

Treatment of Achalasia in the Evidence-Based Medicine Era – A Quest in Search for a Proper Attitude by Reviewing the Present Guidelines

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Rezumat

Tratamentul acalaziei în era medicinei bazate pe dovezi – în căutarea unei atitudini corecte prin revizuirea ghidurilor prezente

Cea mai bună modalitate de a începe o lucrare ca aceasta este cu o citare a lui W. Edwards Deming: “Fără date, ești doar o altă persoană cu o opinie”. În era medicinei bazate pe dovezi (EBM), fiecare procedură chirurgicală trebuie să fie susținută de date statistice solide pentru a oferi pacienților noștri cel mai bun tratament. Dar este EBM întotdeauna calea către adevăr? Am decis să analizăm literatura de specialitate pentru acalazie și să vedem dacă ghidurile și datele sunt suficient de fiabile pentru a justifica o anumită atitudine. Practic, ne-am angajat în acest efort nu pentru că nu avem încredere în declarațiile ghidurilor, ci pentru a vedea dacă un chirurg poate găsi singur atitudinea potrivită în această boală. Acalazia este o tulburare de motilitate a esofagului caracterizată prin relaxarea deficitară a sfincterului esofagian inferior care are ca rezultat disfagia. Există mai multe metode de tratament, cu diverse afirmații în ghiduri. În prezent, fiecare tratament ar trebui să fie susținut de date și statistici, medicina bazată pe dovezi fiind obligatorie atunci când o metodă este preferată. Acest articol trece în revistă mai multe studii și, de asemenea, ghidurile disponibile în căutarea unui răspuns la întrebarea care procedură este cea mai bună.

Cuvinte cheie: acalazie, tratament, medicină bazată pe dovezi, ghiduri

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Abstract

The best way to start a paper like this is with a citation from W. Edwards Deming: “Without data, you’re just another person with an opinion.” In the era of Evidence-Based Medicine (EBM) every surgical procedure has to be backed up by solid statistical data to offer our patients the best treatment. But is EBM always the path to truth? We decided to analyze the literature for achalasia and see if the guidelines and the data are reliable enough to justify a certain attitude. Practically, we engaged in this endeavor not because we do not trust the statements of the guidelines, but to see if a surgeon can find by themselves the proper attitude in this disease. Achalasia is a motility disorder of the esophagus characterized by deficient relaxation of the inferior esophageal sphincter that results in dysphagia. There are several methods of treatment, with various statements in the guidelines. Currently, every treatment should be sustained by data and statistics, evidence-based medicine being mandatory when a method is preferred over another. This article reviews several studies and also the available guidelines in search for an answer to the question which procedure is the best.

Key words: achalasia, treatment, evidence-based medicine, guidelines

Introduction

In 1672 Thomas Willis described achalasia for the first-time and proposed dilatation treatment with cork-tipped whalebone, reporting a successful case in “*Pharmaceutice Rationalis*”. The disease was rare, and the first attempt to treat it surgically was registered in 1901 by Gottstein who reported an anterior extra mucosal myotomy. In 1913, Heller introduces the anterior and posterior myotomy, but other surgeons of the time considered that the proper treatment should be the esophagogastronomy, Heyrovsky (1913) and Grondahl (1916) stated that esophagogastronomy without esophageal resection is the procedure for that particular disease. The results were not very promising and, in 1923, Zaaïjier returns to the anterior myotomy. L. Jacob and Fontaine first proposed the thoracic approach for myotomy in 1951. In 1962, Dor introduces the anterior fundoplication, which will be later used in the surgical treatment of achalasia.

1975 is the year when a Romanian surgeon, Dan Gavriiliu, proposes a “triple operation” for achalasia – anterior myotomy, anterior fundoplication, and anterior extra mucosal pilorectomy to ensure a proper gastric emptying.

The first endoscopic treatment was described in 1987 by Levine who entered the

battlefield with endoscopic dilatation, which is still competing with surgery as the first method of treatment.

After the introduction of laparoscopic surgery, Shimi (1991) reported the first laparoscopic myotomy, followed by Pellegrini (1992) with thoracoscopic myotomy. In 1995 Swanstrom and Pennings associated the Toupet fundoplication to esophageal myotomy for the first time. In Romania, the first reports of laparoscopic treatment of achalasia were published by Duca and Tarcoveanu in 1995.

