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Comprehensive Approaches to the Treatment of Esophageal Achalasia: A Review of Current Methods

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Abstract

Introduction and purpose

Achalasia is the most prevalent primary esophageal motility disorder, marked by improper relaxation of the lower esophageal sphincter (LES), increased resting pressure in the LES, and a lack of peristalsis in the esophagus. Symptoms include difficulty swallowing (dysphagia), regurgitation, chest pain, and weight loss. Due to the nonspecific nature of these symptoms, diagnosis can be delayed by several years. Since the underlying cause of achalasia is still unknown, treatment options focus on alleviating symptoms by targeting the lower esophageal sphincter.

Materials and methods

This paper is based on a literature review sourced from PubMed, using the following keywords: achalasia, POEM, laparoscopic cardiomyotomy, pneumatic dilation, and botulinum toxin injection.

Results

Various treatment options are available for achalasia, each offering unique features and results. The main approaches include Peroral Endoscopic Myotomy (POEM), Laparoscopic Myotomy (LM), Botulinum Toxin Injection, and Pneumatic Dilation (PD).

Conclusion
Each treatment differs in its level of invasiveness, duration of symptom relief, risk of complications, and the likelihood of requiring additional interventions. The selection of the most suitable option is influenced by individual patient factors, such as the type and severity of achalasia, overall health, and personal preference.
Key words: achalasia, POEM, laparoscopic crdiomiotomy, pneumatic dilatation, botulinum toxin injection

Introduction
Achalasia is a primary motility disorder of the esophagus characterized by abnormal relaxation of the lower esophageal sphincter (LES), elevated resting pressure of the LES, and absence of peristaltic waves in the esophageal body. The pathomechanism of achalasia is not fully understood. The disorder in the relaxation of the lower esophageal sphincter is likely due to a decrease in the postganglionic cells of the Auerbach's plexus and reduced secretion of neurotransmitters responsible for LES relaxation, such as VIP (vasoactive intestinal peptide). [1] Achalasia occurs at a frequency of about 1 in 100,000 people, equally common in women and men, most often affecting individuals between the ages of 20 and 40. [2] The symptoms of the disease are not specific. In the absence of characteristic complaints, the diagnosis may be delayed even by several years. It is important to differentiate achalasia from gastroesophageal reflux disease, cardiovascular diseases, and eating disorders. In the diagnosis of achalasia, an upper gastrointestinal endoscopy is performed to assess the mucosa of the esophagus and stomach and to rule out any potential organic causes of esophageal obstruction. Esophagography and manometry, which measure esophageal pressure, are also important diagnostic tools. [3] The Eckardt score is a clinical scoring system used to assess the severity of symptoms in patients with achalasia. It evaluates four key symptoms: Dysphagia, regurgitation, chest pain, weight loss. Each symptom is scored from 0 to 3 based on its severity, leading to a total score ranging from 0 to 12. A higher Eckardt score indicates more severe symptoms. It is commonly used to evaluate the effectiveness of treatment for achalasia, with a score of 3 or less generally considered indicative of treatment success. [4] The condition significantly reduces the quality of life for patients, causing dysphagia, regurgitation, chest pain and weight loss. The goal of treatment is to alleviate symptoms. Currently, both endoscopic and surgical methods are used including pneumatic dilation, botulinum toxin injections, endoscopic and surgical cardiomyotomy. [1],[5]
The aim of this paper is to discuss the available treatment methods for achalasia, including both endoscopic and surgical techniques, based on the available literature.

State of knowledge
Diagnostics
The gold standard in the diagnosis of achalasia is high-resolution manometry. Modern high-resolution manometry (HRM) systems use numerous sensors on a flexible catheter, passed through the nose into the stomach, to measure esophageal pressure. These sensors create color-coded topographic plots known as "Clouse plots." There are two types of HRM systems: water-perfused and solid-state.

