



# **Evolving therapeutic approaches in achalasia:** a comprehensive review of peroral endoscopic myotomy (POEM) vs. Heller's myotomy

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### **Abstract**

This comprehensive narrative review thoroughly explores the treatment landscape for achalasia, a rare esophageal motility disorder. Beginning with an introduction outlining the anatomical and clinical aspects of achalasia, the review delves into its historical perspective, tracing the evolution of treatment options from early nonsurgical methods to advanced surgical techniques such as Heller's myotomy and peroral endoscopic myotomy (POEM). Technical perspectives on surgical interventions, including key steps, clinical practice guidelines, and modifications to POEM techniques, are extensively discussed. A comparative analysis between POEM and Heller's myotomy elucidates their indications, contraindications, efficacy, outcomes, and interventions for persistent symptoms or complications. Furthermore, the review explores the adverse events associated with both procedures, highlighting their safety profiles and management strategies. Finally, from a financial perspective, considerations such as operative time, hospital stay length, readmission rates, and quality-adjusted life years are examined, emphasizing the implications for patient decision-making. This review underscores the importance of a multidimensional approach to understanding and managing achalasia, advocating for further research to enhance treatment efficacy and reduce adverse effects.

Keywords: achalasia, Heller's myotomy, peroral endoscopic myotomy (POEM), surgical interventions

### Introduction

Achalasia is a rare, chronic motility disorder of the esophagus defined by the failure of the lower esophageal sphincter (LES) to relax and by the absence of normal peristalsis<sup>[1]</sup>. This is associated with dysphagia, regurgitation, chest pain, and weight loss. The pathophysiology is an underlying progressive degeneration of inhibitory ganglion cells in the esophageal myenteric plexus, which impairs neural control of esophageal motility<sup>[2]</sup>. The world incidence of achalasia is around 1 per 100 000 individuals per annum with a prevalence of 10 in 100 000. The illness occurs in both

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### **HIGHLIGHTS**

- Comparative analysis: This study provides a comprehensive comparison between peroral endoscopic myotomy (POEM) and Heller's myotomy, elucidating their indications, contraindications, efficacy, outcomes, and interventions for persistent symptoms or complications.
- Technical perspectives: The technical aspects of both procedures, including key steps, clinical practice guidelines, and modifications to POEM techniques, are extensively discussed, offering valuable insights for clinicians performing these interventions.
- Safety profiles and management strategies: The adverse events associated with both POEM and Heller's myotomy are highlighted, along with their respective safety profiles and management strategies, crucial information for clinicians and patients considering these procedures.
- Clinical implications: Understanding the comparative effectiveness and safety profiles of POEM and Heller's myotomy is essential for informed clinical decision-making, and optimizing patient outcomes in the management of achalasia.

genders with equal frequency and more commonly in middle-aged and older adults<sup>[3–5]</sup>.

While the definite etiology of achalasia is unclear, several have been suggested, such as autoimmune reactions, genetic influences, and viral infections<sup>[6]</sup>. One interesting report from Naik *et al*<sup>[7]</sup> is finding varicella-zoster virus DNA in 80% of achalasia patients, positing a possible viral etiology. Environmental components are also implicated since there has been an increase in cases around the globe with no geographic or ethnic predisposition<sup>[7]</sup>.

Achalasia significantly affects the quality of life of patients, not only because of the physical symptoms but also because of psychological distress. Research has shown that women with achalasia are more anxious and depressed than men. The disease can restrict social activities, travel, and daily activities, adding to its burden<sup>[8]</sup>.

The definitive test for achalasia is high-resolution esophageal manometry (HRM) to evaluate LES pressure and peristalsis of the esophagus. HRM results characteristically demonstrate incomplete LES relaxation and a lack of peristalsis. The barium swallow is a valuable adjunct, with a sensitivity of 78.3% and a specificity of 88.0%<sup>[9]</sup>. It demonstrates the typical "bird-beak" appearance of the lower esophagus. Though not the initial diagnostic test, endoscopic examination helps exclude malignancies and other structural lesions. However, endoscopic findings in early achalasia may be normal<sup>[10]</sup>.

Since achalasia is a progressive condition with no cure, management is directed toward relieving symptoms and enhancing esophageal emptying. Nonsurgical interventions include pneumatic dilation, which energetically disrupts the LES, and botulinum toxin (Botox) injections, which are effective in symptom improvement for only a short duration by causing relaxation of the LES. Pharmacologic interventions, including calcium channel blockers and nitrates, are ineffective in the long term<sup>[11]</sup>.

Surgical procedures are the treatment of choice for long-term symptom management. Heller's myotomy, which can be either open or laparoscopic, involves incising the LES muscle fibers to allow food entry into the stomach<sup>[12]</sup>. Peroral endoscopic myotomy (POEM) is a more recent minimally invasive option with good results. Preoperative evaluation is key to the decision-making process, given the heterogeneity of therapeutic approaches<sup>[13]</sup>. The patient's comorbidities, symptoms' severity, and esophagus function determine decision-making. Eckardt Symptom Score (ESS) is a commonly used scoring system to measure the severity of symptoms and monitor the response to therapy. Achalasia treatment is still complicated, with every treatment method offering different levels of efficacy and side effects. Knowing preoperative evaluation criteria and treatment strategies is vital to maximize patient outcomes<sup>[14]</sup>.

# Methodology

This narrative review explores the treatment landscape for achalasia, comparing POEM and Heller's myotomy. An extensive literature search was conducted using PubMed/MEDLINE and Google Scholar databases, with data collected up to 2023. Search criteria included keywords such as "Peroral Endoscopic Myotomy," "POEM," "Heller's Myotomy," "achalasia treatment," "surgical interventions," "clinical outcomes," "adverse events," and "financial implications." The review aimed to identify articles that provided insights into both procedures' therapeutic and diagnostic significance in managing achalasia. Articles not in English were excluded. Screening of titles, abstracts, references, and citations ensured the relevance of selected articles to the topic under discussion.

