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Achalasia Cardia: Balloon, Tunnel, or Knife?

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Abstract

Achalasia cardia is a rare esophageal motility disorder characterized by impaired relaxation of the lower esophageal sphincter during swallowing and aperistalsis of the esophageal smooth muscles. The treatment approaches to achalasia include nonsurgical treatment with medications (nitrates, calcium channel blockers), endoscopic treatment (balloon pneumatic dilation [PD], botulinum toxin injection [BTI], peroral endoscopic myotomy [POEM]), and surgery (laparoscopic Heller's myotomy [LHM]). The subtype of achalasia (the Chicago Classification) governs the ideal treatment. For the commonly encountered achalasia subtype I and II, PD, LHM, and POEM all have similar efficacy. However, for type III achalasia, POEM seems to be the best line of treatment. Among high-risk elderly patients or those with comorbidities, BTI is preferred. The choice of treatment should be minimally invasive therapy with good short-term and sustained long-term effects with negligible adverse events. POEM seems to be evolving as a first-line therapy among the available therapies. Here, we review the treatment options among achalasia cardia patients with special attention to post-POEM gastroesophageal reflux disease and its management.

Keywords

- achalasia cardia
- Heller's myotomy
- peroral endoscopic myotomy
- pneumatic dilation
- treatment

Introduction

Achalasia cardia is an uncommon esophageal motor disorder resulting in failure of relaxation of the lower esophageal sphincter (LES).[1,2] This is associated with a loss of peristalsis in the distal esophagus. Achalasia is considered a rare disorder due to its low incidence of about 1.6 per 100,000 and prevalence of 10 per 100,000 individuals.[3] The frequency of achalasia across the Asia-Pacific countries seems to be increasing gradually. The disease can occur at any age and affects both men and women equally.[4] The etiology of primary achalasia remains largely unknown.[5] Without appropriate treatment, patients with achalasia can have progressive dilation of the esophagus. These patients are also at an increased risk for developing esophageal cancer, though the risk is relatively low.[6] It is therefore necessary to identify the appropriate achalasia subtype and treat it accordingly.

Esophageal Manometry and Achalasia Subtypes

High-resolution manometry (HRM) is preferred to conventional manometry due to its higher sensitivity in diagnosing achalasia.[7,8] Achalasia is diagnosed on HRM by an elevated median integrated relaxation pressure (IRP), which implies impaired relaxation of the esophagogastric junction and absence of normal peristalsis. IRP is the median of the maximal relaxation pressures of the esophagogastric junction in 4 seconds during the 10-second window of relaxation of the esophagogastric junction that follows a swallow.[9] The median IRP value varies based on the various systems, but an

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Table 1 Achalasia cardia subtypes and treatment

Achalasia	Subtype I: classic achalasia	Subtype II: achalasia with esophageal compression	Subtype III: spastic achalasia
IRP and peristalsis	100% failed peristalsis, IRP > ULN	100% failed peristalsis and panesophageal pressurization with ≥ 20% of swallows; mean IRP > ULN	No normal peristalsis, premature contractions with distal latency < 4.5 s and DCI > 450 mm Hg s cm seen in ≥ 20% of swallows, mean IRP > ULN
Treatment	PD, LHM, and POEM have shown similar results	PD, LHM, and POEM have shown similar results	POEM has shown good success rates than others

Abbreviations: DCI, distal contractile integral (amplitude × duration × length; mm Hg s cm); IRP, integrated relaxation pressure; LHM, laparoscopic Heller's myotomy; PD, pneumatic dilation; POEM, peroral endoscopic myotomy; ULN, upper limit of normal.

elevated median IRP is identified as ≥15 mm Hg. Based on the Chicago Classification version 3.0, patterns of esophageal pressurization on HRM findings, achalasia is categorized into three different subtypes.[10] The patterns include types I, II, and III. Type I is the classic achalasia with minimal contractility in the esophageal body, type II with isobaric intermittent periods of panesophageal pressurization, and type III (spastic) with premature or spastic distal simultaneous esophageal contractions (►**Table 1**).[11] Each subtype in patients has very subtle clinical differences but has varied responses to the different treatment modalities (►**Fig. 1**).

