CIRUGÍA ESPAÑOLA

www.elsevier.es/cirugia

Review Article

New Trends and Concepts in Diagnosis and Treatment of Achalasia☆

Marco E. Allaix, Marco G. Patti *

Department of Surgery, Center for Esophageal Diseases, University of Chicago Pritzker School of Medicine, Chicago, IL, United States

ARTICLE INFO

Article history:
Received 15 January 2013
Accepted 16 January 2013
Available online 26 November 2013

Keywords:
Achalasia
Botulinum toxin injection
Endoscopic dilatation
Laparoscopic Heller myotomy
Peroral endoscopic myotomy

ABSTRACT

The last two decades have witnessed a revolution in the treatment of esophageal achalasia. Nowadays, laparoscopic Heller myotomy with partial fundoplication is considered in most centers; the primary treatment modality, while endoscopic treatment, i.e. pneumatic dilatation, is mainly reserved for the management of patients unfit for surgery or in case of surgical failure. Recently, a new approach to achalasia has been proposed: the peroral endoscopic myotomy (POEM), which combines the advantages of endoscopy and surgery.

This article reviews the evolution of the diagnosis and treatment of esophageal achalasia during the last 20 years.

Nuevas tendencias y conceptos en el diagnóstico y tratamiento de la acalasia

Palabras clave:
Acalasia
Inyección de toxina botulínica
Dilatación endoscópica
Miotomía laparoscópica de Heller
Miotomía endoscópica peroral

RESUMEN

En las 2 últimas décadas, hemos sido testigos de una revolución en el tratamiento de la acalasia esofágica. Actualmente, la miotomía laparoscópica de Heller con funduplicatura parcial se considera, en la mayoría de los centros, el tratamiento primario, mientras que el tratamiento endoscópico, es decir la dilatación neumática, se reserva principalmente para el tratamiento de pacientes que no son aptos para la cirugía o para cuando esta fracasa. Recientemente, se ha propuesto un nuevo enfoque para la acalasia: la miotomía endoscópica peroral (POEM), que combina las ventajas de la endoscopia con las de la cirugía.

Este artículo revisa la evolución del diagnóstico y del tratamiento de la acalasia esofágica en los últimos 20 años.

☆ Please cite this article as: Allaix ME, Patti MG. Nuevas tendencias y conceptos en el diagnóstico y tratamiento de la acalasia. Cir Esp. 2013;91:352–357.

* *Corresponding author.*
E-mail address: mpatti@surgery.bsd.uchicago.edu (M.G. Patti).

Introduction

Esophageal achalasia is a primary motility disorder characterized by changes in esophageal manometry, including the absence of esophageal peristalsis and altered relaxation of the lower esophageal sphincter (LES) in response to swallowing. LES pressure is elevated in about 50% of patients.[1] The emptying of food from the esophagus to the stomach is consequently impaired and leads to various symptoms such as dysphagia, regurgitation, heartburn, and chest pain. Since the pathogenesis of achalasia is unknown, the goal of treatment is to improve esophageal emptying and patient symptoms by reducing the functional obstruction at the gastroesophageal junction. This can be achieved by either endoscopic therapy or surgery. Endoscopic treatment modalities include: (1) endoscopic injection of botulinum toxin; (2) pneumatic dilatation; (3) Heller myotomy; and, more recently, (4) peroral endoscopic myotomy (POEM).

The aim of this article is to review the latest trends and concepts in the diagnosis and treatment of esophageal achalasia.

Diagnosis

Esophageal manometry is the gold standard for the diagnosis of achalasia. Classical criteria for the diagnosis of achalasia include: impaired LES relaxation and the absence of peristalsis. Nevertheless, considerable heterogeneity has been documented[2–4] with regard to peristaltic abnormalities and esophageal pressure dynamics in patients with esophageal achalasia.

