The long-term outcome of balloon dilation versus botulinum toxin injection in patients with primary achalasia

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Balloon dilation (BD) is currently the most commonly performed treatment for achalasia. Intrasphincteric botulinum toxin injection (BTI) is also used as an alternative to BD or laparoscopic Heller’s myotomy with partial fundoplication. These treatments reduce lower esophageal sphincter (LES) pressure, resulting in improved esophageal emptying by gravity and in improved symptoms, such as dysphagia, regurgitation, chest pain, and weight loss; however, few studies have identified predictors of the long-term outcomes for BD versus BTI in patients with primary achalasia.

In the current issue of The Korean Journal of Internal Medicine, the long-term outcomes of BD versus BTI in patients with primary achalasia from a single institution were compared and the predictors of remission identified [1]. At a median follow-up of 61 months, BD appeared to be more efficacious than BTI in terms of long-term remission in the enrolled patients with achalasia. Independent factors predicting long-term remission included the treatment type and the difference in LES pressure.

Botulinum toxin (BT) can impede the release of acetylcholine from cholinergic neurons. Chemical denervation after BTI is intended to lower both basal and residual LES pressure, thereby reducing bolus obstruction [2,3]. Commonly, 70% to 80% of referred patients show relieved or improved symptoms within 30 days after the procedure. According to a literature review performed by Basotti and Annese [4], a single injection of BT is effective in approximately 85% of patients with achalasia, but its effect diminishes over time to 50% by 6 months and to 30% by 1 year. According to a review by Vaezi and Richter [5], 26% of patients are resistant to BT and show no clinical response, which is thought to be due to antibodies against the protein [6].

Although BTI is safe and easy to perform, it was found to be effective only in short-term evaluations, with reduced benefit within 2 years after injection and eventually no benefit with repeated injections [7,8]. Because of these limitations, BTI is best reserved for patients who are too ill to undergo surgery, such as those who are elderly, those whose disease is complicated by overlapping diseases, or those who decline surgery or BD [9]. BTI is also suitable as a transition during periods in which more invasive treatments are not possible, for
example, during pregnancy or temporal use of double or triple antiplatelet therapy. In addition, BTI has been used as a rescue treatment after unsuccessful BD or surgical myotomy [10]. However, there is increased difficulty with performing esophagomyotomy after BTI [11].

BD is the most cost-effective treatment for achalasia over a 5- to 10-year postprocedure period [12,13]. BD aims to fracture the muscularis propria forcibly, decreasing LES pressure and thereby improving bolus transit through the cardia. According to a review of 1,144 patients across 24 studies with an average follow-up of 37 months, BD showed good to excellent symptom relief in a graded manner in 74%, 86%, and 90% of patients treated with 30-, 35-, and 40-mm balloons, respectively [8]. Irrespective of the protocol used, a large portion of patients will relapse, mainly during the first year after treatment [14,15]. However, long-term remission, based on symptom recurrence, can be achieved in almost all patients by repeated BD [17]. Those patients with the best outcomes following BD tend to be older (> 40 years), female, and to present with type II patterns on high resolution manometry [14,18-21]. Several studies using long-term follow-up periods are available currently. Eckardt et al. [22] showed a 5-year follow-up response rate of 46% among patients with unique BD, and patients experiencing a relief in symptoms after 5 years were more likely to continue in this way. Zerbib et al. [17] reported estimated efficacies of 97% and 93% after 5 and 10 years, respectively, but most frequently in cases of repeated BD. In a study comprising 209 patients with a mean follow-up of 70 months, a 72% success rate with BD was observed [16]. However, in these studies, BD was not repeated routinely, rather performed on demand only for patients were still symptomatic. In a meta-analysis performed by Weber et al. [23], the 10-year remission rate for BD was 47.9%, while the perforation rate was 2.4%. When performed by experienced operators, BD can achieve good to excellent outcomes (defined as an improved swallowing ability and an improved quality of life); however, only a few patients can be definitively treated by a single dilation, with most needing repeated dilations over a long-term follow-up [24]. A recent Cochrane Review compared 178 patients from six randomized, controlled trials after esophageal BD versus endoscopic BTI. At the 1-year follow-up, up to 74% of patients who underwent BTI experienced treatment failure, compared with 36% of patients who underwent BD [25]. In addition, Campos et al. [26] performed a systematic review and a meta-analysis on 7,855 achalasia patients and found better symptomatic relief in patients treated by BD compared with BTI.

Perforation is the most serious complication of BD, with an overall rate of 1.6% [24,27]. Most such cases should be managed by surgical correction, such as simple closure, second-look operation after simple drainage, or esophagectomy.

Recently, peroral endoscopic myotomy (POEM) has been introduced as a promising alternative to the current treatments. However, the POEM technique is difficult and requires extensive experience with therapeutic endoscopy. POEM is an elegant treatment resulting in excellent short-term results and is considered an alternative for achalasia. BD and laparoscopic Heller’s myotomy have shortcomings, suggesting a need for a better treatment option. A recent POEM survey showed an overall clinical success rate of 98% after a mean follow-up of 9.3 months [28].

Therefore, BD should be used as the first-line treatment in Korean patients with achalasia due to its superior long-term clinical success rate. BTI is best reserved for patients who are too ill to undergo surgery and as a suitable transition during periods in which more invasive treatments are not possible. BTI can also be used as rescue treatment after unsuccessful BD or surgical myotomy. However, the number of effective treatments available for achalasia, such as POEM, is increasing. Short-term follow-up data for POEM are promising; however, more long-term follow-up data and prospective randomized trials comparing POEM with BD or surgical myotomy are needed to determine the potential of POEM as a new treatment option for achalasia.