### **Historical perspective**

To appreciate the evolution of treatments for achalasia, it is essential to explore the different treatment options available and trace their progression over time. The journey begins with pharmacological and nonsurgical treatments and advances in surgical techniques, including Heller's myotomy and POEM.

# Treatment options before LHM and POEM/predecessor techniques for achalasia treatment

The treatment options for achalasia were limited and often couldn't provide long-term relief for patients. Several techniques were attempted, each with its limitations and challenges. Pneumatic dilation, which uses a balloon to stretch the LES, offers promising results but necessitates repeated dilations<sup>[12]</sup>. The botulinum toxin injection (BTI) works by temporarily relaxing the LES muscle, thereby relieving the symptoms of dysphagia. Nevertheless, it is crucial to consider that the effect of BTIs is short-lived, and the cost associated with this treatment option is an added disadvantage<sup>[15]</sup>. Apart from these injections, an alternative approach for managing achalasia is pharmacological therapy, using medications to relax the LES, which lacked consistent efficacy<sup>[16]</sup>.

# Development of POEM

POEM stands as a pioneering and minimally invasive option, diverging from the traditional laparoscopic Heller's myotomy (LHM), to address esophageal motility disorders with remarkable efficacy. In 2010, one of the first case series, which consisted of 17 patients who underwent POEM, was published. The study's outcome was excellent and showed marked improvements in symptoms of achalasia<sup>[17]</sup>. Unlike LHM, which requires an abdominal incision, POEM is completely endoscopic. The approach involves creating a submucosal tunnel in the esophageal wall and performing myotomy, thereby relieving the symptoms of achalasia, hence providing a less invasive and more comfortable experience for patients.

According to a study published in July 2021, 67 patients underwent POEM for achalasia, with pretreatment Eckardt scores ranging between 4 and 12 points. Three months after the procedure, 64 patients achieved an Eckardt score of less than 3, suggesting a success rate of over 95%. Additionally, the procedure's safety profile demonstrates that 91% of patients experienced either no or mild to moderate adverse effects<sup>[18]</sup>. Moreover, the Journal of the Canadian Association of Gastroenterology highlights a study involving 50 patients who underwent POEM. The outcome of this study states that more than 98% of patients achieved a post-POEM Eckardt score of less than 3 more than 3 months after the procedure. The study also reported a post-POEM pathologic reflux incidence of 23%. These findings suggest that POEM is a safe and effective procedure for treating achalasia<sup>[19]</sup>.

### Development of Heller myotomy

Ernst Heller's innovative surgical procedure, known as Heller's myotomy, revolutionized the treatment of achalasia in the early 20th century. The method involved cutting the LES muscles to alleviate the obstruction and improve the passage of food and liquids into the stomach. Initially, the technique involved open surgical myotomy, requiring large incisions in the chest or abdomen. Due to constant advancements in surgical techniques over the years, the procedure for Heller's myotomy evolved into a less invasive approach called LHM. This minimally invasive

technique utilizes small incisions, laparoscopic instruments, and cameras to perform the myotomy.

A significant adverse effect in the realm of surgical treatment for achalasia is the potential emergence of gastroesophageal reflux disease (GERD) following Heller's myotomy. Since myotomy aims to release the resistance at the gastroesophageal junction, it can inadvertently relax the LES, leading to the subsequent reflux of gastric contents into the esophagus. To address this complication, the surgical approach of fundoplication was introduced. Fundoplication involves wrapping the stomach's upper part around the esophagus's lower end to create an anti-reflux barrier. This barrier mitigates the reflux of gastric contents into the esophagus, preventing the incidence of GERD following myotomy.

Several variations of fundoplication techniques exist, each with its own merits and demerits. Nissen fundoplication, popularized in 1958, involves a full wrap around the esophagus, creating a robust anti-reflux mechanism. However, Nissen fundoplication is least preferred for the treatment of achalasia due to the high risk of recurrence of dysphagia postoperatively<sup>[20,21]</sup>. On the other hand, partial fundoplication techniques, such as Dor and Toupet fundoplication, are preferred for the surgical correction of achalasia.

Dor fundoplication, or anterior fundoplication, is a technique in which only the upper part of the stomach, called the fundus, is wrapped anteriorly around the lower esophagus to prevent GERD. A long-term follow-up of a prospective randomized controlled trial (RCT) suggests that the gastroesophageal reflux (GER) and dysphagia scores were slightly worse after HM than after HM + DF<sup>[22]</sup>. In contrast, Toupet fundoplication, or posterior fundoplication, involves the formation of a wrap around the lower esophagus with the wrap positioned posteriorly. A retrospective study shows that Dor and Toupet's fundoplication shows comparable short-term outcomes. However, Dor is preferred due to its reduced requirement for extensive dissection and more mucosal protection<sup>[23]</sup>. An RCT comparing the longterm results of LHM + DF vs. LHM + Nissen mentions that although both techniques achieved long-term GER control, the recurrence rate of dysphagia was significantly higher among the patients who underwent Nissen fundoplication<sup>[20]</sup>.

# **Technical perspective**

Various approaches are considered for a particular surgical intervention, which then affects the procedure's outcome. The patient is given full autonomy to choose the suitable option after discussing it with his physician and weighing the risks, benefits, and finances.

# Peroral endoscopic myotomy

Recently, POEM has gained wide acceptance as a minimally invasive endoscopic treatment for achalasia. It represents a Natural Orifice Transluminal Endoscopic Surgery (NOTES) approach to Heller myotomy<sup>[24]</sup> and is performed in a fashion similar to the technique described by Inoue and colleagues<sup>[25]</sup>.

The POEM technique contains five key steps:

### 1. Diagnostic endoscopy and taking measurements

An initial upper endoscopy identifies and measures the submucosal entry site proximal to the gastroesophageal junction (GEJ), usually 10–15 cm.