Pandolfino et al.[5] have recently reported 3 manometric patterns of esophageal body contractility in achalasia that are quite distinct: (1) with minimum pressurization; (2) with esophageal compression, either located in the distal esophagus or in the entire length of the esophagus; and (3) compression attributable to spastic contractions. These authors found that patients with type II are much more likely to respond to treatment than type I or III. In a logistic regression analysis, type II was a predictor for positive response to treatment, while type III was a predictor for negative response to treatment.[6]

In conclusion, although the 3 subtypes show deteriorated LES relaxation and absence of peristalsis, they are distinct pathophysiological conditions and, therefore, may provide a possible explanation for the variability observed in the response to treatment.

In 2013, the use of high-resolution manometry (HRM) is widespread and has replaced conventional manometry in most hospitals. However, further studies with long-term follow-up are needed to define the clinical utility of this new classification in the diagnosis and treatment of patients with achalasia.

Treatment

Endoscopic Botulinum Toxin Injection

The purpose of endoscopic botulinum toxin injection is to reduce the pressure of the LES by suppressing the release of acetylcholine in the presynaptic cholinergic nerve endings.

Although this treatment is safe and provides immediate relief or improvement of symptoms in 80%–85% of patients, the effect gradually decreases over time, and after 12 months[7] only 30%–40% of patients are asymptomatic. Most need to repeat the botulinum toxin injections, and long-lasting clinical benefits are limited. In addition, there is often transmural inflammation and fibrosis in the gastroesophageal junction, which makes Heller myotomy difficult and the outcome becomes less predictable.[8,9]

Compared to pneumatic dilatation, botulinum toxin injection is associated with a higher rate of recurrence of symptoms within 12 months.[10] Similarly, this type of treatment is less effective than laparoscopic Heller myotomy after 2 years of follow-up.[11]

In conclusion, treatment with botulinum toxin injection should be limited to patients who are not candidates for more effective therapies, such as pneumatic dilatation and laparoscopic Heller myotomy (LHM).

Minimally Invasive Surgery

In the last two decades, the widespread acceptance of minimally invasive surgery has led to a gradual change in the treatment algorithm of achalasia.

In 1991, the first minimally invasive esophageal myotomy was performed in the United States by left thoracotomy.[12] Despite the obvious improvements in the results obtained with this technique in terms of increased postoperative comfort, shorter hospital stay, faster return to daily activities and relief of dysphagia compared to open surgery, laparoscopy became the technique of choice for most hospitals.[13,14] The technical reasons supporting this change are better exposure of the gastroesophageal junction and the ability to perform fundoplication, which reduces the risk of postoperative gastroesophageal reflux, occurring in approximately 60% of patients after thoracoscopy.[15]

Consequently, although LHM is considered the gold standard for the treatment of achalasia in most centers, endoscopic dilation is being increasingly used when Heller myotomy fails.[16]

LHM entails controlled cutting of the longitudinal and circular muscle fibers (myotomy) of the lower esophagus (6 cm) and proximal gastric wall (2.0–2.5 cm), followed by partial fundoplication.

In order to sufficiently expose the esophagus for a proper myotomy, both pillars of the diaphragm and the mediastinal esophagus are dissected, releasing the front and sides. During this stage of the process, the anterior and posterior vagus nerves are identified and preserved. In patients with sigmoid esophagus, the dissection is expanded proximally in the posterior mediastinum and behind the esophagus to straighten the esophageal axis and reduce the risk of food stasis after myotomy.[17] Afterwards, the short gastric vessels are divided. The fat is then removed to provide full exposure of the gastroesophageal junction. Myotomy is performed with hook electrocautery in the 11 o'clock position. After reaching the submucosal plane at a point about 3 cm above the gastroesophageal junction, the myotomy is extended upwards about

6 cm and 2.0–2.5 cm toward the gastric curve.[18,19] Patients previously treated with an intrasphincteric injection of botulinum toxin may present fibrosis at the gastroesophageal junction, which is associated with the loss of normal anatomic planes. Under these circumstances, myotomy can be very challenging, with an increased risk of esophageal perforation and less predictable clinical outcomes.[8,20,21]

After completion of the myotomy, approximately 40% of the circumference of the mucosa is exposed.

