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EDITORIAL

Post-POEM esophageal reflux in a Mexican population ☆



Reflujo esofágico post-POEM en población mexicana

The first case of treatment of achalasia took place in 1674, when the renowned anatomist, Sir Thomas Willis (the Willis circle) described a patient whose esophagus was "dilated" due to the presence of a whale bone.¹ Although 345 years have passed since that original report, management of achalasia continues to be palliative, focused on opening the dysfunctional lower esophageal sphincter, thus improving the distal esophageal obstruction and enabling its emptying by the force of gravity. Different methods have emerged for that purpose, including calcium channel blockers and nitrates, the intra-esophageal injection of acetylcholine blocking agents (botulinum toxin), pneumatic dilation, and surgical ablation of the lower esophageal sphincter through Heller myotomy. Originally introduced by Ernest Heller in 1913,² the intervention has evolved notably, from its trans-abdominal and transthoracic approaches to the minimally invasive techniques through thoracoscopy, laparoscopy, and more recently, robotic surgery.

In the past decade, we have witnessed another novel technologic advance in the management of achalasia: peroral endoscopic myotomy (POEM). POEM is a myotomy with no external incision that has the particularity of not altering the diaphragmatic hiatus or the phreno-esophageal membrane.³ First described in 2008 in Japan by Inoue et al.,⁴ it at least partially owes its debut to the culmination of research on natural orifice transluminal endoscopic surgery (NOTES) in an experimental animal model at the Johns Hopkins Medical Center,⁵ to studies on the creation of the "third space" conducted at the Mayo Clinic,⁶ as well as to the creativity and talent of Dr. Inoue, trained as a thoracic and laparoscopic surgeon.³

Since its appearance and up to the present, there have been several thousand case reports in the literature on the experience with POEM,⁷ and its use has been extended to include virtually the entire world, and more recently, Latin

American countries.⁸ POEM has been shown to be safe and reproducible, with a reported efficacy of close to 91% at 2 years of observation,⁹ and 87% at a 5-year follow-up.¹⁰ Mean procedure duration is 99.6 to 101 ± 29 min^{7,11} and 95% of the patients are discharged at 24 h.¹¹ Nevertheless, at least one recent study suggests that the majority of patients can be released the same day as the intervention.¹² Operative mortality is <0.01% and the risk for perforation and bleeding is 1.4%.¹³ The most frequent complication is capno-pneumoperitoneum or capno-pneumothorax, which resolves spontaneously in most patients.¹⁴ The procedure has been reported as successful in patients of all ages and it has recently been shown to be exceptionally beneficial (89-91%) in patients with type III achalasia¹⁵ and in other spastic esophageal disorders, such as "jackhammer" esophagus and distal esophageal spasm.¹⁶ Those virtues have made treatment through POEM superior to pneumatic dilation, whose efficacy is around 60-88%,¹⁷ and comparable to surgical myotomy, which is perceived as more invasive. Despite its inherent advantages, long-term effectiveness and durability (> 10 years), as well as its possible complications (peptic stricture, Barrett's esophagus, dysplasia) have not been sufficiently characterized.

In the study published in the *Revista Mexicana de Gastroenterología*, Hernández-Mondragón et al.¹⁸ reported on the Mexican experience with POEM and specified the incidence of the most common post-POEM complication: gastroesophageal reflux disease (GERD). The authors described a group of patients with achalasia treated with POEM that were longitudinally observed: n=68 (12 months); n=58 (24 months), n=47 (36 months), n=39 (48 months), and n=25 (60 months) to determine the postoperative incidence of GERD. The selected population had a mean age of 47.8 ± 14.3 years and 57.3% were women. They included patients with type I achalasia (n=10) (14.7%), type II (n=37) (54.4%), and type III (n=6) (8.9%). Fifteen patients (22%) had undergone previous treatment for achalasia (14 laparoscopic Heller myotomies and 1 redo-POEM). The presence of GERD was evaluated through 3 modalities: a validated questionnaire, pH monitoring, and endoscopy (based on the

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Los Angeles classification). The pH study, endoscopy, and questionnaire were positive, post-POEM, in 73, 28, and 18% patients (at 3 months); in 48, 35, and 13% (at 6 months); and in 55, 30, and 15% (at 12 months). Once treatment with proton pump inhibitors was begun, those figures decreased to 3, 1, and 4% (at 60 months), respectively. The most frequent complication was pneumoperitoneum in $n = 15/68$ (22%) patients, requiring needle decompression in $n = 5$ (33%) patients. No relation between the efficacy of POEM and the presence or intensity of GERD, or complications secondary to its presence, was observed.