Solid-state systems offer more detailed pressure data, but water-perfused systems can also be used with the correct normative values. HRM provides real-time, integrated assessments of esophageal function, though differences between systems necessitate using appropriate normative values for accurate interpretation. [6]

Manometry identifies the following six features:

1. Integrated Relaxation Pressure (IRP): Reflects the relaxation of the lower esophageal sphincter (LES) in response to swallowing. A median IRP of less than 15 mmHg in the supine position and less than 12 mmHg in the upright position is considered normal for Medtronic systems.
2. Distal Contractile Integral (DCI): Used to assess the strength of smooth muscle contractions in the esophagus, taking into account the length, amplitude, and duration of the contraction. In conventional manometry, this is equivalent to pressure amplitude. The upper limit of normal is considered to be 5000 mmHg x s x cm.
3. Contractile Deceleration Point (CDP): Marks the point where the wavefront of the contraction slows down.
4. Contractile Front Velocity (CFV): Measures the speed of the wavefront of the esophageal contraction.
5. Distal Latency (DL): Refers to the time delay before distal esophageal contraction.
6. Peristaltic Break: Represents interruptions in the peristaltic wave. [7]

Based on this examination, three types of achalasia are distinguished according to the Chicago classification:

Type I is classic achalasia with impaired peristalsis in 100% of swallowing events,

Type II is achalasia with esophageal compression without normal peristalsis, where elevated pressure persists throughout the esophagus in 20% of swallowing events

Type III is spastic achalasia without normal peristalsis, with partially preserved peristalsis in the distal segment, where at least 20% of swallowing events are characterized by rapidly propagating contraction waves or spastic simultaneous contraction. [8]

Upper digestive endoscopy plays a crucial role in the diagnosis of achalasia, primarily by helping to exclude other potential causes of esophageal obstruction, such as strictures, tumors, or other structural abnormalities. Tumors at the esophagogastric junction can cause pseudoachalasia, which presents with a clinical picture similar to classic achalasia but occurs more frequently in older patients, with significant weight loss and a shorter duration of symptoms. [4] Endoscopy allows for the direct visualization of the esophagus, LES (lower esophageal sphincter), and stomach lining to check for mucosal changes, inflammation, or other signs that could suggest a different underlying condition. Although endoscopy alone is not diagnostic for achalasia, it can reveal features suggestive of the disorder, such as retained food or saliva in the esophagus, longitudinal esophageal stripes (present in 41-94% of patients with achalasia), a dilated esophagus, or difficulty passing the endoscope through the LES due to increased pressure. Endoscopy is also used to evaluate patients after achalasia treatment to rule out gastroesophageal reflux. An additional benefit is the ability to implement therapeutic methods using endoscopy, such as pneumatic dilation of the esophagogastric junction (EGJ) or botulinum toxin injections. [5,7]

Esophageal fluoroscopy allows visualization of the shape of the organ and highlights any possible narrowing.
A characteristic finding is the "bird-beak" appearance. The sensitivity of fluoroscopy is limited, ranging from 56% to 69% in patients with achalasia. Sensitivity can be improved by evaluating esophageal passage after 1 and 5 minutes. In most healthy individuals, barium exits the esophagus after 1 minute and in all cases after 5 minutes. In diagnosing untreated achalasia, a barium column height of 5 cm at 1 minute has a sensitivity of 94% and a specificity of 71%, while a height of 2 cm at 5 minutes has a sensitivity of 85% and a specificity of 86%. [7,9] Based on radiological examination, four stages of esophageal spasm can be distinguished:

- Stage I: X-ray without abnormalities
- Stage II: Esophageal width <4 cm
- Stage III: Esophageal width 4-6 cm
- Stage IV: Esophageal width at least 8 cm or sigmoid esophagus [4]