Since the laparoscopic approach aims to relieve dysphagia and prevent gastroesophageal reflux, the role and the type of fundoplication have been widely investigated. The exclusive use of LHM is associated with postoperative gastroesophageal reflux (in 50%–60% of patients) and with the risk of developing Barrett's esophagus or stenosis.[20,22,23] Moreover, total fundoplication is associated with an increased risk of persistent or recurring dysphagia.[24] Therefore, the addition of a partial fundoplication to myotomy produces better results than total fundoplication as it takes into account the lack of peristalsis.[24] Recently, a multicenter, randomized, controlled study compared anterior partial fundoplication (Dor) with posterior fundoplication (Toupet) and found no significant differences in the incidence of postoperative gastroesophageal reflux.[25] Currently, anterior partial fundoplication is performed more frequently because it is easier to perform and covers the exposed esophageal mucosa.[26]

LHM is associated with minimal postoperative pain, shorter hospital stay (1–2 days) and a rapid return to daily activities (2–3 weeks). In 90%–95% of patients, the symptoms are still better after 5 years, and in 80%–90% improvement is still present after 10 years. Recurrence of symptoms occurs mainly in the first 2–3 years of follow up, and may be secondary to the fibrosis developed at the distal edge of the myotomy. Most cases can be successfully treated by endoscopy and pneumatic dilatation.[13]

Advanced age and the diameter of the esophagus have not been associated with adverse results. Therefore, LHM should also be performed in patients with dilated and sigmoid esophagus, while esophagectomy should be considered only if LHM does not work.[17,27]

Postoperative gastroesophageal reflux is present in 25% of the patients and is generally well controlled with medication.[13]

Pneumatic Balloon Dilatation Versus Laparoscopic Heller Myotomy

Pneumatic dilatation in the LES is the most effective endoscopic treatment for achalasia.[13] Under fluoroscopic or endoscopic control, a balloon is inflated at the gastroesophageal junction in order to break the muscle fibers, while preserving the mucosa intact.

In the 1980s, the most frequently used balloons were non-expanding, low distensibility balloons with increasing diameters, which were associated with a low risk of perforation. As a result, pneumatic dilation was considered the primary treatment for patients with achalasia, while surgery played a secondary role and was reserved for cases in which dilatation failed.[28,29] Compared to pneumatic dilatation, LHM obtains better results in terms of improvement of postoperative dysphagia and gastroesophageal reflux rates, with a significantly lower risk of needing another operation.[30] Although the results in the short-term follow-up are similar, long-term monitoring shows that most patients are asymptomatic after LHM, but only 50% of patients with multiple pneumatic balloon dilatations are.[31] Several studies have shown better results after LHM than after pneumatic dilatation in patients under the age of 40.[32] In addition, previous endoscopic treatment with either botulinum toxin injection or pneumatic balloon dilatation may compromise the clinical results of LHM. In several series of patients previously treated with endoscopy, higher intraoperative complication rates were observed along with worse long-term clinical outcomes after LHM. These findings may be related with scar tissue at the gastroesophageal junction, which makes surgical dissection of the anatomical planes much more difficult.[9]

In 2011, Boeckxstaens et al.[29] published the results of a multicenter, randomized study comparing pneumatic dilatation (95 patients) with LHM and Dor fundoplication (106 patients) for esophageal achalasia with no previous treatment. The rate of perforation during pneumatic dilatation and LHM was 4% and 12%, respectively. Therapeutic success was defined as an Eckardt score of less than 3. The study showed similar success rates for LHM (90%) and pneumatic balloon dilatation (86%) in a follow-up period of two years.

