Current Treatment Options in Esophageal Achalasia

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Abstract

Achalasia is a disorder of the esophagus characterized by aperistalsis and failure of the lower
esophagus to relax, resulting in symptoms such as dysphagia, regurgitation, chest pain and weight loss. Manometric study is the gold standard for diagnosis, which must at least meet the criteria of the absence of or abnormal swallowing relaxation of the LES, and aperistalsis of the esophageal body. However, endoscopes and radiologic tests are often as important in distinguishing secondary achalasia caused by malignancy. Therapeutic trends for the treatment of esophageal achalasia have changed a great deal in past decades. These changes include endoscopic and minimally invasive surgical procedures such as laparoscopic or thoracoscopic cardiomyotomy, or more aggressively, cardioplasty or esophageal resection. In this review article, we discuss the benefits and outcomes of each individual option. To date, the results of minimally invasive surgical treatment seem to be better when compared to medical management or endoscopic procedures, despite the higher initial expenses, and pneumatic dilation provides the most cost-effective treatment option for achalasia under most clinically reasonable circumstances. Finally, one new trend in alternative treatment, botulinum toxin injection therapy, is used only in a small number of older of high-risk patients.
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Key Words：Esophageal achalasia, Pneumatic dilatation, Botulinum toxin, Minimally invasive surgical myotomy

Introduction

Achalasia is one of the primary motility dysfunctions of the esophagus, of which the pathophy-siology is well understood. In the United States, such a disorder is relatively uncommon, with a prevalence estimated at about 10 in 10,000 and an incidence rate in the range of 0.5 new cases per year per 100,000 of the general population1. Most cases occur in middle age, and affect both sexes and all races equally. The selective loss of inhibitory neurons of the myenteric plexus which produces VIP, nitric oxide and inflammatory infiltrate are responsible for abnormal lower esophageal sphincter (LES) dysfunction2. This results in an unopposed excitation of the LES, and dysfunction or failure of the LES to relax in response to each swallow3-5.

Since pharmacological therapies have had a low success rate in treating the disease6-7, the goal of this article is to review and discuss current treatment trends available in Taiwan. This includes pneumatic dilation, botulinum toxin (BT) injection therapy, and minimally invasive surgery.

Diagnosis

Clinical diagnosis is always symptom-based. Dysphagia to both liquid and solid foods is the most common symptom. Food regurgitation is one of the patients' major problems, producing pulmonary complications ranging from a minor cough to severe aspiration pneumonia. Weight loss usually occurs as a result.

Three examinations are very important:

esophageal manometric study, radiology and esophagogastroduodenoscopy (EGD). Manometry is still the standard diagnostic test for achalasia. This must at least meet the criteria of the absence or abnormal swallowing relaxation of the LES, and the absence of peristalsis in the esophageal body (Fig. 1)1,8,9 . Barium ingestion and fluoroscopy or videoflurographic pharyngoesophageal study can be carried out as an alternative diagnosis. A classic "bird-beak" of the GE junction, with atonia and a dilated esophageal body, are the typical radiological signs (Fig. 2). In some early stage patients, the size of the lumen may be normal but peristalsis is still absent. EGD is

always necessary to distinguish this from the secondary form of achalasia due to malignancy. Furthermore, in addition to the endoscopic ultrasound, biopsies are always performed on suspected lesions.

Current treatment options

As mentioned earlier, there are currently 3 main treatment modalities: medical pneumatic dilation, surgery and botulinum toxin injection therapy. Whichever treatment options are chosen, the goal is to relax the LES, and relieve the symptoms. The durability of a successful treatment, complication rates, and cost-benefits are the

primary concerns.