### 2. Esophageal mucosotomy creation

A submucosal cushion is created by using saline solution mixed with a blue dye, and a 2 cm longitudinal mucosal incision is made to lift the mucosal wall and enter the submucosal space.

### 3. Submucosal tunnel creation

It is created using techniques similar to that of endoscopic submucosal dissection. The plane of dissection is maintained closest to the muscularis propria, and it is ensured that mucosal injury (MI) is avoided during the dissection. The submucosal tunnel is extended ~3 cm distal to the GEJ to ensure complete myotomy of the LES.

### 4. Selective circular myotomy

A selective myotomy of the circular muscle layer is then performed, usually proximal to distal. The submucosal tunnel's length is usually 3–5 cm longer than the total myotomy length. The mucosa is carefully inspected to detect any tears.

### 5. Mucostomy closure

Mucosal entry is then closed with endoscopic hemostatic clips or other endoscopic methods. [25,26]

According to the clinical practice guidelines for POEM<sup>[27]</sup>:

# 1. Diagnostic workup before POEM

Gastrointestinal upper endoscopy, timed barium swallow, and high-resolution manometry are performed for the diagnosis of esophageal achalasia and decision-making before offering POEM<sup>[28,29]</sup>.

# 2. Preoperative assessment

Risk assessment for general anesthesia with endotracheal intubation is critical in these patients. <sup>[17]</sup> No dietary liquid or food should be in the esophagus during the procedure, so a few days of fasting and endoscopic cleansing should be done <sup>[27]</sup>. The method should be performed with  $CO_2$  insufflation <sup>[30]</sup> and patients should be supine with both arms at their sides or in the semi-left lateral decubitus position <sup>[24]</sup>.

# 3. Intraoperative

Pneumoperitoneum frequently occurs with POEM and if its degree is sufficient to affect circulation, then paracentesis should be performed to remove the gas.<sup>[26]</sup>

The starting point of the myotomy is the oral side of the abnormal luminal obstructive contractions in the esophageal body, and the endpoint is 1–2 cm into the gastric side to secure the LES incision. The location recommended for myotomy in POEM is the anterior or posterior wall<sup>[31,32]</sup>. A method should be selected to verify that the myotomy is extended to the gastric side at the proper length, such as:

- The double-scope method
- Endoscope insertion depth
- Anatomical landmarks
- Scope resistance

The double-scope method is beneficial because it allows direct vision to verify that the myotomy extends down to the stomach.

### 4. Postoperative care

Vital signs must be monitored on the day of the procedure. Upper GI endoscopy and esophagography should be performed after POEM, and the patient can be started on an oral diet after confirmation of no leak or adverse event (AE). A medical interview should be conducted, and GERD should be assessed by endoscopy. If necessary, acid secretion inhibitors should be started<sup>[27]</sup>.

### Modifications to the POEM technique

Since its initial description, several modifications have been proposed to its technique, which follows the basic principles of submucosal endoscopy which is given in Table 1.

 Orientation of myotomy: Anterior, posterior, and greater curvature

Anterior: The initial description involves POEM at the 1–2 o'clock position with patients lying supine. It aims to avoid damage to the angle of his and an important antireflux mechanism, the sling muscle fibers located over the fundus at the stomach's greater curvature.

Posterior: It begins with a mucosal incision and the development of the submucosal tunnel at the 5–6 o'clock position. [33] In a global International Per Oral Endoscopic Myotomy Survey (IPOEMS) enrolling 16 expert centers, most centers performed anterior myotomy, and only 2 performed posterior myotomy. [25]

Greater curvature: In some cases, myotomy by conventional routes is not feasible due to anatomical reasons or submucosal fibrosis because of previous. In these cases, endoscopic myotomy can be performed successfully via a greater curvature approach, that is, 8 o'clock.

# 2. Thickness of myotomy: Complete (full thickness) vs. selective circular

A circular muscle myotomy, which preserves the longitudinal outer esophageal muscular layer is often recommended. Still, since the longitudinal muscle fibers are extremely thin and fragile, the completeness of myotomy is the basis for the excellent results of conventional surgical myotomy. However, this modification needs to be further analyzed. [34]

3. Length of myotomy: Short vs. standard (long)

Short follow-up and lack of a comparison arm were the main limitations proving either method was better.

Since GERD is the most common adverse after POEM in the long term, as proven by RCTs when compared to Heller myotomy with fundoplication<sup>[35,36]</sup>, there have been alterations to the procedure that intend to reduce GERD after POEM such as:

4. Anti-reflux POEM: Sling fibers preservation during posterior POEM, NOTES fundoplication

Tanaka *et al*<sup>[37]</sup> compared the incidence of reflux esophagitis in 114 patients who underwent POEM either by conventional or sling fiber technique. Grade B esophagitis was lower when sling fibers were preserved, but symptomatic reflux was not significantly different.<sup>[37]</sup>

Inoue *et al*<sup>[38]</sup> performed endoscopic fundoplication in 21 patients who underwent POEM via the anterior route. They concluded it might help mitigate GERD and serve as a minimally invasive endoscopic alternative to a laparoscopic Heller–Dor procedure.<sup>[38]</sup> But more extensive trials are required