Nevertheless, some of the limitations of this study may affect the interpretation of the results. First of all, the selection criteria for the surgeons who participated in the study are not clearly specified: a perforation rate of 12% during LHM is much higher than in the largest prospective series of untreated patients, which raises questions about the experience of some of the surgeons who participated in the study. Second, the myotomy was only extended 1–1.5 cm under the gastroesophageal junction and no technical details were provided about the anterior partial fundoplication, such as separating the edges of the muscle, and the number and location of the sutures. Third, the study showed that patients <40 years of age should be treated with LHM. Finally, the 2-year follow-up study is short. Several studies have shown that the success rate of pneumatic dilatation after 10–15 years is only 40% or 50%, even after several endoscopic sessions.[31]

Peroral Endoscopic Myotomy

Peroral endoscopic myotomy (POEM) was recently presented as a new approach to achalasia.[33] This procedure is performed under general anesthesia with endotracheal intubation.

A submucosal injection of 10 ml of saline with 0.3% indigo carmine is administered in the mid-esophagus about 13 cm proximal to the gastroesophageal junction at the 2 o'clock position. A 2 cm longitudinal incision is made on the surface of the mucosa to create an entrance to the submucosal space. This way, a descending anterior submucosal tunnel is created, passing through the gastroesophageal junction and reaching up to about 3 cm in the proximal stomach. Further sequential injections of indigo carmine solution mark the progression of the tunnel and aid in hemostasis and hydrodissection. After the submucosal tunnel is finished, the

circular muscle fibers are cut approximately 2–3 cm distal to the mucosa entrance, about 7 cm above the gastroesophageal junction. Myotomy is continued distally until it reaches the gastric submucosa, extending approximately 2–3 cm distal to the gastroesophageal junction.

After identification and dissection of the circular muscle fibers in the lower esophagus and proximal stomach, the mucosa entry site is closed with hemostatic clips.

This technique was proposed to have several advantages. First, the endoscopic approach should theoretically minimize postoperative pain. Secondly, a longer myotomy can be performed, extending to the middle third of the esophagus just below the aortic arch. Finally, concomitant antireflux surgery may not be necessary thanks to the selective sectioning of the circular muscle fibers without dissection at the gastroesophageal junction plane.

At present, the data available about clinical outcomes are from small series of patients with very short follow-up periods.

In 2010, Inoue et al.[33] published their first experience with POEM performed in 17 consecutive patients with achalasia. Mean operative time was 126 min, with an interval ranging from 100 to 180 min. Mean myotomy length was 8.1 cm, of which about 6 cm were in the esophagus and 2.0 cm in the stomach. One patient presented pneumoperitoneum, which caused a temporary increase in intraperitoneal pressure; abdominal wall puncture allowed for rapid recovery with no clinical repercussion. None of the 17 patients presented clinically evident postoperative subcutaneous emphysema. In all cases, POEM significantly reduced LES resting pressure (from a mean of 52.4 mmHg to 19.9 mmHg, P=.0001). During a mean follow-up of 5 months, none of the patients developed recurring symptoms of dysphagia, but reflux esophagitis (grade B, Los Angeles classification) was diagnosed in a patient who was treated successfully with medication. None of the patients required additional surgical or endoscopic treatment.

In 2012, von Renteln et al.[34] published the results of the first prospective POEM trial conducted in Europe. The primary end point was relief of symptoms after 3 months. The secondary outcomes were related with adverse events due to the procedure, LES pressure, reflux symptoms and use of medication before and after POEM. Peroral endoscopic myotomy was performed under general anesthesia in 16 patients. Three months after the POEM procedure, the treatment was considered successful in 94% of patients, defined by an Eckardt score $\leq$3. The mean pressure in the LES was reduced significantly from pre-POEM 27.2 mmHg to 11.8 mmHg after surgery (P<.001). No patients developed symptoms of gastroesophageal reflux after treatment. None of the patients required medical treatment after POEM.

