoplication in which a fundoplication is performed during the initial POEM through a transmural dissection and plication all performed endoscopically have been described by Inoue and colleagues in 2018.[39] Anti-reflux mucosectomy (ARM)[40] approaches to bolster the LES have been described and may hold promise in the future of management of post-myotomy reflux, but given the rarity of the clinical need for these treatments, large studies and long-term data would be needed to demonstrate a real clinical benefit.

Training and Education

For a new technique to gain widespread adoption, training and education must be optimized such that new practitioners can not only learn the procedure but also implement it successfully into their practice. Initial studies evaluating the learning curve in POEM suggested that for a novice interventional endoscopist, between 70 and 100 cases were required to decrease the risk of technical failures, adverse events, and clinical failure, which would take years for the average surgeon to complete, if ever.[41] However, for practitioners with previous advanced therapeutic endoscopic expertise, this learning curve can be as low as 15–25 cases[12, 42, 43] and adoption may be further facilitated by performing pre-clinical procedures in animal models before attempting POEM in live human subjects.[44, 45] This highlights the importance of good endoscopic training for general surgeons and established programs to assist in the adoption of POEM.

The problem with this is that while basic endoscopy remains a graduation requirement for general surgeons, there is currently no ACGME residency standard for exposure to advanced therapeutic or interventional endoscopy in general surgery residency.[46] As a result, many surgeons coming out of training lack the advanced therapeutic endoscopic skills needed to be able to rapidly adopt POEM. This training challenge is compounded by the fact that despite enthusiasm for the adoption of POEM throughout the USA, there is a paucity of training programs that adequately prepare learners to independently implement a POEM practice. Only a handful of currently accredited minimally invasive surgery fellowships in the USA perform POEM at a volume sufficient to train their fellows in this technique for independent practice. For surgeons who are already in practice, hands-on POEM training courses are offered throughout the country with multi-day experience designed to introduce POEM and a strict curriculum has been shown to effectively translate to improving POEM skills.[47] However, implementing a POEM practice and continuing to progress through the learning curve after attending a course requires both institutional support and expert proctoring, which can be difficult to come by. As barriers to surgeons learning POEM continue to arise, many may find them insurmountable and may choose to abandon the procedure altogether or leave it to the gastroenterologists.

Insurance and Reimbursement

After many golden years of POEM adoption, there has been an unsettling phenomenon in the USA in which insurance carriers have begun to deny reimbursement for the procedure, belatedly describing it as “experimental” and citing the lack of prospective randomized controlled trials to validate clinical efficacy. Unfortunately, given the near equivalent outcomes demonstrated in retrospective trials when comparing with alternate therapeutic options, many hundreds of patients would be required in each arm to have any statistical power in such a study, which would be nearly impossible given the rarity of the disease and patient preferences for the less invasive option.[9] However, when patients are faced with the choice of self-pay or simply taking an alternate procedure, most are unable to shoulder the financial burden of proceeding with POEM. This has led to frustration on the part of both patients and providers alike, who tire of continually appealing denials and simply give up the fight.

The Future of Poem and the Third Space

The success of the POEM procedure in terms of its widespread adoption and excellent outcomes has shown the incredible promise of “third space” endoscopy in the future of natural orifice and endoluminal surgery. POEM techniques have been successfully applied in a growing number to perform per-oral pyloroplasty (POP), also called Gastric-POEM (G-POEM).[48] As comfort in the submucosal space has expanded, submucosal tumor endoscopic resections (STER) are being used with increasing frequency, and even full-thickness resections of masses extending into the mediastinum, all through a submucosal approach.[49, 50]

Future technologic development will aid in the ongoing evolution of the POEM procedure and its offspring. It is likely that as POEM becomes standard of care, more POEM-specific

equipment will appear on the market to aid in better visualization, easier dissection, or more accurate intraoperative monitoring and myotomy assessment. More novel technologies like robotic endoscopes will allow for the boundaries of POEM and third space procedures to continue to expand.

What Does Poem Need?

Despite the sterling track record and promising potential of POEM, the procedure continues to struggle as a bit of an orphan with minimal societal ownership. Even with a decade of strong data, no major GI or surgical society has issued a statement in support of the efficacy of POEM, and as a result, hospitals, training programs, and insurers can continue to hold it at the fringe if they desire. For POEM to become standard care, medical society support will be paramount.

Conclusion

Per-oral endoscopic myotomy (POEM) was truly the first widespread clinically accepted application of Natural Orifice Transluminal Endoscopic Surgery (NOTES) and continues to serve as the torch bearer for surgical innovation in GI surgery.[12] It is a safe and effective treatment for esophageal motility disorders that is gaining in popularity throughout the world and is a valid, and perhaps the most valid treatment option for achalasia. With more than a decade of robust data, POEM is a proven approach and attempts to define it as "experimental" are unfounded and unethical. Its applications will likely continue to grow as endoscopic equipment and expertise improve and the indications for the procedure broaden.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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