Table 1.
The modification to the POEM techniques over time

|   |                              | Technique  | Current evidence   | Future directions   |
|---|------------------------------|--|--|---|
| 1 | Orientation<br>of<br>myotomy | Ant, post, greater curvature                             | RCTs show clinical success similar at 1 year follow-up period <sup>[33,39,40]</sup> with mucosal injuries being higher after anterior POEM and GERD being higher after posterior POEM <sup>[41]</sup>                              | Long-term follow-up studies   |
| 2 | Thickness of myotomy         | Selective circular vs.<br>full-thickness<br>myotomy      | A comparative study shows similar clinical success, reduced procedure duration with full-thickness myotomy, and GERD may be similar or higher after full-thickness myotomy <sup>[34]</sup>   | RCTs should be done, and the impact on GERD needs further evaluation                                  |
| 3 | Length of myotomy            | Short vs. Standard myotomy                               | RCTs and comparative studies show similar clinical success similar at 1 year <sup>[42–44]</sup> Procedure duration was shorter in the shorter myotomy group and GERD may be similar or higher after a long myotomy <sup>[45]</sup> | Long-term follow-up studies are required to<br>confirm the durability of response to short<br>myotomy |
| 4 | Diverticular<br>POEM         | Septotomy vs. no septotomy                               | POEM alone may be sufficient and septotomy may not be required   | Long-term results of POEM without septotomy, comparative studies between the two techniques           |
| 5 | Anti-reflux<br>POEM          | Sling fiber<br>preservation,<br>NOTES-<br>fundoplication | Both techniques may potentially prevent post-POEM reflux   | RCTs required to confirm the utility of anti-reflux POEM techniques                                   |
| 6 | Submucosal fibrosis          | OPEN-POEM, double tunnel POEM                            | Both techniques appear to be useful in cases with severe SMF (No RCTs)   | The safety of O-POEM needs evaluation in future studies   |

before incorporating NOTES fundoplication into routine clinical practice.

5. Diverticular POEM (D-POEM) (septotomy vs. no septotomy)

D-POEM is emerging as a safe and effective treatment in cases with epiphrenic diverticula of the esophagus (EED). It involves submucosal tunneling, exposure of the septum, and division of the septum.

### Heller's myotomy

Heller esophagomyotomy is considered the primary treatment for achalasia which provides the most durable symptom relief, without needing to intervene repeatedly. In the procedure, the constricting muscle fibers of the lower esophagus and upper stomach are divided, which improves esophageal emptying as these fibers contribute to the LES mechanism. [46,47]

There are several techniques for this procedure:

### Open technique (trans-abdominal or transthoracic)

This was the first technique to be developed, and it was mostly performed in patients with persistent dysphagia after pneumatic dilatation was done for achalasia.<sup>[48]</sup> Initially, it consisted of two simultaneous trans-abdominal extra mucosal myotomies on the esophagus's anterior and posterior walls, but now myotomy on the anterior wall is done only.

Abdominal access is given through an incision. The phrenoesophageal ligament is divided, and the diaphragmatic crura is opened. The anterior mediastinal esophagus is dissected, and the short gastric vessels are divided to mobilize the fundus. The anterior gastric fat pad and anterior vagus nerve are dissected free from the stomach and esophagus. A full-thickness myotomy is performed to at least 5 cm proximal and 3–4 cm distal to the GEJ which is recognized by typical anatomical findings, as the periesophageal fat, the his angle and changes of the muscle fibers. [25]

Both approaches are effective in the treatment of dysphagia, but studies have shown that the trans-abdominal approach resulted in a higher incidence of postoperative GERD. Adding a partial anterior fundoplication to the trans-abdominal approach reduces its rate. [49]

# Minimally invasive techniques (laparoscopic/thoracoscopic or laparoscopic with Dor fundoplication)

In the last three decades, we've seen a shift from open to minimally invasive LHM, which, along with robotic surgery, is currently the standard of care with better short-term outcomes and similar long-term functional results compared to open surgery. [47]

A potential side effect of Heller's myotomy is GERD, which can be reduced by combining the laparoscopic procedure with an antireflux procedure: an anterior (Dor) fundoplication, as proved by a meta-analysis combining multiple retrospective and prospective cohort studies. As a result, laparoscopic esophagectomy with partial fundoplication has become the primary treatment for the disease. [46] Patient outcomes were comparable in a long-term symptomatic follow-up of a prospective RCT to

compare the two procedures, providing support for either method.  $^{[22]}$ 

Douard *et al*<sup>[50]</sup> designed a prospective non-randomized study to compare functional outcomes after laparoscopic and open myotomy with Dor fundoplication. It was concluded that laparoscopic was favorably compared with open surgery regarding dysphagia and GERD relief and the overall clinical score indicated gradual improvement in patient functional status during 12-month follow-up. [50]

### New approaches: Robotic myotomy

Recently, a robotic technique for a minimally invasive Heller's myotomy for achalasia has been successfully adopted. Although the robotic approach appears to have some advantages over standard laparoscopy, data on this topic is still controversial, with no definite conclusions drawn.

In a multicenter, retrospective analysis using the University Health System Consortium database, 2683 patients with achalasia underwent Heller myotomy between October 2007 and June 2011. Of these, 418 patients underwent open surgery (OM), 2116 under the laparoscopic approach (LM), and 149 under the robotic approach (RM). Compared to OM, the perioperative outcomes were superior in the LM and RM groups. The perioperative outcomes for the LM and RM groups are comparable, with the robotic group having slightly improved results, although with increased costs<sup>[46]</sup>. The authors concluded that robotic surgery is equivalent in safety and efficacy to LHM. They felt that the increased cost should come down as surgeons and manufacturers should work together on cost-reduction strategies.<sup>[47]</sup>

A systematic review with meta-analysis was conducted to compare the safety and postoperative outcomes of Laparoscopic versus robotic-assisted Heller myotomy. In 3214 patients, the only factor to be statistically different was the intraoperative esophageal perforation rate, which was lower in robotic myotomy. [51]

# Laparoscopic single-site approach

This surgery represents a shift to more minimally invasive which is feasible, safe, and efficacious. it increases operative time but does not increase procedure-related morbidity or hospital length of stay and avoids apparent umbilical scarring.<sup>[52]</sup>

# POEM vs. Heller's technical perspective: A comparison

POEM has been regarded as a relatively safe procedure when performed by experts at 12 tertiary care centers in 1826 patients in an international, multicenter case-control study with an overall 7.5% prevalence of AEs, with severe AEs rare. [26]

In a retrospective study comparing patient-reported outcomes with more than 1 year of follow-up at a single institution between Laparoscopic HM and POEM, there was a nonsignificant trend towards better outcomes with POEM. However, the two procedures had significant demographic and clinical differences in patient selection. [53]

# Clinical perspective

In treating achalasia, physicians consider both POEM and Heller myotomy as viable options. POEM is a minimally invasive endoscopic procedure, while Heller myotomy is a traditional surgical approach with a long track record of success. Each method has its own set of risks, benefits, and recovery profiles. The choice of procedure is tailored to the patient's medical condition, preferences, and overall health status, with a thorough discussion between the patient and physician to ensure an informed decision that best suits the patient's needs and lifestyle.