Finally, Swanstrom et al.[35] recently published the symptomatic and physiologic results after 6 months of 18 patients who had undergone POEM for achalasia. The average length of myotomy was 9 cm (range 7–12 cm), and the average duration of the operation was 135 min (range 90–260 min). Three intraoperative complications were reported (2 gastric mucosal tears and one full-thickness esophagotomy). All complications were repaired endoscopically without sequelae. Mean hospital stay was one day and the average return to normal activity was 3 days (range 3–9 days). All patients experienced relief of their dysphagia during the mean follow-up of 11.4 months. Postoperative manometry and barium swallow showed significant improvement in LES relaxation and esophageal emptying, respectively. Gastroesophageal reflux was objectively diagnosed by 24-h pH monitoring in 46% of patients 6 months after POEM.

Only one study has retrospectively compared POEM and LHM.[36] It compared 18 non-randomized patients who underwent POEM with 55 patients treated for LHM. There were no differences in myotomy length, rate of complications or duration of hospital stay. During surgery, decompression with a Veress needle was required for pneumoperitoneum in 7 patients (39%) treated with POEM. POEM treatment was considered successful (Eckardt score $\leq$3) in 16 patients (89%) in an average follow-up of 6 months. Six weeks after POEM, routine follow-up manometry and barium timed-esophagogram (with barium swallowed at intervals) showed normalized pressures in the gastroesophageal junction and contrast column heights.

From the limited evidence available, POEM seems to be a promising procedure. However, there are some concerns to be raised about this new technique:

(1) Endoscopic myotomy is a very demanding technique that requires great skill and the learning curve is quite long.
(2) Although several studies have reported a significant reduction in pressure in the LES, demonstrated by manometry, the pressure was between 15 and 20 mmHg. As we know, a predictor of long-term success is an LES pressure around 10 mmHg.[37]
(3) Gastroesophageal reflux was reported in up to 50% of patients after POEM, which replicates the results obtained when only myotomy is performed without an anti-reflux procedure.
(4) Revisional surgery in patients with recurrent dysphagia after POEM can be challenging. The presence of adhesions between the submucosa and the longitudinal muscle layer after POEM could make dissection very difficult in this area.

Conclusions

Although the results of pneumatic balloon dilation and LHM seem similar in the short-term, long-term follow-up data show that LHM with partial fundoplication should be considered the procedure of choice for achalasia. Pneumatic dilatation should be reserved for cases where surgical skill is not available and for the treatment of recurrent dysphagia after myotomy. Only prospective studies with long-term follow-up comparing POEM and LHM with fundoplication will be able to determine the role of this new technique in the treatment of esophageal achalasia.

Conflict of Interest

The authors have no conflict of interests to declare.