Treatment

POEM

Peroral endoscopic myotomy (POEM) is a new type of endoscopic myotomy introduced in 2009. [10] It is the first-line treatment for patients with type III achalasia, where the highest success rate is achieved. [7] POEM involves inserting an endoscope into the submucosal tunnel of the esophagus and then cutting the fibers of both layers of smooth muscle in the lower part of the anterior esophageal wall and the cardia. [11] It has been demonstrated that POEM resulted in a reduction in dysphagia severity and a decrease in LES pressure. [12]
In a single-center prospective cohort study, the effectiveness of POEM was evaluated in 610 patients with achalasia over a 10-year period. The authors report an adverse event rate of 3.4%. Gastroesophageal reflux symptoms developed in 20.5% of patients after POEM. The researchers assessed POEM as an effective and safe method for treating achalasia, with a 90% success rate over a 5-year period. [13]
In randomized multicenter clinical trial comparing the effectiveness of POEM and pneumatic dilation in patients with achalasia, POEM (92%) was found to be significantly more effective than pneumatic dilation (54%). No differences were found in IRP values or barium column height between the two groups. The incidence of GERD was higher among patients who underwent POEM(41%) in comparison to those who underwnt PD (7%). [10]
POEM offers a less invasive alternative to traditional surgical methods for treating achalasia, such as open or laparoscopic myotomy. It has shown superior efficacy in reducing symptoms and improving patient outcomes. While both POEM and pneumatic dilation are effective, POEM is often preferred for its lower complication rates and long-term success.

Pneumatic dilation

Pneumatic dilation (PD) uses graded size polyethylene balloons (3.0, 3.5, and 4.0 cm) for treating achalasia and can be performed with or without fluoroscopy. [7] It is the most commonly used method for treating achalasia worldwide. [10]

In a study comparing the effectiveness of pneumatic dilation with laparoscopic Heller myotomy (LHM), 201 patients were evaluated, with 95 undergoing PD. The effectiveness of PD was 90% after one year and 86% after two years, compared to corresponding rates of 93% and 90% for LHM. A complication of esophageal perforation was noted in 4% of patients who underwent PD. [14]

The risk of esophageal perforation during pneumatic dilation depends on the size of the balloon used. The risk is 1% for a 30 mm balloon and 3.2% for a 35 mm balloon. The safety of the procedure increases when gradual dilation is applied. [7]

In a publication discussing the outcomes of treatment using pneumatic dilation in a group of 209 patients, it was reported that 66% of patients did not require further intervention after PD. A repeat procedure was performed in 23% of the patients involved in the study after 79 ± 8 months. The characteristics of patients who did not benefit from the first procedure were also discussed. These were more often younger individuals with higher LES pressure after treatment. Studies have shown that higher LES pressure after pneumatic dilation is a predictive factor for symptom recurrence. [15]

The authors of a multicentre study concluded that both Heller myotomy and pneumatic dilation can be preferred methods for first-line treatment in patients with achalasia, and their effectiveness is comparable. However, 25% of patients who underwent PD required repeat procedures. [16]

Laparoscopic cardiomyotomy

Laparoscopic cardiomyotomy involves a longitudinal incision through all the transverse fibers of the circular muscle layer down to the submucosal layer. The extent of the procedure should cover 2-3 cm above the narrowing and 1-1.5 cm in the distal direction. To minimize the risk of GERD, it is recommended to complement the myotomy with a fundoplication procedure, most commonly using the Dor technique. [17] According to ACG guidelines, it is recommended to perform fundoplication using the Dor or Toupet technique. [5]

Surgical myotomy is the treatment of choice in the following groups of patients: individuals younger than 40 years of age, patients who do not respond to less invasive treatments, patients at higher risk of failure with less invasive methods, and patients for whom surgical myotomy is the preferred method. [12]

In a meta-analysis comparing Heller myotomy and pneumatic dilation, myotomy was found to be the more effective method, but both methods demonstrated similar safety profiles. The Heller method was supplemented with an antireflux procedure. The authors found that the incidence of GERD complications was similar for both procedures. In both LHM (Laparoscopic Heller Myotomy) and PD (Pneumatic Dilation), the most serious complication was esophageal perforation, and its frequency did not significantly differ depending on the procedure performed. [18]