#### Indications for POEM

All patients with types I, II, and III achalasia can be treated by POEM<sup>[54]</sup>. Patients who have received previous treatments for achalasia, including PD (pneumatic dilation), BTI, LHM, or prior POEM, are all competent for undergoing POEM<sup>[55–57]</sup>. Though POEM is traditionally performed to relieve the symptoms of achalasia, it is also being used in other hypertensive motor disorders associated with dysphagia and chest pain, such as Jackhammer esophagus<sup>[32]</sup>, Esophageal epiphrenic diverticulum (ED)<sup>[58]</sup>, distal esophageal spasm (DES)<sup>[59]</sup> and nutcracker esophagus<sup>[60]</sup>. Furthermore, POEM has been documented to be utilized in the stomach (known as endoscopic pyloromyotomy) as a treatment approach for specific individuals suffering from gastroparesis<sup>[61]</sup>.

### Contraindications for POEM

POEM is contraindicated for individuals with severe cardiopulmonary disease or other significant medical conditions that pose an unacceptable surgical risk, as well as those diagnosed with pseudo-achalasia<sup>[62]</sup>. Additionally, it may not be feasible in cases where the creation of the submucosal tunnel is hindered due to extensive fibrosis and adhesion. Mild or moderate esophagitis without esophageal stricture is generally acceptable. Still, severe esophagitis and/or large ulcers in the lower esophagus or esophagogastric junction (EGJ) should be considered relative contraindications<sup>[27]</sup>.

# Indications for LHM

LHM is primarily indicated for the treatment of benign achalasia. The procedure aims to relieve dysphagia, addressing the challenges associated with swallowing. Patients with achalasia also experience distressing symptoms like regurgitation and retrosternal pain, all of which can be alleviated through this surgical intervention, providing symptomatic relief<sup>[63]</sup>. In cases where other treatments, such as pneumatic dilation, have proven ineffective in providing adequate relief, LHM may be considered an alternative option<sup>[46]</sup>. It is important to note that previous pneumatic dilation should not be seen as a contraindication for undergoing LHM, contrary to popular belief<sup>[64]</sup>.

#### Contraindications for LHM

LHM is contraindicated for individuals with prohibitive surgical risk factors, such as underlying medical conditions that make them unfit for surgery, should not undergo this procedure<sup>[65]</sup>. Moreover, patients who refuse to undergo surgery or have previously experienced a failed Heller myotomy are not suitable candidates. In cases where an LM is not feasible, particularly when there is associated intra-abdominal pathology that cannot be treated using laparoscopy, an open procedure may be considered an alternative [66]. Additionally, some surgeons believe that patients with megaesophagus or grade IV dilatation (diameter greater than 8 cm) may not experience significant relief from dysphagia following myotomy, making it a potential contraindication. Lastly, patients with anemia and hypertension are considered to have physiologic contraindications for laparoscopic surgery<sup>[65]</sup>.

# Efficacy of POEM vs. LHM

Both POEM and Heller myotomy have demonstrated effectiveness in treating achalasia. POEM has the benefit of being minimally invasive, leading to potentially fewer complications<sup>[67]</sup>. On the other hand, Heller myotomy is a well-established procedure with proven long-term success<sup>[68]</sup>. The decision between the two methods largely relies on factors such as the patient's unique condition, the medical team's expertise, and patient preferences.

### Clinical outcomes of POEM vs. LHM

- 1. Operative time: POEM generally has a shorter operative time than LHM, making it a more time-efficient procedure<sup>[69]</sup>.
- 2. Blood loss: POEM is associated with less blood loss during the procedure than LHM, reducing the risks of significant bleeding<sup>[69]</sup>.
- 3. Pain: Patients who undergo POEM typically experience less postoperative pain than LHM, improving patient comfort and recovery<sup>[69]</sup>.
- 4. Dysphagia relief: POEM is more effective than LHM in providing short-term relief from dysphagia (difficulty swallowing) in patients with achalasia<sup>[70]</sup>.
- Reflux incidence: One notable concern with POEM is the higher incidence of pathologic reflux compared to LHM. This can lead to other complications and require additional management<sup>[71]</sup>.

Table 2.

The different aspects of the POEM such as success rate, rate of adverse events, operative time, and length of stay

|   | Authors                              | Success rate | Rate of adverse events | Operative time | Length of stay |
|---|--------------------------------------|--------------|------------------------|----------------|----------------|
| 1 | Khashab <i>et al</i> <sup>[72]</sup> | 94.3%        | 19.2%                  | 106 min        | 1.9            |
| 2 | Kumagai <i>et al<sup>[73]</sup></i>  | 90.5%        | n/a                    | 121 min        | n/a            |
| 3 | Ramirez <i>et al</i> <sup>[25]</sup> | 94.2%        | n/a                    | n/a            | 1.3            |
| 4 | Kumbhari <i>et al<sup>[74]</sup></i> | 98%          | 6%                     | 102            | 3.3            |
| 5 | Bhayani <i>et al<sup>[75]</sup></i>  | n/a          | n/a                    | 120            | 1.1            |

Table 3.