The authors should be congratulated for their excellent work and effort that brought together the experience of a national referral center (the Department of Digestive Endoscopy of the *Hospital de Especialidades Centro Médico Nacional Siglo XXI*) with POEM. The study is unique in that it objectively shows the efficacy of the procedure (Eckardt score and high-resolution manometry), as well as the incidence of GERD and the possible post-POEM complications in a sample ($n = 68$) of the Mexican population. In addition, the authors included 3 instruments for evaluating the presence of GERD (pH-monitoring, a validated questionnaire, and endoscopy). The longitudinal follow-up, at a minimum of 12 months, and then in a smaller sample ($n = 25$) up to 60 months, provided valuable information.

Among the outstanding observations was the efficacy of the procedure, which was clinically maintained in 24/25 patients (Eckardt score), as well as manometrically maintained (residual lower esophageal sphincter relaxation pressure or integrated relaxation pressure [IRP] of 2 mmHg, min-max 0-3) for 5 years. The incidence of post-POEM GERD, defined by the "gold standard" of pH-monitoring was high at the short and medium terms (73% at 3 months, 48% at 6 months, and 55% at 12 months) and up to 30% of the patients developed some grade of esophagitis (the majority, grade A, 20%). The multivariate analysis did not demonstrate any association with GERD, according to the different factors included: clinical success, manometric success, type of myotomy (partial vs. total), approach (anterior vs. posterior), or weight gain. No patient presented with any other type of major complication secondary to GERD (Barrett's esophagus, stricture, or esophageal adenocarcinoma) during the 60 months of post-POEM follow-up.

As was to be expected, the destruction of the fibers of the dysfunctional esophago-gastric barrier through POEM, with no coadjuvant protection (fundoplication), accelerated the appearance of iatrogenic reflux. Hernández-Mondragón et al. emphasize the frequency of that post-POEM complication in their study. Their figures for GERD are comparable to those in the international literature, in which the values for post-POEM GERD vary from 9 to 58%.^{14,19-21} That variability is due to the differences in the methods used for reporting GERD (symptoms, endoscopy, or pH study), among studies. The study by Hernández-Mondragón et al.¹⁸ leads the way in providing information on a national population, utilizing 3 methods of evaluation and clearly demonstrating the superiority of pH-monitoring in the detection of GERD. Using that diagnostic method, the incidence of GERD was obviously higher, at 48 to 73% of the population, manifested at the different follow-up times.

For both the clinical gastroenterologist and the surgeon, those findings are important because they emphasize

several practical concepts: 1) the recognized lack of a relation between GERD symptoms, endoscopy, and pH study; 2) the high incidence of post-POEM GERD; 3) the importance of diagnosing and treating post-POEM GERD through the most objective method (pH-monitoring); and 4) the need to identify patients with GERD and treat them promptly with acid-inhibiting agents.

The abovementioned is of particular relevance, given the recent studies that have described cases of post-POEM Barrett's esophagus. Teitelbaum et al.²² reported the appearance of Barrett's esophagus (with no dysplasia) in one of 15 patients followed for 5 years, post-POEM. An additional article reported the development of neo-epithelium consistent with Barrett's esophagus in 2 cases, as well as one patient with a 2 cm peptic stricture, in a post-POEM follow-up at 24 months.²³ Strikingly, the appearance of Barrett's esophagus has been observed not only post-POEM, but also after surgical myotomy.^{24,25} The development of Barrett's esophagus (and peptic stricture) in that small, but significant, case series begs the question of what the real risk of post-POEM Barrett's esophagus is. At any rate, those observations suggest that the post-POEM patient requires longitudinal following, objective identification of reflux (pH study), and long-term acid suppression in patients with abnormal acid exposure. Likewise, those findings illustrate the importance of the integrity of the esophageal gastric junction as a barrier of protection and defense in the development of possible complications of GERD, such as Barrett's esophagus.