Treatment Options

Treatment is directed at relieving symptoms, and so far no cure has been found for the disease. Treatment is aimed at reducing the resting pressure in the LES so that it does not impede the passage of ingested food. This is achieved by disruption of the muscle fibers of the LES by a pharmacological reduction in LES pressure (botulinum toxin injection, use of oral nitroglycerin, calcium channel blockers [smooth muscle relaxants]), pneumatic balloon dilation, surgical myotomy, or peroral endoscopic myotomy (POEM).[1] The efficacy of these seems to reduce with time. Unfortunately, no treatment normalizes swallowing; they merely improve it. Achalasia cardia has been thought to exist for more than 300 years.[12] The earliest reports suggest a surgical approach (Heller's myotomy, 1914 to present),[13,14] followed by pneumatic balloon dilation (1960 to present)[15,16] and the more recent minimally invasive endoscopic therapy POEM (2010 to present).[17] The long-term efficacy data of pneumatic dilation (PD) first emerged in the early 1980s.[18] We discuss

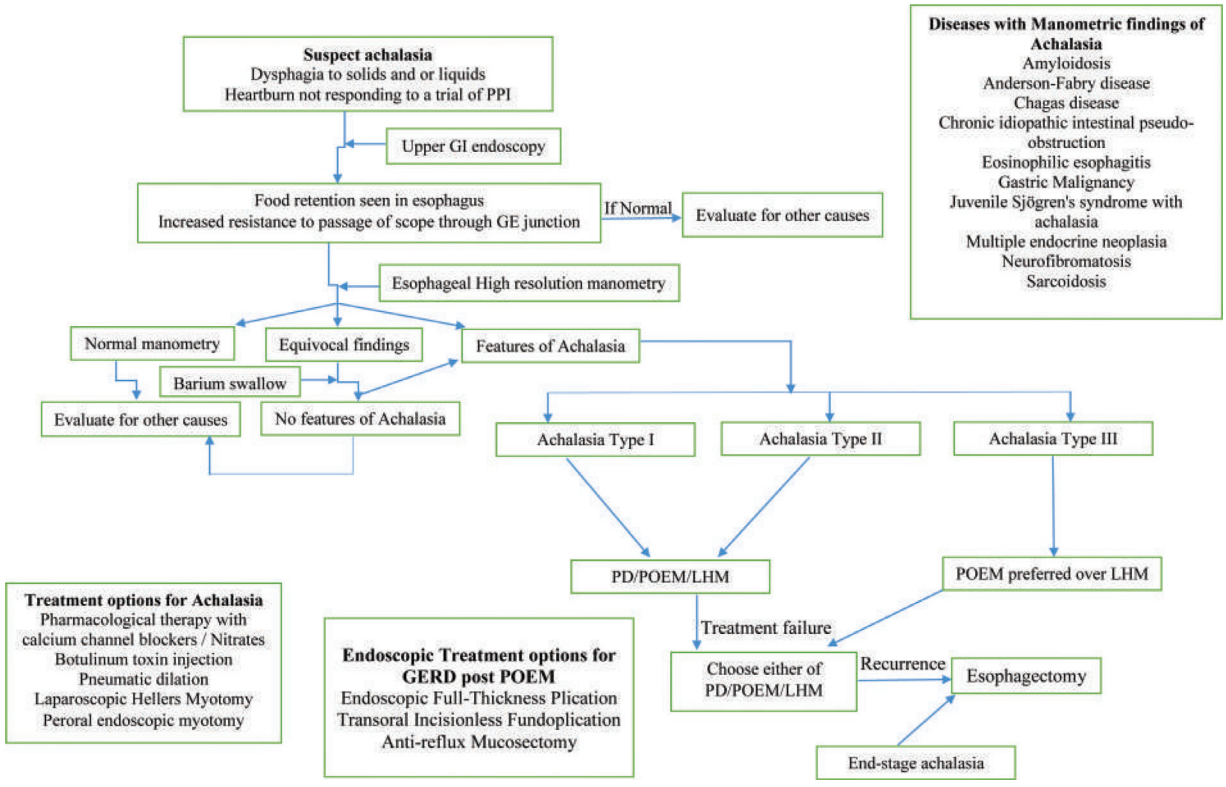

Fig. 1 Achalasia diagnosis and management flowchart.

the outcomes of these procedures and optimizing the available treatment options in these patient populations.

Balloon

The initial response to pneumatic balloon dilation over the years has been found to be 71 to 90%.[19–23] However, the recurrence rate over 5 years has been found to be about 50%.[24] There is a requirement for repeated dilatations in 33% of patients. Prospective studies of PD with few patients (7–29 patients) using Rigiflex balloons have shown success rates of 53 to 93%, but the postprocedural follow-up was less than 2 years.[25,26] Two larger prospective studies of 50 patients with 4 years' follow-up showed a remission rate of 26 to 40%.[27,28] PD in children with achalasia when followed up for 6 years had the overall success rate (up to three sessions) of 87%, with older children more likely to respond to PD.[29] In pregnant patients, PD is associated with a much lower risk of complications and hence should be attempted before other options. The predictors of outcome following PD are postdilation LES characteristics, age, female gender, and achalasia subtype.[19,21] A postdilation decrease in LES pressure to approximately 10 mm Hg is found to be a reasonable goal of PD. Younger age is a poor predictor of response to PD and may require repeat therapy. Females have a more favorable PD treatment response. Type II achalasia has also been associated with a good response to PD.[30] There is a risk of perforation in up to 21%[31] and postoperative chest pain in 15% of patients. Bleeding, esophageal mucosal tears, intramural hematomas, and diverticula at the gastric cardia have also been seen. Currently, more than 25 centers all over India are performing POEM procedure and the trend appears to have changed over the years from balloon dilation toward POEM with the availability of long-term results regarding its safety and efficacy.