The different aspects of the LMH such as success rate, rate of adverse events, operative time, and length of stay.

|   | Authors                              | Success rate | Rate of adverse events | Operative time | Length of stay |
|---|--------------------------------------|--------------|------------------------|----------------|----------------|
| 1 | Khashab <i>et al</i> <sup>[72]</sup> | 88.5%        | 9.6%                   | 263 min        | 2.3            |
| 2 | Kumagai <i>et al<sup>[73]</sup></i>  | 90%          | n/a                    | 100 min        | n/a            |
| 3 | Ramirez <i>et al</i> <sup>[25]</sup> | 91.4%        | n/a                    | n/a            | 2.1            |
| 4 | Kumbhari <i>et al<sup>[74]</sup></i> | 80.8%        | 27%                    | 264            | 3.2            |
| 5 | Bhayani <i>et al<sup>[75]</sup></i>  | n/a          | n/a                    | 149            | 2.2            |

# Success rate, rate of AEs, operative time, and length of stay after POEM vs. LHM

Tables 2 and 3 present the results of studies comparing POEM and LHM procedures for treating achalasia. The success rates of POEM range from 90.5% to 98%, while the success rates of LHM range from 80.8% to 91.4%. The rates of AEs for POEM range from 6% to 19.2%, while those for LHM range from 9.6% to 27%. The operative time for POEM ranges from 102 to 121 minutes, while the operative time for LHM ranges from 100 to 263 minutes. The length of stay for both procedures ranges from 1.1 to 3.3 days.

Overall, POEM appears to have higher success rates and lower rates of AEs than LHM. However, the operative time for POEM is shorter than that of LHM in some studies but longer in others. The length of stay is similar for both procedures. Further studies are needed to compare the long-term efficacy and safety of POEM and LHM.

### Eckardt score

The ESS is a commonly used grading system to assess symptoms, disease stages, and treatment effectiveness in achalasia. It assigns points (ranging from 0 to 3) to four key symptoms of the condition: dysphagia, regurgitation, chest pain, and weight loss, with a total possible score of 0–12. The scores are categorized as follows: 0–1 points indicate clinical stage 0, 2–3 points correspond to stage I, 4–6 points represent stage II, and a score greater than 6 indicates stage III (Table 4).

### Posttreatment improvement in Eckardt score

Several studies have examined the posttreatment improvement in the Eckardt score, a measure used to assess the severity of achalasia symptoms, particularly comparing two treatment approaches: Peroral Endoscopic Myotomy (POEM) and LHM (Table 5).

# Interventions for persistent symptoms or complications after POEM or HM

The specific intervention or procedure used after POEM or HM will depend on the underlying cause of persistent symptoms or complications. Some of the interventions that might be considered include:

- Repeat POEM or HM: In some cases, if the initial procedure did not achieve the desired result, a repeat POEM or HM may be performed to improve the outcome<sup>[78]</sup>.
- 2. Balloon dilation: Balloon dilation involves inflating a balloon inside the esophagus to stretch and widen the LES. This can be done either endoscopically or surgically and may help in cases of recurrent narrowing (stricture) of the LES.<sup>[79]</sup>.
- 3. BTI: Botox can be injected into the LES to relax the muscle temporarily. This is a less invasive option but is usually considered for elderly or high-risk patients who may not be suitable for more extensive interventions<sup>[80]</sup>.
- 4. Anti-reflux procedures: If patients develop significant reflux (backflow of stomach contents into the esophagus) following POEM or HM, additional anti-reflux procedures may be considered to manage this issue<sup>[81]</sup>.

### **AEs of POEM vs. LHM**

The safety and efficacy of any treatment approach hinge upon thoroughly examining the potential complications involved. While both Heller's myotomy and POEM have shown promising results in treating achalasia, it is important to evaluate the risks involved with each technique. Each procedure is associated with certain AEs that can occur peri and postoperatively.

POEM demonstrates a favorable AE profile in addition to the other advantages of being an incision-less approach compared to LHM. The rate of complications or AEs is higher after LHM than POEM. One multicenter RCT reported a 7% and 3% incidence of serious AEs in LHM plus Dor's fundoplication and POEM groups, respectively<sup>[36]</sup>. In another multicenter

Table 4.

The Eckardt score for evaluation in achalasia

| Score | Weight loss (kg) | Dysphagia  | Retrosternal pain | Regurgitation |
|-------|------------------|------------|-------------------|---------------|
| 0     | None             | None       | None              | None          |
| 1     | <5               | Occasional | Occasional        | Occasional    |
| 2     | 5–10             | Daily      | Daily             | Daily         |
| 3     | >10              | Each meal  | Each meal         | Each meal     |

Table 5.

The posttreatment improvement in Eckardt score comparing POEM vs. LMH.

|   | Study                                 | Treatment | Outcome measure | Results   |
|---|---------------------------------------|-----------|-----------------|---|
| 1 | Kumbhari <i>et al</i> <sup>[74]</sup> | POEM      | Eckardt score   | Superior clinical response compared to LHM                  |
|   |                                       | LHM       | Eckardt score   | There is no significant difference between POEM and LHM     |
| 2 | Kahaleh <i>et al</i> <sup>[76]</sup>  | POEM      | Eckardt score   | Lower Eckardt scores after POEM compared with LHM           |
|   |                                       | LHM       | Eckardt score   | POEM is more effective than LHM based on short-term results |
| 3 | Zhang <i>et al</i> [77]               | POEM      | Eckardt score   | Lower Eckardt scores after POEM compared with LHM           |
|   | -                                     | LHM       | Eckardt score   | There is no significant difference between POEM and LHM     |

comparative study, it was observed that the overall rate of AEs was significantly higher in the Heller's myotomy (LHM) cohort, with a rate of 27.0%, compared to only 6% in the POEM group<sup>[74]</sup>. However, it is crucial to note that not all studies have consistently supported these findings.

In contrast, a subset of research (Ref) has reported divergent results, indicating that POEM may be associated with higher rates of AEs. A recent meta-analysis has shown that the rate of any AE related to POEM was 24.8% vs. 13.3% for LHM<sup>[82]</sup>. Similarly, another study revealed that the complication rates for POEM and LHM were 20.6% and 10.0%, respectively, during the learning curve<sup>[83]</sup>. The occurrences of AEs tend to reduce considerably after the completion of the learning curve<sup>[84]</sup>. When performed by experienced hands, POEM has established itself as a safe and effective procedure, boasting a low incidence of post-operative AEs.