Future long-term studies on POEM (> 10 years) are needed to determine the real incidence of Barrett's esophagus in the population with *de novo* reflux and establish whether it is a reason for concern or represents isolated cases. Likewise, the biologic behavior of the neo-epithelium in the "environment" of the aperistaltic esophagus has not been determined. For example, compared with patients that have undergone Heller myotomy, acid exposure measured through pH-monitoring is much higher in post-POEM patients than in those that have undergone surgical myotomy (total acid exposure: 48.4 vs. 13.6%; $p < 0.001$, abnormal DeMeester score 54.8 vs. 17.4%; $p = 0.005$, respectively).²⁶ That "excess" of acid in an "aperistaltic" environment of achalasia could potentiate the risk for cellular degeneration and induce the dysplastic epithelium of Barrett's esophagus.

In addition, the study by Inoue et al., in which POEM was successfully combined with simultaneous endoscopic fundoplication in a case series of 21 "concept test" patients, is of considerable interest.²⁷ Those authors suggest the possibility of integrating a valuable measure for mitigating POEM-induced reflux. Their observations need to be confirmed by long-term studies with a larger number of patients, but it is a new technique that promises to be of great usefulness for preventing post-POEM GERD.

In summary, there have been important advances in achalasia management over the past decade, following the introduction of POEM. The work of Hernández-Mondragón et al. illustrates the frequency and importance of the most frequent post-POEM complication: GERD. Their findings provide valuable and practical information for both the gastroenterologist and the surgeon and suggest the need for the opportune and objective diagnosis (pH study) of those patients, treating them appropriately and

following them longitudinally. Long-term studies (>10 years) will enable us to better understand the durability and efficacy of POEM, its impact on the management of achalasia, its potential complications, and the real incidence of Barrett's esophagus. Promising information awaits us with the recent introduction of fundoplication in simultaneous coordination with POEM. Further studies will determine whether that novel intervention should be systematically incorporated for the prevention of the frequent and important post-POEM complication that is GERD. Only additional prospective research can help discern whether, through POEM, we have changed the course of achalasia to that of GERD and its complications.

Conflict of interest

The author declares that there is no conflict of interest or financial relation.