Thirty years after Levine, another endoscopist, Inoue, came back into force in 2010 and discovered Per Oral Esophageal Myotomy (POEM).

Materials and Method

We performed a MEDLINE/PubMed to identify relevant international guidelines, and original publications on the search for therapeutic options for achalasia, articles which were extracted and fully accessed. In particular meta-analyses of treatment outcomes for achalasia were sought including older studies.

Finally, we generated a comprehensive narrative review and a comparison of guidelines by summarizing the most updated data on the management of achalasia focusing on

the latest updates from the last 10 years. Three inclusion criteria were applied: the articles must be available full text, written in English and pertaining to adult patients with achalasia. The exclusion criteria were as follows: published in languages other than English, animal studies, studies of adolescents or children, medical treatment and esophagectomy.

Results

Current Stage

One must not forget that the primary goal of the treatment is to eliminate the dysphagia by eliminating the relaxation disorder of the lower esophageal sphincter, allowing the food to pass through the hypo/a peristaltic esophagus under the force of gravity.

Taking that into consideration, we identified the following types of treatment for achalasia:

1. Medical treatment – calcium blockers, nitrates – low efficacy
2. Endoscopic treatment:
 - a. Botulinum toxin injection (BTX)
 - b. Pneumatic dilatation (PD)
 - c. Peroral esophageal myotomy (POEM)
3. Surgical treatment:
 - a. Heller myotomy - laparoscopic/ thoracoscopic/open with/without anti-reflux valve
 - b. Esophagectomy – rare, reserved for severe cases, failures for other types of treatment

There are several important guidelines at the moment, the International Society for Diseases of Esophagus (ISDE), the SAGES (Society of American Gastrointestinal and Endoscopic Surgeons) guidelines, the ACG (American College of Gastroenterologists) guidelines, the American Society for Gastrointestinal Endoscopy (ASGE), “2019 Seoul Consensus on Esophageal Achalasia Guidelines” and the European guidelines on achalasia, stating almost the same facts, but not identical, based on a thorough research of literature concerning the topic and we will

come back to them at the end of this paper. We decided not to study the literature for medical treatment and esophagectomy, seldom used in the management of achalasia, and concentrate our efforts on the other methods, which are used more frequently.

Description of Present Options of Treatment

Botulinum toxin injection

The procedure implies the injection of botulinum toxin at the level of lower esophageal sphincter and a subsequent acetylcholine release blocking with the reestablishment of the balance between neuro mediators. It determines an inflammatory reaction at this level. It has a limited therapeutic value, only 30% of the patients will be symptom-free after one year of treatment, several injections are required. The method is addressed to patients who cannot undergo the definitive therapies, considered having a high risk for dilatation or surgery (1).

Pneumatic dilatation

A balloon is inflated at the level of esophago-gastric junction under endoscopic guidance until the circular muscular fibers are ruptured with mucosal integrity preservation. The success rate is 70-80%, but almost 50% of the patients will require more than one dilatation. The esophageal perforation rate is about 5%. The incidence of post-procedural reflux disease is 30%. It appears to be a procedure addressed to patients with high risk for surgery (2).

Per oral esophageal myotomy (POEM)

It is an endoscopic procedure performed under general anesthesia with endotracheal intubation. A submucosal tunnel is created, and the circular fibers are severed beginning 7 centimeters above the esophagogastric junction until 3 centimeters below that level, followed by the mucosal closure. It is, though appealing, a difficult technique with a long learning curve. About 50% of the patients will experience reflux disease after the procedure (3,4).

Surgical treatment – myotomy

The procedure is based on the circular fibers cutting. There are several approaches – open/ minimally invasive, thoracic/ abdominal. The common approach is laparoscopic, where a 5-6 centimeters myotomy is performed on the esophagus associated with a 1.5-2 centimeters myotomy on the stomach. The results are very good, 85-95% success rate, with 20% risk of reflux disease after the operation. Association of the anti-reflux valve was a subject of debate for many years, currently, an anterior fundoplication being recommended (5).

Review of the Literature

Faced with so many options, both patients and doctors may wonder which the right way is. Evidence-based medicine should shed light on the matter and clear the situation. The importance of EBM was emphasized by David Sackett, quoting: “Evidence-based medicine is the integration of best research evidence with clinical expertise and patient values”.