REFERENCES

1. Fisichella PM, Raz D, Palazzo F, Niponmick I, Patti MG. Clinical, radiological, and manometric profile in 145 patients with untreated achalasia. World J Surg. 2008;32:1974–9.
2. Goldenberg SP, Burrell M, Fette GG, Vos C, Traube M. Classic and vigorous achalasia: a comparison of manometric, radiographic, and clinical findings. Gastroenterology. 1991;101:743–8.
3. Todorczuk JR, Aliperti G, Staiano A, Clouse RE. Reevaluation of manometric criteria for vigorous achalasia. Is this a distinct clinical disorder? Dig Dis Sci. 1991;36:274–8.
4. Hirano I, Tatum RP, Shi G, Sang Q, Joehl RJ, Kahrilas PJ. Manometric heterogeneity in patients with idiopathic achalasia. Gastroenterology. 2001;120:789–98.
5. Pandolfino JE, Ghosh SK, Rice J, Clarke JO, Kwiatek MA, Kahrilas PJ. Classifying esophageal motility by pressure topography characteristics: a study of 400 patients and 75 controls. Am J Gastroenterol. 2008;103:27–37.
6. Pandolfino JE, Kwiatek MA, Nealis T, Bulsiewicz W, Post J, Kahrilas PJ. Achalasia: a new clinically relevant classification by high-resolution manometry. Gastroenterology. 2008;135:1526–33.
7. Allescher HD, Storr M, Seige M, Gonzales-Donoso R, Ott R, Born P, et al. Treatment of achalasia: botulinum toxin injection vs pneumatic balloon dilation. A prospective study with longterm follow-up. Endoscopy. 2001;33:1007–17.
8. Patti MG, Feo CV, Arcerito M, de Pinto M, Tamburini A, Diener U, et al. Effects of previous treatment on results of laparoscopic Heller myotomy for achalasia. Dig Dis Sci. 1999;11:2270–6.
9. Smith CD, Stival A, Howell DL, Swafford V. Endoscopic therapy for achalasia before Heller myotomy results in worse outcomes than Heller myotomy alone. Ann Surg. 2006;243:579–86.
10. Vaezi MF, Richter JE, Wilcox CM, Schroeder PL, Birgisson S, Slaughter RL, et al. Botulinum toxin versus pneumatic dilatation in the treatment of achalasia: a randomised trial. Gut. 1999;44:231–9.
11. Zaninotto G, Annese V, Costantini M, del Genio A, Costantino M, Epifani M, et al. Randomized controlled trial of botulinum toxin versus laparoscopic Heller myotomy for esophageal achalasia. Ann Surg. 2004;239:364–70.
12. Pellegrini CA, Wetter LA, Patti MG, Leichter R, Mussan G, Mori T, et al. Thoracoscopic esophagomyotomy. Initial experience with a new approach for the treatment of achalasia. Ann Surg. 1992;216:291–6.
13. Stefanidis D, Richardson W, Farrell TM, Kohn GP, Augenstein V, Fanelli RD, Society of American Gastrointestinal and Endoscopic Surgeons. SAGES guidelines for the surgical treatment of esophageal achalasia. Surg Endosc. 2012;26:296–311.
14. Patti MG, Fisichella PM, Perretta S, Galvani C, Gorodner MV, Robinson T, et al. Impact of minimally invasive surgery on the treatment of esophageal achalasia: a decade of change. J Am Coll Surg. 2003;196:698–705.
15. Patti MG, Arcerito M, de Pinto M, Feo CV, Tong J, Gantert W, et al. Comparison of thoracoscopic and laparoscopic Heller myotomy for achalasia. J Gastrointest Surg. 1998;2:561–6.
16. Patti MG, Pellegrini CA, Horgan S, Arcerito M, Omelanczuk P, Tamburini A, et al. Minimally invasive surgery for achalasia. An 8-year experience with 168 patients. Ann Surg. 1999;230:587–93.
17. Sweet MP, Nipomnick I, Gasper WJ, Bagatelos K, Ostroff JW, Fisichella PM, et al. The outcome of laparoscopic Heller myotomy for achalasia is not influenced by the degree of esophageal dilatation. J Gastrointest Surg. 2008;12:159–65.
18. Oelschlager BK, Chang L, Pellegrini CA. Improved outcome after extended gastric myotomy for achalasia. Arch Surg. 2003;138:490–7.
19. Bello B, Gullo R, Patti MG. Laparoscopic Heller myotomy and partial fundoplication for esophageal achalasia. In: Nguyen NT, Scott-Conner CE, editors. The SAGES manual: vol. 2: advanced laparoscopy and endoscopy LLC: Springer Science+Business Media; 2012. http://dx.doi.org/10.1007/978-1-4614-2347-8_11.