Interestingly, no standardized classification system exists for grading the severity of AEs associated with POEM. Nonetheless, several categorizations have been employed in various studies, such as the ASGE Lexicon, Clavien–Dindo, and the IPOEMS survey classification, leading to a wide range of reported overall AE incidence rates (3.2%–23%)<sup>[85]</sup>. In most cases, AEs are managed through medical or endoscopic means, without adverse consequences.

AEs that may arise during POEM or the perioperative period primarily include insufflation-related complications, mucosal injuries, bleeding, pain, and, more rarely, aspiration pneumonia. Notably, the management of most intraoperative AEs can be addressed concurrently without adverse consequences. Certain postoperative AEs, such as leaks, delayed bleeding, and delayed mucosal perforations, may present distinct diagnostic and management challenges.

# Mucosal injury

MI emerges as one of the most feared and prevalent intra-procedural events impacting the short-term outcomes of POEM. The incidence of MI has been reported in varying ranges from 1.6% to 25.8%<sup>[26,85]</sup>. A recent single-center study revealed MI occurrences in 44 out of 206 patients (21.4%) who underwent POEM<sup>[85]</sup>. Similarly, another study conducted on 610 consecutive POEM patients documented accidental mucosal injuries in 64 patients (10.5%)<sup>[86]</sup>. In a larger cohort involving a total of 1826 patients who underwent POEM, a total of 51 (2.8%) inadvertent mucosal injuries were recorded<sup>[26]</sup>. The significance of severe MI lies in the potentially serious consequences, such as esophageal leak and mediastinitis, impacting the overall procedure outcome and prolonging hospital stays. Addressing mucosal tears immediately is crucial, as they tend to expand rapidly,

typically requiring closure with end clips. However, other options such as glue and over-the-scope clips are also utilized<sup>[87,88]</sup>.

#### Esophageal perforation

The most critical intraoperative complication specifically associated with Heller's myotomy (LHM) is esophageal perforation<sup>[83,89]</sup>. They can pose serious risks since they require immediate interventions. It can be managed with esophageal stenting<sup>[90]</sup>. It is important to note that esophageal perforation can also occur during POEM, necessitating similar prompt management strategies.

### Gastroesophageal reflux disease

While both POEM and LHM have demonstrated significant dysphagia relief as effective treatment options for achalasia, it is worth noting that GERD stands as a noteworthy long-term AE following POEM<sup>[36]</sup>. It is a common occurrence, with varying incidences reported across multiple studies. POEM has been associated with noticeably greater rates (19%–50%) of post-operative GERD<sup>[82]</sup>. A meta-analysis of 36 studies encompassing 2,373 patients revealed an overall incidence of GERD in 8.5%<sup>[91]</sup>. Similarly, an analysis of 500 patients noted occurrences in 16.8% at 2 months and 21.3% at a 3-year follow-up period<sup>[92]</sup>.

# Reflux esophagitis

Studies have shown remarkable differences in the incidence of reflux esophagitis post-POEM compared to LHM<sup>[93,94]</sup>. POEM is known to show a higher incidence of esophagitis. This can be attributed to acid reflux that occurs post-procedure. Reflux esophagitis was seen in 11 (39.3%) cases in a case series of 28 patients who underwent POEM<sup>[95]</sup>.

### Intra-procedural bleeding

POEM, like any endoscopic procedure, is not immune to intraprocedural bleeding, which is a frequent AE that may arise independently or occasionally as a result of MI. According to a recent study, 52.3% of patients with MI experienced intraprocedural bleeding during POEM<sup>[85]</sup>.

### Pneumoperitoneum and pneumothorax

Minor operative AEs like pneumoperitoneum pneumothorax occur in 30% and 11%, respectively. They usually resolve spontaneously, in rare cases perioperative decompression is carried out to alleviate the condition<sup>[96]</sup>.

### Technical challenges

Both POEM and Heller's myotomy involve significant skillful difficulties. POEM requires advanced endoscopic skills for complex submucosal tunneling and precise myotomy, which presents a steep learning curve. Heller's myotomy, on the other hand, involves surgical precision and can lead to complications like esophageal perforation, which also demands immediate intervention and management<sup>[93,94]</sup>.

# **Financial perspective**

When a patient is identified as having achalasia, the doctor often offers both medicinal and surgical alternatives to treat the condition's symptoms and avoid recurrence. The two methods of treating GERD most frequently advised worldwide are POEM and Heller's myotomy. The patient and the doctor can agree upon the best course of therapy by considering all the essential variables. Finances are the primary consideration among the many others that may affect the patient's choice. Operative time, hospital stay length, readmission rate, and quality-adjusted life years (QALY) are some of the factors that may be used to compare the cost as a whole [97,98] (Fig. 1).

### Duration of the procedure

The POEM and Heller's myotomy are surgical procedures that call for following the appropriate OT protocols, which involve preoperative and postoperative care. The length of a procedure significantly impacts its ultimate cost since it is directly tied to the cost of the entire course of therapy. The cost increases and decreases based on the length of the operation. POEM patients had a greater median myotomy length (11 vs. 8 cm, P = 0.001) and a shorter median operating duration (106 minutes vs. 145 minutes, P = 0.003)<sup>[97]</sup>. Despite having a more extensive myotomy (16 vs. 8 cm; P = 0.01), POEM patients' mean procedure times were substantially lower than those of LHM patients (102 vs. 264 minutes; P = 0.01)<sup>[74]</sup>.

### Length of hospital stay

The length of the hospital stay (LOS) directly relates to how much the treatment costs. More extended hospital stays naturally result in higher daily costs for healthcare services, medications, and other operating costs, significantly impacting the treatment's total cost. The length of hospital stay did not differ substantially between POEM and LHM (3.3 vs. 3.2 days; P = 0.68, respectively). The POEM group experienced fewer AEs (6 % vs. 27 %; P = 0.01). Another study indicates that hospital stays were similar in length, averaging 1 day each<sup>[99]</sup>.