There are many studies comparing different treatment options. The questions to be answered can be summarized as follows:

1. Botulinum toxin injection (BTX) or pneumatic dilatation (PD)?
2. Botulinum toxin injection (BTX) or myotomy?
3. Pneumatic dilatation (PD) or myotomy?
4. Laparoscopic or thoracoscopic myotomy?
5. Laparoscopic Heller myotomy (LHM) - with or without fundoplication?
6. Type of anti-reflux valve associated to the myotomy?
7. POEM or myotomy?

Botulinum toxin injection or pneumatic dilatation?

Some randomized trials compared the two methods. First, published by Vaezi et al (6) in 1999 stated that pneumatic dilatation (PD) is more effective when compared to botulinum toxin injection (BTX) when the results are assessed after 1 year after treatment, symptom improvement being parallel with the correction of the manometry parameters. The

second, published by Mikaeli et al (7) in 2001, found the same thing, that the pneumatic dilatation is better, one dilatation being as effective as two botulinum toxin injections. PD and BTX treatment are equally effective in the short term, while PD is the more effective endoscopic treatment in the long term (greater than six months) (8).

Botulinum injection (BTX) or myotomy?

A randomized controlled trial published by Zaninotto et al (9) in 2004 found that surgical myotomy is as safe as botulinum toxin injection, but myotomy offers a real chance for a definitive cure to the majority of patients. Assessing the disease-free patients two years after treatment, they found a statistically significant difference, 87.5% after surgery versus 34% after botulinum injection ($p < 0.05$). The conclusion of the study was that botulinum toxin injection should be offered as an alternative treatment to high-risk patients or as an intermediate step to more effective methods such as pneumatic dilatation or surgery.

In 2019 Seoul Consensus on Esophageal Achalasia Guidelines botulinum toxin injection is recommend for achalasia patients whose general condition renders them unsuitable for surgery (10).

Pneumatic dilatation or myotomy?

This is the topic that generated the most intense debate. In 1995, Patti et al (11) published a prospective study based on patient and/or doctor preference. Their conclusion was that myotomy is superior to pneumatic dilatation from dysphagia amendment and post-procedural reflux.

A retrospective study published in 2002 included 249 patients followed for more than 5 years. The results showed that after 15 years of follow-up after dilatation the success rate is quite low, around 40%, the average number of procedures required is 4 (12).

The European Achalasia Trial was a large multicenter randomized trial that published the first results in 2011 (13). After two years of follow-up the group found comparable results for myotomy and pneumatic dilatation, but

better results for patients under the age of 40 after myotomy.

During the same year, 2011, Reynoso et al (14) compared both methods stratifying the patients after the severity of the illness. They found that myotomy has comparable or superior results in the group of patients with the mild and moderate disease. The pneumatic dilatation had comparable or superior results for patients with advanced or extreme disease. The same study showed that esophageal perforation is significantly higher after pneumatic dilatation (2.4% for pneumatic dilatation versus 0.4% after laparoscopic myotomy, $p < 0.001$).

In 2013, the European Achalasia Trial revealed more results showing that the outcomes of treatment depend on manometric subtype. Both methods had a higher success rate in type II achalasia, compared to types I and III. In type II, pneumatic dilatation had a better outcome. In type III, myotomy seemed to offer better results (15).

Interesting data came from a single-center experience retrospective study that showed results after a long-term follow-up of patients after pneumatic dilatation. It turned out that recurrence is frequent after dilatation, for good long-term results close follow-up and repeated procedures are necessary (16).

If the surgeon reading this article feels confused and eager for a conclusion on this topic, what follows will probably only deepen the bewilderment.

Several papers stated that pneumatic dilatation is the first option in achalasia management and surgery should be reserved to failures after dilatation (17,18), but myotomy performed after endoscopic procedures (pneumatic dilatation, botulinum injection) has worse results with more complications and worse outcome (19,20).

There were high expectations from meta-analysis results. In 2012 a large meta-analysis including 36 randomized studies (2001-2011), 3211 patients with 5 years follow-up was published (21). The results showed that myotomy offers better long-term results, but

with a significantly higher risk of esophageal perforation (4.8% vs. 2.4%, $p < 0.05$). One year later, in 2013, another meta-analysis including 3 randomized studies (2007-2011), 346 patients with one-year follow-up was published (22), the conclusion was the same, myotomy offers better results, with a significantly lower risk of esophageal perforation (0.6% vs. 4.8%, $p = 0.04$). The difference between the two studies in terms of risk can be explained; the second study included more recent papers with series coming probably from the fact that groups surpassed the initial surgical experience.