20. Richards WO, Torquati A, Holzman MD, Khaitan L, Byrne D, Lutfi R, et al. Heller myotomy versus Heller myotomy with Dor fundoplication. A prospective randomized double-blind clinical trial. Ann Surg. 2004;240:405–15.
21. Portale G, Costantini M, Rizzetto C, Guirroli E, Ceolin M, Salvador R, et al. Long-term outcome of laparoscopic Heller-Dor surgery for esophageal achalasia. Possible detrimental role of previous endoscopic treatment. J Gastrointest Surg. 2005;9:1332–9.
22. Burpee SE, Mamazza J, Schlachta CM, Bendavid Y, Klein L, Moloo H, et al. Objective analysis of gastroesophageal reflux after laparoscopic Heller myotomy: an anti-reflux procedure is required. Surg Endosc. 2005;19:9–14.
23. Falkenback D, Johansson J, Oberg S, Kjellin A, Wenner J, Zilling T, et al. Heller's esophagomyotomy with or without a 360 degrees floppy Nissen fundoplication for achalasia. Longterm results from a prospective randomized study. Dis Esophagus. 2003;16:284–90.
24. Rebecchi F, Giaccone C, Farinella E, Campaci R, Morino M. Randomized controlled trial of laparoscopic Heller myotomy plus Dor fundoplication versus Nissen fundoplication for achalasia. Ann Surg. 2008;248:1023–30.
25. Rawlings A, Soper NJ, Oelschlager B, Swanstrom L, Matthews BD, Pellegrini C, et al. Laparoscopic Dor versus Toupet fundoplication following Heller myotomy for achalasia: Results of a multicenter, prospective, randomized-controlled trial. Surg Endosc. 2012;26:18–26.
26. Patti M, Herbella FA. Fundoplication after laparoscopic Heller myotomy for esophageal achalasia: what type? J Gastrointest Surg. 2010;14:1453–8.
27. Mineo TC, Pompeo E. Long-term outcome of Heller myotomy in achalasic sigmoid esophagus. J Thorac Cardiovasc Surg. 2004;128:402–7.
28. Eckardt VF, Gockel I, Bernhard G. Pneumatic dilation for achalasia: late results of a prospective follow-up investigation. Gut. 2004;53:629–33.
29. Boeckxstaens GE, Annese V, des Varannes SB, Chaussade S, Costantini M, Cuttitta A, et al., European Achalasia Trial Investigators. Pneumatic dilation versus laparoscopic Heller's myotomy for idiopathic achalasia. N Engl J Med. 2011;364:1807–16.
30. Wand L, Li YM, Li L. Meta-analysis of randomized and controlled treatment trials for achalasia. Dig Dis Sci. 2009;54:2303–11.
31. West RL, Hirsch DP, Bartelsman JFWM, de Borst J, Ferwerda G, Tytgat GNJ, et al. Long term results of pneumatic dilation in achalasia followed for more than 5 years. Am J Gastroenterol. 2002;97:1346–51.
32. Alderliesten J, Conchillo JM, Leewenburgh I, Steyenberg EW, Kuipers EJ. Predictors for outcome failure of balloon dilatation in patients with achalasia. Gut. 2011;60:10–6.
33. Inoue H, Minami H, Kobayashi Y, Sato Y, Kaga M, Suzuki M, et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia. Endoscopy. 2010;42:265–71.

34. Von Renteln D, Inoue H, Minami H, Werner YB, Pace A, Kersten JF, et al. Peroral endoscopic myotomy for the treatment of achalasia: a prospective single center study. Am J Gastroenterol. 2012;107:411–7.
35. Swanstrom LL, Kurian A, Dunst CM, Sharata A, Bhayani N, Rieder E. Long-term outcomes of an endoscopic myotomy for achalasia: the POEM procedure. Ann Surg. 2012;256: 659–67.
36. Hungness ES, Teitelbaum EN, Santos BF, Arafat FO, Pandolfino JE, Kahrilas PJ, et al. Comparison of perioperative outcomes between peroral esophageal myotomy (POEM) and laparoscopic Heller myotomy. J Gastrointest Surg. 2013;17:228–35 [Epub ahead of print].
37. Eckardt VF, Aignherr C, Bernhard G. Predictors of outcome in patients with achalasia treated by pneumatic dilation. Gastroenterology. 1992;103:1732–8.