**Conflict of interest**

No potential conflict of interest relevant to this article was reported.

**REFERENCES**

1. Jung HE, Lee JS, Lee TH, et al. Long-term outcomes of balloon dilation versus botulinum toxin injection in
patients with primary achalasia. Korean J Intern Med 2014;29:738-745.
2. Jankovic J, Brin MF. Therapeutic uses of botulinum toxin. N Engl J Med 1991;324:1186-1194.
3. Roberts KE, Duffy AJ, Bell RL. Controversies in the treatment of gastroesophageal reflux and achalasia. World J Gastroenterol 2006;12:355-361.
4. Bassotti G, Annese V. Review article: pharmacological options in achalasia. Aliment Pharmacol Ther 1999;13:1391-1396.
5. Vaezi MF, Richter JE. Current therapies for achalasia: comparison and efficacy. J Clin Gastroenterol 1998;27:21-35.
6. Pamphlett R. Early terminal and nodal sprouting of motor axons after botulinum toxin. J Neurol Sci 1989;92:181-192.
7. Pasricha PJ, Rai R, Ravich WJ, Hendrix TR, Kalloo AN. Botulinum toxin for achalasia: long-term outcome and predictors of response. Gastroenterology 1996;110:1410-1415.
8. Richter JE. Update on the management of achalasia: balloons, surgery and drugs. Expert Rev Gastroenterol Hepatol 2008;2:435-445.
9. Martinek J, Siroky M, Plottova Z, Bures J, Hep A, Spicak J. Treatment of patients with achalasia with botulinum toxin: a multicenter prospective cohort study. Dis Esophagus 2003;16:204-209.
10. Annese V, Basciani M, Perri F, et al. Controlled trial of botulinum toxin injection versus placebo and pneumatic dilation in achalasia. Gastroenterology 1996;111:1410-1424.
11. 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;243:579-584.
12. O’Connor JB, Singer ME, Imperiale TF, Vaezi MF, Richter JE. The cost-effectiveness of treatment strategies for achalasia. Dig Dis Sci 2002;47:1516-1525.
13. Karanicolas PJ, Smith SE, Inculet RI, et al. The cost of laparoscopic myotomy versus pneumatic dilation for esophageal achalasia. Surg Endosc 2007;21:1198-1206.
14. Vela MF, Richter JE, Khandwala F, et al. The long-term efficacy of pneumatic dilatation and Heller myotomy for the treatment of achalasia. Clin Gastroenterol Hepatol 2006;4:580-587.
15. West RL, Hirsch DP, Bartelsman JF, et al. Long term results of pneumatic dilation in achalasia followed for more than 5 years. Am J Gastroenterol 2002;97:1346-1351.
16. Hulselmans M, Vanuytsel T, Degreef T, et al. Long-term outcome of pneumatic dilation in the treatment of achalasia. Clin Gastroenterol Hepatol 2010;8:30-35.
17. Zerbib F, Theiot V, Richy F, Benajah DA, Message L, Lamoulle H. Repeated pneumatic dilations as long-term maintenance therapy for esophageal achalasia. Am J Gastroenterol 2006;101:692-697.
18. Boeckxstaens GE, Annese V, des Varannes SB, et al. Pneumatic dilation versus laparoscopic Heller’s myotomy for idiopathic achalasia. N Engl J Med 2011;364:1807-1816.
19. Rohof WO, Salvador R, Annese V, et al. Outcomes of treatment for achalasia depend on manometric subtype. Gastroenterology 2011;141:78-79.
20. Vaezi MF, Baker ME, Achkar E, Richter JE. Timed barium oesophagram: better predictor of long term success after pneumatic dilation in achalasia than symptom assessment. Gut 2002;50:765-770.
21. Vantrappen G, Hellemans J, Deloof W, Valemoipa B, Vandenbroucke J. Treatment of achalasia with pneumatic dilatations. Gut 1971;12:268-275.
22. Eckardt VF, Gockel I, Bernhard G. Pneumatic dilation for achalasia: late results of a prospective follow up investigation. Gut 2004;53:620-631.
23. Weber CE, Davis CS, Kramer HJ, Gibbs JT, Robles L, Fisichella PM. Medium and long-term outcomes after pneumatic dilation or laparoscopic Heller myotomy for achalasia: a meta-analysis. Surg Laparosc Endosc Percutan Tech 2012;22:289-296.
24. Richter JE, Boeckxstaens GE. Management of achalasia: surgery or pneumatic dilation. Gut 2011;60:869-876.
25. Leyden JE, Moss AC, MacMathuna P. Endoscopic pneumatic dilation versus botulinum toxin injection in the management of primary achalasia. Cochrane Database Syst Rev 2006;(4):CD005046.
26. Campos GM, Vittinghoff E, Rabl C, et al. Endoscopic and surgical treatments for achalasia: a systematic review and meta-analysis. Ann Surg 2009;249:45-57.
27. Vanuytsel T, Lerut T, Coosemans W, et al. Conservative management of esophageal perforations during pneumatic dilation for idiopathic esophageal achalasia. Clin Gastroenterol Hepatol 2012;10:142-149.
28. Stavropoulos SN, Modyal RJ, Friedel D, Savides T. The International Per Oral Endoscopic Myotomy Survey (IP-OEMS): a snapshot of the global POEM experience. Surg Endosc 2013;27:322-338.