Another study conducted by Lois AW *et al*<sup>[100]</sup> stated that the adverse effects were few and almost uniform in both procedures.

#### Readmissions

The entire cost of therapy is negatively impacted by surgery or disease with a higher readmission rate, which may be primarily brought on by recurrence or any complications following the procedure. In severe cases, readmission might result in extra hospital stays or additional surgical procedures, further increasing the expense. Readmission often suggests the need for more testing. As readmissions have a higher mortality rate and longer hospital stays than index admissions, they burden the healthcare system. The mortality risk for readmission was much more significant for the LHM group, although there was no difference in readmission rates between those receiving POEM or LHM<sup>[101]</sup>.

### Quality-adjusted life years

QALY is a fully credited parameter today as it deals with the long-term efficacy of the treatment option. An option with better QALY and high initial cost is more valued than one with a lower primary cost but less QALY. QALYs in the POEM group were marginally greater than those in the LHM group (0.434 0.215 vs. 0.332 0.222, P = 0.397). According to the incremental cost-utility ratio, employing POEM would cost an extra US\$ 9046.41/QALY gained<sup>[2]</sup>. According to the ICER, utilizing POEM would add an extra \$18 536 to the cost per QALY gained<sup>[102]</sup>.

#### Reimbursements

Even though POEM is less expensive overall than Heller's in the industrialized world, especially the United States, it is not favored because there are no refunds. Despite POEM's median hospital expenditures being much lower than LHM's (\$3658 vs. \$14 152, P = 0.002), the median hospital reimbursement was significantly lower. The maximum cost-effective reimbursement for POEM, including all professional and facility expenses, ranged from \$8033.37 to \$8223.14<sup>[103]</sup>. Since POEM is difficult for the health-care insurance system to compensate for, patients frequently choose Heller's myotomy instead of POEM. This is another instance of how financial considerations significantly influence a person's choice. It is believed that POEM will only be preferred as the best option if it is remunerated with equality regardless of its numerous benefits over Hellers<sup>[104]</sup>.

### Overall cost

From 2010 to 2017 it is estimated that the usage of POEM increased 19-fold from 1.1% to  $18.9\%^{[4]}$ . In a study conducted

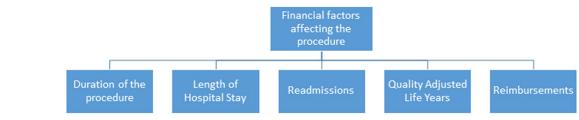


Figure 1. Highlights the factors affecting these procedures.

by Conte *et al*<sup>[98]</sup>, there were 40 patients in total – 20 POEM patients and 20 LHM patients. POEM and LHM's ultimate costs were US\$ 2619.19 399.53 and US\$ 1696.44 412.21, respectively (P = 0.001). Attaar *et al*<sup>[104]</sup>, in their study concluded that inflation-adjusted hospital costs were lower for POEM than for LHM (35.5 12.8 vs. 30.7 10.3 in thousands of US dollars, P = 0.006).

Given that POEM is more affordable than Heller's myotomy, we can confidently conclude that it is preferable. In comparison to LHM, POEM had a shorter LOS and operational duration, a longer myotomy length, and a better ability to resolve dysphagia. Although POEM expenditures are substantially lower than LHM, they are not well compensated. POEM in comparison to LHM, assumes at least a 10% cost reduction in cost-minimization analysis or at least a 44% cost reduction in cost-effectiveness analysis<sup>[103]</sup>.

### Conclusion

As evidenced by the articles used in this review, numerous techniques are used to treat achalasia, including pharmacological and surgical methods. Compared with pharmacological measures, surgical techniques are proven more efficacious and provide a longer-lasting effect. Heller's myotomy and POEM are widely accepted as the mainstay for surgical treatment of achalasia. Recently, POEM has been gaining more popularity because it is less invasive, rendering it safer than HM and with fewer complications. Compared to LHM, POEM is a time-efficient surgery with shorter operative and postoperative recovery times, less incidence of postoperative pain, and reduced risk of massive blood loss. However, POEM involves complex technical challenges that require advanced endoscopic skills.

On the other hand, Heller's myotomy is a procedure used for ages and has gained the trust of both patients and surgeons. Although the success rate is higher and the incidence of adverse effects is lower with POEM than with HM, it is still preferred as its cost is well compensated by insurance. In the long run, the overall cost is significantly lower for POEM than LHM due to its shorter hospital stays, fewer test requirements, and fewer complications.

We believe this article can help overcome the challenges by comprehensively comparing two of the most widely used surgical modalities for treating achalasia. Besides the historical significance and nonsurgical options, we have also discussed the intricacies of the procedure, indications/contraindications, adverse effects, and the technical and financial effects of both methods. Per our existing research evidence, POEM is comparable to LHM and an emerging treatment option for achalasia. Finally, we strongly feel that further research should be conducted to determine the long-term effectiveness of both procedures and to find ways to reduce the adverse effects.

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Ethics approval was not required for this review.

# Consent

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### **Author's contribution**

Conceptualization, writing – original draft, final approval, and agreeing to the accuracy of the work: K.A.; conceptualization, writing – original draft, final approval, and agreeing to the accuracy of the work: S.A.R.; writing – original draft, final approval, and agreeing to the accuracy of the work: T.H.; writing – original draft, final approval, and agreeing to the accuracy of the work: A.S.; writing – original draft, final approval, and agreeing to the accuracy of the work: R.A.; writing – original draft, final approval, and agreeing to the accuracy of the work: N.A.K.; reviewing and editing: H.H.S.; reviewing and editing: M.A.H.

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The authors declare that there is no conflict of interest.

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It will be available on reasonable request.

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