1. Pneumatic dilation

This simple forceful bougie dilation method began when Willis treated his patient with a whalebone many centuries ago. However, much greater strength of stretching is usually required for dilation to cause an effective mechanical tear to the muscle fiber of the LES. The modern dilator's fully inflated diameter usually ranges from 3 centimeters or more to achieve a satisfactory result, and is able to achieve maximal pressure. The most commonly used dilator is the Regiflex dilator10. The number of dilation sessions and the inflation time needed for a successful dilation varies from operator to operator. Some have suggested a single dilation session is enough, but recommend dilation with a bigger dilator, based on the patients' symptom scores11-12. Others have suggested more progressive methods, such as a series of dilations on the same or successive days, with a larger dilator. Some have suggested a balloon inflation time of 10 seconds, while others have achieved statisfactory results only after 5 minutes of continuous inflation. Immediate and short-term results have reportedly been good in most series13. The most important concern is the long term durability of such results after forceful dilation. In the first five to ten years of follow-up studies in the literature, approximately 20-75% of patients needed a second or even more dilatations. Half of the patients improved after repeated dilations14. Those who did not respond eventually sought help from a surgeon. The response to pneumatic dilation is usually based on subjective improvements in symptom scores of the patient15. However, objective parameters rarely return to normal. About half of the dilated patients achieve short-term reduction in LES pressure and scintigraphic retention, and about one quarter have changes in esophageal diameter6,15. A post-dilated LES pressure of below 10 mmHg accounts for a better long-term response6. Complications due to pneumatic dilation are uncommon. The most severe complication is perforation (1-10 %). These perforations are usually minor, and conservative treatment with antibiotics and parenteral alimentations are suggested whenever possible, although the hospital stay may be extended16,17. Reflux is not commonly seen post dilation (less than 2 %). If it does occurs, it is only for a short period of time. Unfortunately, the long-term success rate of pneumatic dilation is rather low, resulting in permanent successful treatment of achalasia in only 40-50% of patients14,18. Furthermore, it must be remembered that achalasia is a risk factor for esophageal cancer19.

2. Botulinum toxin (BT) injection

BT is a biological toxin derived from Clostrid-ium botulinum that causes paralysis of both voluntary and involuntary muscles. BT is used in various di-sorders of muscle overactivity, such as spasticity in both children and adults, and dystonic conditions

such as blepharospasm, cervical dystonia, spasmo-dic dysphonia, writer's cramp, hemifacial spasm and headache20. Its main action is at the terminal nerve endings of myoneural junctions by preventing the release of acetylcholine from vesicles, thus causing chemical denervation which may persist for months. Because of its wider safety range and fewer complications, BT has been an important therapeutic modality in different branches of medicine and surgery, such as in treating achalasia20-22. Local injection of the toxin to the LES muscle of patients with achalasia lowers LES tone, and the patient becomes asymptomatic21-22. This new treatment has been widely practiced in past decades with excellent immediate responses (success rates of more than 90 %), but these results last only 6-9 months on average in most patients, and only half of all patients benefit for more than 1 year22-24. Like post-pneuma-tic dilation patients, there is significant improvement in all objective tests for esophageal functions, such as lowering of LES pressure, increase of esophageal diameter and improvement of transit time by scinti-graphy22. Complications of BT therapy for achalasia are minor, because the dosage used is too small to induce serious adverse effects such as generalized paralysis. About one quarter of the patients suffer from transient chest pains and less than 5% complain of reflux symptoms22.

Achalasia treatment in elderly patients is a matter of controversy. It has been reported that the long-term success is highest among elderly patients and in patients with an LES pressure not exceeding the upper normal level prior to treatment23-26. The effect of BT injections wanes with time in elderly patients, necessitating repeated injections to keep the patients symptom-free. Due to the number of repeated injections required, this procedure is more expensive than endoscopic dilation by 50 % or more. Also, younger patients (< 55 years) with a severe increase in LES pressure do not seem to benefit from BT injections, and pneumatic dilation or minimally invasive myotomy may be more advantageous to them24. In general, pneumatic dilatation is more efficacious than BT for sustained symptomatic relief in patients with achalasia. The efficacy of a single pneumatic dilatation is similar to that of 2 BT injections27.

BT is as good as pneumatic dilatation in achieving an initial improvement in achalasia. It is also effective in patients with tortuous megaesophagus and previous failed pneumatic dilatations. However, as mentioned earlier, dysphagia often recurs during 1-year follow up28. Furthermore, one report has shown that previous BT injections made subsequent minimally invasive myotomy riskier and more difficult29. Therefore, taking into account the lower long-term efficacy of BT injection therapy, it is a suitable alternative only for a minority of older or high-risk patients30.

3. Surgical myotomy

Myotomy of the LES is the most direct method used and by far the best treatment modality for satisfactory long-term results, regardless of the fact that only about 60 %

of myotomy patients remain in remission 10 years after surgery31-33. Sometimes, an esophageactomy may be needed for those with recurrent and disabling symptoms. There is significant improvement of objective parameters of response, increase in the opening of gastroesophageal junction, narrowing of the lumen and improved esophageal transiting for at least 3 to 7 years34,35. LES pressure has fallen significantly, usually less than 10 mmHg for those who respond. Increases in peristalsis and LES relaxations are seen post-surgery. Although post-operation complications are rare (less than 4 %), those most commonly seen are mucosal leakage, fistula, splenic injury and pneumonia. Such morbidity and the longer hospital stay are costly, and lead to psychological insecurity.