Knife

Surgical myotomy (Heller's myotomy) is performed laparoscopically. LES disruption during this surgical procedure can cause reflux of stomach contents into the esophagus. To prevent this, it is combined with an antireflux procedure such as partial fundoplication (Dor or Toupet fundoplication).

Symptom relief is seen in 90 to 97% of patients at 12 to 36 months.[32,33] In one study that included 62 patients who had undergone surgical myotomy and partial fundoplication at a mean follow-up of 19 months, 38% of patients reported some dysphagia.[34] This shows that the effect of surgery wanes off over time. Surgery appears to be less cost-effective when compared with PD mainly due to the recovery period and associated complications. The latter include bleeding, perforation, gastroesophageal reflux disease (GERD), pneumothorax, and infection. The occurrence of GERD is much lower when an antireflux procedure is performed (9 vs. 47%).[35] PD has also been tried in patients who fail to improve following surgical myotomy.

Knife versus Balloon

The efficacy and durability of LHM are superior to a single session of PD. However, the superiority of LHM is less evident when compared with graded PD, as needed by the clinical response. In a retrospective study of 179 patients, the success of Heller's myotomy was comparable with PD after 6 years of follow-up (57 vs. 44%).[36] Success was defined as dysphagia or regurgitation less than three times per week or freedom from alternative treatment. A meta-analysis that compared graded PD with LHM included three randomized trials with 346 patients published between 2007 and 2011.[37] After up to 1 year of follow-up, surgical myotomy was more effective than PD (86 vs. 77%) and was associated with fewer adverse events (0.6 vs. 5%). However, there were no differences in postprocedure LES pressure, rate of GERD, and quality of life.[37]

The largest trial in the meta-analysis included 201 patients who were assigned to either PD or LHM. Patients were followed for a mean of 43 months.[38] In an intention-to-treat analysis, there was no significant difference between the groups with regard to therapeutic success. At a 1-year follow-up, the success rate for PD was 90%, and for LHM it was 93%. After 2 years, the success rates were 86 and 90%, respectively. In addition, after 2 years of follow-up, there was no significant difference between the groups with regard to LES pressure, esophageal emptying, quality of life, or esophageal acid exposure. Subgroup analyses found that patients younger than 40 years were at increased risk of requiring redilation after PD. After 5 years of follow-up, there was no significant difference in success rates between the two groups.[38]

Tunnel

POEM, a natural orifice transluminal endoscopic surgery, is an endoscopic method for performing myotomy of the LES.[17] POEM has shown favorable outcomes in achalasia that often do not respond to conventional therapies, such as type III (spastic) achalasia and markedly dilated, sigmoid esophagus, and in patients who have failed prior therapies. In a Japanese retrospective study of 500 consecutive patients (61 patients followed for >3 years), clinical success was observed in 91% at 1 to 2 years after POEM, which decreased to 88% at 3 years.[39] POEM is safe and associated with a low rate of postoperative adverse events.[40] Although rare, pneumoperitoneum, pneumothorax, mucosal tear, mediastinitis, bleeding, and gastroesophageal reflux have been encountered. All patients should be evaluated for the risk of cardiovascular complications. A preoperative baseline echocardiogram (ECG), 2 dimensional echocardiography (2D-ECHO), and routine laboratory parameters should be ideally checked prior to POEM.

Akintoye et al in 2016 performed a meta-analysis with 36 studies involving 2,373 patients who underwent POEM.[41] Clinical success (Eckardt score ≤ 3) was achieved in 98% of patients after the procedure. The mean Eckardt score improved from 6.9 ± 0.15 preoperatively to 0.77 ± 0.10, 1.0 ± 0.10, and 1.0 ± 0.08 at 1, 6, and 12 months, respectively.

After 8 months of follow-up, the rates of symptomatic GERD, esophagitis, and abnormal acid exposure were 8.5, 13, and 47%, respectively.[41]

Tunnel or Knife?