Those results were confirmed in 2015 by another study by Markar et al (23), stating that surgery is more effective, because dilatation often needs to be repeated. The risk for esophageal perforation can be managed more easily during surgery.

Finally, the European Achalasia Trial revealed (24) the analysis that took into consideration the Eckardt Score, necessity of reintervention, LES pressure measurement, esophageal emptying, and complication rate. Both methods, myotomy and pneumatic dilatation, had a comparable success rate, but 25% of patients with dilatation required reintervention. The conclusion was that any of those two can be first intention treatment.

If the reader feels that it is a draw, one should know that the debate is not over yet. The Centre for Reviews and Dissemination from the University of York in cooperation with National Institute for Health Research started in January 2016 a new project, PROSPERO – the international prospective register of systematic reviews, the objective being the investigation of the standard of clinical and patient-reported outcome reporting in achalasia randomized controlled trials. The conclusions were that, for the treatment of esophageal achalasia, LHM and PD were found to be similar in terms of their long-term efficacy, as well as in terms of the post-treatment GER rates. However, the perforation rate appears to be lower when LHM is employed (25).

Laparoscopic or thoracoscopic myotomy?

That debate was quickly ended by a retrospective study published by Patti MG (26), which concluded that laparoscopic myotomy is superior in terms of postoperative morbidity, post procedural reflux disease, with a shorter hospital stay.

Laparoscopic myotomy - with or without fundoplication?

A randomized control trial from 2004 (27) stated that the association of an antireflux fundoplication reduces significantly the risk of post-myotomy reflux, with no differences in dysphagia improvement. Another randomized control trial published in 2006 (28) concluded that the association fundoplication increases the period with good quality of life and is cost-effective after ten years follow-up. Currently, minimally invasive Heller myotomy with partial fundoplication is the standard surgical treatment of achalasia (29). On the basis of these data, LHM plus partial fundoplication is considered in most centers worldwide as the gold standard modality for the approach to achalasia.

Type of anti-reflux valve associated to the myotomy?

It was demonstrated that fundoplication is beneficial in association with myotomy, but the type of valve that has to be created was another topic for debate. A randomized prospective study from 2008 (30) compared Nissen fundoplication with Dor in association to myotomy. There were no differences in the incidence of postoperative reflux, but dysphagia occurred more frequent after Nissen fundoplication (15% vs 2.8%, $p < 0.001$). A multicenter, prospective, randomized-controlled trial from 2012 (31) compared Toupet valve with Dor, with no differences in the incidence of postoperative reflux and dysphagia. Technically the Dor fundoplication is a more standardized procedure, is easier to perform, on the other hand, the Toupet fundoplication is less standardized and technically demanding. In summary the

choice of the partial fundoplication should be left to surgeon experience (32).

POEM or myotomy?

POEM was recently discovered, so the numbers of cases and centers where it is performed are small. Only retrospective studies were available. A paper published in 2013 by Hungness et al (33) compared the two methods and found no differences in terms of length of myotomy, complication rate or hospital stay. The success rate after POEM was high, 89% after 6 months, but 39% of patients developed pneumoperitoneum after the procedure, resolved with Verres needle. Two other studies (34,35) revealed the same postoperative results and the same incidence of postoperative reflux, but a shorter hospital stay for POEM. In a study published in 2019 (36), POEM demonstrated similar results compared to laparoscopic Heller myotomy with regards to improvement of dysphagia, post procedure reflux, and surgical time, with the benefit of shorter length of hospital stay. Therefore, POEM can be considered an option for patients with achalasia.

At the end of our search, we tried to summarize all the debates and the results (Table 1).

Discussion

After these conclusions drawn from the literature review, we returned to the existent and most used guidelines in the past 10 years.

Table 1. Questions and answers from our own research regarding the methods of treatment of achalasia

QUESTION	ANSWER
Botulinum injection or pneumatic dilatation?	Pneumatic dilatation
Botulinum injection or myotomy?	Myotomy
Pneumatic dilatation or myotomy?	Unclear result, some studies favor myotomy
Laparoscopic or thoracoscopic myotomy?	Laparoscopic myotomy
Laparoscopic myotomy - with or without fundoplication?	Laparoscopic myotomy with fundoplication
Anterior or posterior fundoplication?	Dor (anterior) fundoplication
POEM or myotomy?	Unclear result, further studies needed

The International Society for Diseases of Esophagus (ISDE) Guidelines Committee proposed and endorsed the Esophageal Achalasia Guidelines (I-GOAL) in 2018 to offer clinicians and patients with an up-to-date framework for making informed decisions on managing the disease. Out of 3183 articles were initially retrieved (including 61 articles added with the updated 2017 search) and 128 were added by the panelists; 22 articles were added after the updated literature search in January 2018. In total, 466 articles were considered for the preparation of the Guidelines (37).