Fortunately, minimally invasive surgery by either laparoscopy or thoracoscopy, as applied to myotomy in achalasia patients, has been safely introduced in past decades36,37. Less discomfort and shorter hospital stays are the most attractive factors38-45. Complications, such as incomplete myotomy and mucosal perforation, may still occur due primarily to the lack of tactile perception resulting in technical problems. Evidence indicates that the laparoscopic approach is superior to thoracoscopic procedure due to a shorter operative time and a shorter hospital stay44-46.

Intraoperative endoscopy during videoscopic Heller myotomy guides the extent and adequacy of myotomy by utilizing a focused dissection with preservation of the natural antireflux mechanisms around the gastroesophageal junction, and by limiting the extent of myotomy along the cardia. By doing so, postoperative reflux symptoms are minimized. A concomitant EGD during Heller myotomy to guide myotomy, and routine fundoplication are clinically necessary46. Although reported gastrointestinal reflux in a review of 25 series was about 11%, there is still disagreement about the fundoplication procedure47. Some surgeons routinely perform antireflux procedure during surgery, but reflux can still occur in long-term follow-up studies34.

The surgical treatment for stage III achalasia with a markedly dilated and sigmoid-shaped esophagus is a matter of controversy. Some authors recommend esophagectomy as the primary treatment because they believe that Heller myotomy cannot improve dysphagia in such cases48. Besides esophagectomy and laparoscopic Heller-Dor surgery, another alternative is laparoscopic esophagogastrostomy with posterior semifundoplication. Because of the wide side-to-side anastomoses, there is no risk of persisting stenosis such as that reported for the Heller operation. Although the procedure is certainly less invasive than esophagectomy, it presents about the same degree of technical difficulty43.

Controversy also surrounds the choice of laparoscopic cardiomyotomy as the primary

treatment for achalasia, or as second-line treatment following the failure of nonsurgical intervention. Some doctors believe that laparoscopic cardiomyotomy can be more difficult technically following pneumatic dilatations49. However, reports show that laparoscopic cardiomyotomy can be as safe and effective as a primary or second-line treatment, even after the failure of pneumatic dilatations50. Although pneumatic dilatation is said to relieve dysphagia in achalasia if it decreases lower esophageal sphincter (LES) pressure to 10 mmHg, it does not guarantee relief from dysphagia6. Surgery is still necessary if dilation does not relieve dysphagia, despite the low LES pressure51. However, esophagectomy should always be reserved only for those cases in which simpler operations have failed.

Generally, laparoscopic myotomy is as safe and effective as pneumatic dilation in the treatment of achalasia52. However, when considering the cost-effectiveness of treatment strategies for achalasia, laparoscopic myotomy has a higher initial cost, and pneumatic dilation is the most cost-effective treatment option for adults with achalasia53.

In conclusion, when compared with medical management or endoscopic procedures, the minimally invasive surgical treatment seems to have the better results. However, when medical expenses are considered, pneumatic dilation is still the most cost-effective method for the time being, as BT has the disadvantage of uncertainty with regard to its long-term relapse rates, which may prove costly despite its excellent immediate and short-term reponse.

Fig.1. Achalasia (A) Manometric study showed the absence of LES relaxation in response to a wet swallow, and exaggerated overshoot. LES pressure is approximately 45 mmHg. (B) Aperistalsis in the esophageal body with simultaneous isobaric contractions of about 25 mmHg.

Fig.2. A classic 'bird-beak" of the GE junction with atonia and a dilated esophageal body detected by radiography.

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下食道弛緩不能症 (Achalasia)：現有治療法之最佳選擇 (綜說)

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摘　　要

下食道弛緩不能症 (　achalasia) 起因於吞嚥時食道無法產生有效的蠕動波 (aperistalsis)，且下擴約肌無法鬆弛而造成吞嚥困難，食物逆流、胸痛、體重下降等症狀。食道動力學檢查發現食道無蠕動波和吞嚥時擴約肌無法鬆弛乃診斷之依據。當然內視鏡 (甚至於內視鏡超音波) 和放射線檢查有助以鑑別診斷其癌病變之存在。在過去十幾年以來，無論是內科或外科之治療法，皆有長足的進步。本篇文章的目的主要是探討其各種治療法，並針對其長，短期之療效和經濟觀點來作個綜論，以作爲日後醫師和患者選擇治療法之最佳參考。結論是，以微小侵略性手術之療效最好且併發症少惟其初期所花費稍高。氣球撐開術 (pneumatic dilation) 之安全性佳且單次所花費不高但長期療效不理想。局部注射肉毒桿菌 (botulinum toxin) 治療目前以治療老人或手術之高危險病患爲主。