References

- Willis T. *Pharmaceutic rationalis: sive diatriba de medicamento- rum; operatimibus in humano corpore*. London: Hagae-Comitis; 1674.
- Heller E. Extramuköse cardinplastik beim chronischen cardiospasmus mit dilation des oesophagus. *Mitt Grenzgeb Med Chir*. 1914;27:141–5.
- Kroch DA, Grimm IS. POEM for Achalasia. *Am Surg*. 2018;84:489–95.
- Inoue H, Minami H, Kobayashi Y, et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia. *Endoscopy*. 2010;42:265–71.
- Pasricha PJ, Hawari R, Ahmed I, et al. Sumucosal endoscopic esophageal myotomy: a novel experimental approach for the treatment of achalasia. *Endoscopy*. 2007;39:761–4.
- Sumiyama K, Gostout CJ, Rajan E, et al. Transesophageal mediastinoscopy by submucosal endoscopy with mucosal flap safety valve technique. *Gastrointest Endosc*. 2007;65:679–83.
- Shiwaku H, Inoue H, Onimaru M, et al. Multicenter collaborative retrospective evaluation of peroral endoscopic myotomy for esophageal achalasia: analysis of data from more than 1300 patients at eight facilities in Japan. *Surg Endosc*. 2019 <https://doi.org/10.1007/s00464-019-06833-8>
- Kahaleh M, Xu MM, Zamarripa F, et al. POEM in Latin America: The rise of a new standard. *J Clin Gastroenterol*. 2019;53:e352–5, <http://dx.doi.org/10.1097/MCG.0000000000001161>.
- Stavropoulos SN, Desilets DJ, Fuchs KH, et al. Per-oral endoscopic myotomy white paper summary. *Gastrointest Endosc*. 2014;80:1–15.
- Li QL, Wu QN, Zhang XC, et al. Outcomes of per-oral endoscopic myotomy for treatment of esophageal achalasia with a median follow-up of 49 months. *Gastrointest Endosc*. 2018;87:1405–12.
- Hungness ES1, Sternbach JM, Teitelbaum EN, et al. Per-oral endoscopic myotomy (POEM) after the learning curve: durable long-term results with a low complication rate. *Ann Surg*. 2016;264:508–17.
- Benias PC, Korrapati P, Raphael KL, et al. Safety and feasibility of performing peroral endoscopic myotomy as an outpatient procedure with same-day discharge. *Gastrointest Endosc*. 2019 <https://doi.org/10.1016/j.gie.2019.04.247>
- Zhang XC, Li QL, Xu MD, et al. Major perioperative adverse events of peroral endoscopic myotomy: a systematic 5-year analysis. *Endoscopy*. 2016;48:967–78.
- Zaninotto G, Leusink A, Markar SR. Management of achalasia in 2019. *Curr Opin Gastroenterol*. 2019 <https://doi.org/10.1097/MOG>
- Kahrilas PJ, Pandolfino JE. Treatments for achalasia in 2017: how to choose among them. *Curr Opin Gastroenterol*. 2017;33:270–6.
- Chandan S, Mohan BP, Chandan OC, et al. Clinical efficacy of per-oral endoscopic myotomy (POEM) for spastic esophageal disorders: a systematic review and meta-analysis. *Surg Endosc*. 2019 <https://doi.org/10.1007/s00464-019-06819-6>
- Zheng Z, Zhao C, Su S, et al. Peroral endoscopic myotomy versus pneumatic dilation - result from a retrospective study with 1-year follow-up. *Z Gastroenterol*. 2019;57:304–11.
- Hernández-Mondragón OV, Solórzano-Pineda OM, González-Martínez M, et al. Gastroesophageal reflux disease after peroral endoscopic myotomy: Short-term, medium-term, and long-term results. *Rev Gastroenterol Mex*. 2019 <https://doi.org/10.1016/j.rgmx.2019.04.001>
- Song S, Itawi EA, Saber AA. Natural orifice transluminal endoscopic surgery (NOTES). *J Investig Surg*. 2009;22:214–7.
- Kumbhari V, Familiari P, Bjerregaard NC, et al. Gastroesophageal reflux after peroral endoscopic myotomy: a multicenter case control study. *Endoscopy*. 2017;49:634–42.
- Rösch T, Repici A, Boeckxstaens G. Will reflux kill POEM? *Endoscopy*. 2017;49:625–8.
- Teitelbaum EN, Dunst CM, Reavis KM, et al. Clinical outcomes five years after POEM for treatment of primary esophageal motility disorders. *Surg Endosc*. 2018;32:421–7.
- Werner YB, Costamagna G, Swanström LL, et al. Clinical response to peroral endoscopic myotomy in patients with idiopathic achalasia at a minimum follow-up of 2 years. *Gut*. 2016;65:899–906.
- Gossage JA, Devitt PG, Watson DI, et al. Surveillance endoscopy at five or more years after cardiomyotomy for achalasia. *Ann Surg*. 2014;259:464–8.
- Csendes A, Braghetto I, Burdiles P, et al. Very late results of esophagomyotomy for patients with achalasia: Clinical, endoscopic, histologic, manometric, and acid reflux studies in 67 patients for a mean follow-up of 190 months. *Ann Surg*. 2006;243:196–203.
- Sanaka MR, Thota PN, Parikh MP, et al. Peroral endoscopic myotomy leads to higher rates of abnormal esophageal acid exposure than laparoscopic Heller myotomy in achalasia. *Surg Endosc*. 2018 <https://doi.org/10.1007/s00464-018-6522-4>
- Inoue H, Ueno A, Shimamura Y, et al. Peroral endoscopic myotomy and fundoplication: a novel NOTES procedure. *Endoscopy*. 2019;51(161) <https://doi.org/10.1055/a-0820-2731>

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