A review of 105 articles involving 7,855 patients who underwent endoscopic botulin toxin injection (EBTI), endoscopic balloon dilation (EBD) or surgical myotomy with or without a fundoplication compared the safety and efficacy of these three treatment methods. Laparoscopic myotomy combined with an antireflux procedure achieved the best symptom relief (90%) and had a low complication rate (6.3%). Adding fundoplication to laparoscopic

myotomy reduced the incidence of postoperative gastroesophageal reflux (GER) significantly (31.5% without fundoplication vs. 8.8% with). [19]
Laparoscopic myotomy is a highly effective treatment for achalasia, offering significant symptom relief and a low complication rate. When combined with an antireflux procedure, such as fundoplication, it provides superior outcomes compared to other methods.

Botulinum toxin injection

Botulinum toxin is a neurotoxic protein produced by the bacterium *Clostridium botulinum*. It is one of the most potent toxins known and functions as a powerful neurotoxin by blocking the release of acetylcholine at the neuromuscular junction. This action prevents nerve signals from stimulating muscle contractions, leading to muscle paralysis. By inhibiting the release of acetylcholine, botulinum toxin effectively reduces the stimulation of smooth muscle cells in the LES. This leads to a decrease in muscle contraction and, consequently, a reduction in the high resting pressure of the LES and the abnormal contractions that characterize achalasia. Botulinum toxin injections are typically used as a temporary treatment for achalasia. [5]
Botulinum toxin is administered using sclerotherapy needles in four quadrants, slightly above the esophagogastric junction or the Z-line, at a dose of 20-25 units per quadrant. [20]
In a meta-analysis evaluating 9 studies discussing the role of botulinum toxin in the treatment of achalasia, the effectiveness of the method was described at various time points. At 1 month, the effectiveness was reported as 78.7%, at 3 months as 70%, and at 12 months as 40.6%. Additionally, 46.6% of patients required at least one additional botulinum toxin injection.
Botulinum toxin injection is considered a safe method. The most commonly reported side effect is transient chest pain. [20]
Studies report that subsequent botulinum toxin injections result in less significant improvement, likely due to the development of antibodies that diminish its effect. Currently, it is believed that this method should be reserved for patients who are not eligible for other treatment options, such as POEM or laparoscopic myotomy. [21] It has been observed that a higher response rate to treatment occurred in patients over the age of 50. The reasons for this phenomenon are not known. [22]
In a study comparing botulinum toxin injection and laparoscopic myotomy with fundoplication, the following conclusions were drawn: effectiveness after 6 months was higher for laparoscopic myotomy (82% vs. 66%), the reduction in esophageal diameter was more significant after laparoscopic myotomy (10% vs. 5%), and the decrease in LES pressure was similar for both methods. Absence of achalasia symptoms 2 years after treatment was observed in 87,5% of patients after laparoscopic myotomy and 34% of patients after botulinum toxin injection. [22]
While BT injection can provide symptom relief and is generally considered safe, its effects are often short-lived, and repeated injections may be needed due to the development of antibodies that can diminish effectiveness over time. The treatment is typically reserved for those unable to undergo other therapies.

Conclusion

Overall, POEM and laparoscopic myotomy are the most effective long-term treatments, while botulinum toxin injections and pneumatic dilation are less invasive but may require ongoing management. The choice of treatment depends on patient-specific factors, including age, health status, and the severity of the disease.

Disclosure

Author contributions:

All authors contributed to the article. Conceptualization: Nadia Miga-Orczykowska; methodology: Nadia Miga-Orczykowska; software: Nadia Miga-Orczykowska; check: Nadia Miga-Orczykowska; formal analysis: Nadia Miga-Orczykowska; investigation: Nadia Miga-Orczykowska; resources: Nadia Miga-Orczykowska; data curation: Nadia Miga-Orczykowska; writing-rough preparation: Nadia Miga-Orczykowska

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