

# Considering the first randomized trial of peroral endoscopic myotomy versus surgical myotomy for achalasia

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Achalasia is a rare disorder of primary esophageal motility, characterized by defective relaxation of the lower esophageal sphincter (LES) along with impairment of esophageal peristalsis. Unfortunately at this time, the disease remains incurable. Current management pursues instead the palliation of symptoms through relieving the functional obstruction of the LES by means of tearing or cutting the circular muscle layer (1). The newest arrival to the therapeutic armamentarium, peroral endoscopic myotomy (POEM), has been successfully deployed for nearly 10 years and has been acknowledged to achieve at least similar levels of efficacy and safety to those of pneumatic dilation (PD) and surgical myotomy. However, to date, only retrospective studies, systematic reviews, and meta-analyses comparing endoscopic versus surgical myotomy have been published, possibly due to the intersection between the low prevalence of the disease and the rarity of POEM-capable centers.

Given the above, we read with great enthusiasm the study by Weneke et al. recently published in the *New England Journal of Medicine*, which is a multicenter, open-label, prospective, randomized controlled noninferiority trial comparing POEM and laparoscopic Heller's myotomy plus Dor's fundoplication (LHMD) (2). The primary outcome of the study was posttreatment clinical efficacy at 24 months. Secondary outcomes included procedural characteristics, morbidity, tolerability, side-effect profiles, and complication rates. The study included 241 symptomatic primary achalasia patients diagnosed with high-resolution manometry, regardless of Chicago subtype. Notable exclusion criteria were having Chagas disease or a history, upper gastrointestinal surgery, Barrett's esophagus, esophageal varices and active esophageal disease, strictures, large hiatal hernia or excessive dilatation of esophagus (>7 cm). Notably, prior endoscopic treatment for achalasia was not an exclusion criterion.

Patients were one-to-one randomized to undergo either POEM or LHMD among the eight participating centers. Procedures were performed by expert endoscopists and surgeons according to accepted standards.

Twenty of the 241 patients were excluded and the remaining 221 were assigned into POEM (n= 112) or LHMD (n=109 patients) groups, constituting the modified intention-to-treat (mITT) population. The final per-protocol population (PP) consisted of 211 patients (n=108 POEM cases and 103 LHM cases) after 10 more patients' exclusion during the study as per the same exclusion criteria. The two treatment groups did not differ in consideration of demographic characteristics, Chicago subtype, or pretreatment symptom score. The primary endpoint, clinical success, was defined as per the Eckardt score, which is a clinical grading of four major symptoms of achalasia, i.e., regurgitation, weight loss, chest pain, dysphagia, awarded up to four points each for a possible total of 12 points. As clinical success, a score of less than or equal to three points without the need for further treatment was used as per previous literature (3). Ultimately, the clinical success rates per the mITT protocol at 24 months were 83.0% in the POEM group and 81.7% in the LHMD group, revealing a nonstatistically significant difference. Further, the clinical efficacy rates for subtype 3 patients were 83% in the POEM group and 78% in the LHMD group, while other subgroup analyses for clinical efficacy did not demonstrate any notable interaction between demographics, previous treatment, or achalasia subtype.

As an objective measure for post-procedure esophageal function, integrated relaxation LES pressure was calculated and values were found not to be different between the groups. For clinical measures, a validated questionnaire of the Gastrointestinal Quality of Life Index was used and the results in this regard were also similar for

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the POEM and LHMD groups. POEM procedure time was generally shorter by 13.8 minutes (CI: 6.26-21.36), while time to discharge outcomes were similar between the groups. Postoperative symptom recurrence between 6-24 months was observed in 12 patients in the LHMD group and 16 patients in the POEM group. Among those, all three patients in the LHMD group and two patients in POEM group undergone PD, and two patients in LHMD undergone LHMD as reintervention. On the subject of side effects, no mortalities were observed in either group, while serious adverse events that required reintervention or which prolonged the hospitalization period were observed in eight patients in the LHMD group and three patients in the POEM group. The postprocedure gastroesophageal reflux was evaluated by means of assessing symptoms, conducting endoscopy, and pH monitoring. Along these lines, pH monitoring at 24 months demonstrated a lower reflux rate in the LHMD group than in the POEM group (33% vs. 44%). Similarly, the LHMD group had a proportionally lower rate of esophagitis at 24 months (29% vs. 44%).