In a randomized trial of 221 patients with idiopathic achalasia, POEM (112 patients) and LHM with Dor fundoplication (109 patients) were equally successful in controlling symptoms at 2 years (83 vs. 82%).[42] Compared with LHM, POEM was associated with a lower rate of severe adverse events (2.7 vs. 7.3%) but a higher rate of reflux symptoms (57 vs. 20% at 3 months; 44 vs. 29% at 2 years). POEM was noninferior to LHM plus Dor fundoplication in controlling symptoms of achalasia at 2 years. GERD was more common among patients who underwent POEM than among those who underwent LHM.[42]

Marano et al performed a systematic review and meta-analysis of randomized studies of LHM versus POEM for achalasia with 486 patients (196 in POEM and 290 in LHM).[43] There were no differences between POEM and LHM in reduction in Eckardt score ($p = 0.217$), operative time ($p = 0.36$), postoperative pain scores ($p = 0.268$), analgesic requirements ($p = 0.445$), and complications ($p = 0.796$). Length of hospital stay was significantly lower for POEM ($p = 0.049$). There was a trend toward a significant reduction in symptomatic GERD in favor of LHM compared with the POEM group ($p = 0.017$).[43]

In a meta-analysis of over 7,000 patients in over 70 cohort studies, POEM was more effective than LHM in relieving dysphagia.[44] Predicted probabilities for improvement in dysphagia at 12 months were 93.5% for POEM and 91% for LHM, and at 24 months were 92.7% for POEM and 90% for LHM, both statistically significant. However, POEM was associated with higher incidences of pathologic reflux by multiple measurements (symptoms, erosive esophagitis, and abnormal pH studies) and a slightly longer hospital stay (by 1 day) than LHM. Studies on LHM had significantly longer follow-up than POEM (41.5 vs. 16.2 months); longer-term data on POEM are required before the durability of the two procedures can be directly compared. POEM and LHM are equally effective in improving symptoms, but POEM results in more reflux, and LHM has more adverse events.[44]

Tunnel versus Balloon

In a trial of 133 treatment-naive patients with achalasia, POEM resulted in a higher rate of treatment success than PD at 2 years (92 vs. 54%, $p < 0.001$).[45] No procedure-related adverse events occurred after POEM, while one perforation occurred with PD; reflux esophagitis developed more frequently after POEM than after PD (41 vs. 7%, $p = 0.002$). PD may play a role in treating recurrent dysphagia after POEM or LHM.[45]

GERD and POEM

The commonest late adverse event seen with POEM is GERD. Based on endoscopic-proven erosive esophagitis and/or abnormal pH study, the prevalence of GERD after POEM varies between 20 and 57%.[46] A 2018 meta-analysis found the prevalence of GERD to be higher after POEM than after LHM with fundoplication, in terms of symptoms (19% for POEM vs. 8.8% for LHM), abnormal pH study (39% for POEM vs. 17% for LHM), and esophagitis (28% for POEM vs. 7.6% for LHM).[47] GERD symptoms and true GERD post POEM are different and can be due to stasis or fermentation.[48] The sling fibers of the stomach are spared during POEM with an anterior approach. This reduces the occurrence of postprocedure GERD. With a posterior approach, there is risk of cutting sling fibers, thereby increasing the risk of GERD.[49] To counter the future risk of developing esophageal cancer, antireflux surgery is imperative in post-POEM patients. The available various endoscopic antireflux surgeries include POEM with fundoplication, endoscopic full-thickness plication after POEM, transoral incisionless fundoplication after POEM, and antireflux mucosectomy post POEM.

Endoscopic fundoplication was added to the standard POEM (POEM + F) procedure by Inoue et al in 21 patients.[50] POEM + F was technically feasible in all cases and created a visually recognizable fundoplication. However, the results of POEM + F from another center were not convincing.[51] Twenty patients underwent the POEM + F procedure, with 17/20 (85%) technical success. At 1-month follow-up endoscopy, 5/17 (29.4%) patients had loosening of the fundal wrap and 3/17 (17.6%) patients had ulceration in the fundus and gastroesophageal junction due to underlying hemoclips. At 3 months, loosening of the fundal wrap was seen in 7/17 (41.2%) patients. A 24-hour pH-metry revealed abnormal esophageal acid exposure in 7/17 (41.2%) patients, while it was normal in those patients in whom the fundal wrap was maintained.[49] POEM + F is technically feasible with reasonable short-term success. The authors concluded that the durability, early success, and safety of POEM + F need reassessment in long-term studies. Endoscopic full-thickness plication after POEM can be promising and deserves further evaluation in controlled studies.

Summary

Achalasia cardia is the most commonly studied esophageal motility disorder. The treatment modalities have shown good to excellent palliation of symptoms in up to 90% of patients. For all the invasive therapies, results are best for patients with type II achalasia. The ideal treatment of achalasia should be universally applicable, easy to perform, reproducible, minimally invasive, and cost effective, with good short-term effects, sustained long-term effects, and minimal adverse events. All patients will require long-term follow-up and frequently need repeated or alternative treatments. Despite the absence of definite therapy from the currently available treatment options, POEM seems to be emerging as a front-line therapy for achalasia.

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Conflict of Interest
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