Among the three therapeutic options available for achalasia, PD stands out as being technically simple and cost-effective and was thus considered as one of the potential first-line therapies in a recent consensus (4). However, major concerns related to PD remain in existence: first, its efficacy is limited in a subgroup of patients including those with Chicago subtype 3, while, second, the efficacy declines over time, requiring repeat procedures or additional treatments (5). These factors warrant the introduction of surgical and endoscopic myotomies as preeminent alternatives for PD, being that they are one-time interventions with comparable efficacy and safety profiles that achieve a longer duration of remission (6). For surgical myotomy, LHM plus fundoplication is currently the widely accepted technique. On the other hand, POEM is a newer technique endorsed for being less invasive than surgery and more successful in type 3 patients. Studies to date comparing the two myotomy techniques reported near equal or better efficacy rates for POEM but higher rates of gastroesophageal reflux and its related complications. A recent meta-analysis covering 53 studies and 5,834 patients revealed a 91.0% efficacy rate for POEM versus that of 90.0% for LHM at 24 months ( $p=0.01$ ). The development of gastroesophageal reflux disease (GERD) was more frequent in relation to POEM relative to LHM (OR: 1.69, 95% CI: 1.33-2.14). However, studies published to date lack randomization and long-term follow-up data (7).

This study is notable as the first randomized evaluation of two preeminent therapies for achalasia. There have remained two questions when considering our previous knowledge up to this point: whether the efficacy and whether the safety of POEM versus LHM would still be valid after a randomized comparison. This study answers the two questions: first, POEM's clinical efficacy rate of 82.4% was noninferior to the 80.6% efficacy rate reported for LHMD for a medium-term follow-up period of two years. This noninferiority was also endorsed by similar posttreatment manometric findings. Second, adverse event rates were similar between the two groups with the exception of GERD, which, in the POEM group, occurred significantly more frequently. Fundoplication has a definite role in this outcome as it has been combined with LHM to overcome the potential for posttreatment GERD. Current POEM protocols may benefit from the involvement of an analogous method to prevent reflux. In this manner, a same-session transoral incisionless fundoplication procedure was combined with POEM in a case of type 2 achalasia, yielding very good results (8). This approach is promising and circumvents the reflux problem inherent with POEM.

The last 20 years have witnessed substantial progress in the management of achalasia with high-resolution manometry, improved surgical techniques, and POEM. However, there remains a long road ahead where we must elucidate the etiology, look for curative treatments, and optimize the current therapies.

## REFERENCES

1. Boeckxstaens GE, Zaninotto G, Richter JE. Achalasia. *Lancet* 2014; 383: 83-93. [\[CrossRef\]](#)
2. Werner YB, Hakanson B, Martinek J, et al. Endoscopic or Surgical Myotomy in Patients with Idiopathic Achalasia. *N Engl J Med* 2019; 381: 2219-29. [\[CrossRef\]](#)
3. Taft TH, Carlson DA, Triggs J, et al. Evaluating the reliability and construct validity of the Eckardt symptom score as a measure of achalasia severity. *Neurogastroenterol Motil* 2018; 30: e13287. [\[CrossRef\]](#)
4. Zaninotto G, Bennett C, Boeckxstaens G, et al. The 2018 ISDE achalasia guidelines. *Dis Esophagus* 2018; 31: doi: 10.1093/dote/doy071. [\[CrossRef\]](#)
5. Elliott TR, Wu PI, Fuentealba S, Szczesniak M, de Carle DJ, Cook JJ. Long-term outcome following pneumatic dilatation as initial therapy for idiopathic achalasia: an 18-year single-centre experience. *Aliment Pharmacol Ther* 2013; 37: 1210-9. [\[CrossRef\]](#)
6. Bonifácio P, de Moura DTH, Bernardo WM, et al. Pneumatic dilatation versus laparoscopic Heller's myotomy in the treatment of achalasia: systematic review and meta-analysis based on randomized controlled trials. *Dis Esophagus* 2019; 32: doi: 10.1093/dote/doy105. [\[CrossRef\]](#)

7. F. Schlottmann DJ, Luckett J, Fine NJ, Shaheen, M. G. Patti, Laparoscopic Heller Myotomy Versus Peroral Endoscopic Myotomy (POEM) for Achalasia: A Systematic Review and Meta-analysis. *Ann Surg* 2018; 267: 451-60. [\[CrossRef\]](#)

8. Brewer Gutierrez OI, Benias PC, Khashab MA. Same-Session Per-Oral Endoscopic Myotomy Followed by Transoral Incisionless Fundoplication in Achalasia: Are We There Yet? *Am J Gastroenterol* 2020; 115: 162. [\[CrossRef\]](#)