The “2019 Seoul Consensus on Esophageal Achalasia Guidelines” were developed based on evidence-based medicine; the Asian Neurogastroenterology and Motility Association and Korean Society of Neurogastroenterology and Motility served as the operating and development committees, respectively. The Medline, EMBASE, and Cochrane Library databases were searched for all relevant studies published during the period 2000-2018 and the development of the guidelines began in June 2018, and a draft consensus based on the Delphi process was achieved in April 2019. The guidelines consist of 18 recommendations: 2 pertaining to the definition and epidemiology of achalasia, 6 pertaining to diagnoses, and 10 pertaining to treatments. The endoscopic treatment section is based on the latest evidence from meta-analyses. The treatment recommendations for primary esophageal achalasia were classified as “strong for” “weak for” “weak against” “strong against” or “no recommendation”. The evidence level, clinical applicability, and benefits and harms were the evaluation criteria (10).

The European Guidelines on achalasia published in 2020 (8) are the result of an electronic literature search performed on 18 October 2018 using MEDLINE, EMBASE (accessed via Ovid), The Cochrane Database of Systematic Reviews (The Cochrane Library) and the Cochrane Central Register of Controlled Trials (CENTRAL) without restrictions of language or publication year based on a systematic review of the literature. The certainty of evidence was assessed using the

GRADE methodology (www.gradeworking-group.org) and, for each outcome, graded into four levels: high, moderate, low or very low quality. Based on the certainty of evidence and the balance between desirable and undesirable outcomes, patient values and preferences, applicability, feasibility, equity and costs/resources, recommendations were categorized into four final categories (strong or conditional recommendations in favor of or against an intervention).

The American Society for Gastrointestinal Endoscopy (ASGE) guideline on the management of achalasia was prepared by a working group of the Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy. It includes a systematic review of available literature along with guidelines for the role of endoscopy in management of achalasia. After evidence synthesis, recommendations were drafted by the full panel during a face-to-face meeting on March 16, 2018, and approved by the Standards of Practice committee members and the ASGE Governing Board. The aim of this document is to provide evidence-based recommendations for the treatment of achalasia, based on an updated assessment of the comparative effectiveness, adverse effects of achalasia therapies (38).

In the ACG guidelines (39), issued in 2020, the resultant conclusions were based on the best available evidence or, in the absence of quality evidence, expert opinion. The statements of interest for this paper are that either laparoscopic myotomy with partial fundoplication or pneumatic dilatation can be recommended as initial therapy at those patients fit and willing to undergo surgery (strong recommendation, moderate-quality evidence), in high-volume centers of excellence (strong recommendation, low-quality evidence), but the choice of initial therapy should be guided by patients' age, gender, preferences and local institutional expertise (weak recommendation, low-quality evidence). Botulinum toxin injections are recommended for patients unfit for surgery or pneumatic dilatation (strong recommendation, moderate-quality evidence).

The SAGES guidelines reviewed and approved by the Board of Governors of the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) in Apr 2021 (40), are based on a systematic review of the literature, performed by the SAGES Guidelines Committee to inform the panel's evidence-based deliberations and recommendations (41). The statements of interest are that laparoscopic myotomy with partial fundoplication should be considered the treatment of choice to treat achalasia (strong recommendation, high-quality of evidence), when performed by appropriately trained surgeons offers best results (strong recommendation, high-quality of evidence). The surgical treatment should provide laparoscopic approach (strong recommendation, moderate-quality evidence), partial (weak recommendation, low-quality evidence) fundoplication (strong recommendation, high-quality of evidence), with no recommendation for anterior or posterior type valve. Pneumatic dilatation should be considered in selected non-surgical patients (who are unwilling or unfit for surgery) (strong recommendation, high-quality of evidence). Botulinum toxin injection should be reserved for patients who are poor candidates for dilatation or surgery (strong recommendation, high-quality of evidence).

In search for an answer to the question which procedure is the best, we made a

comparison of guidelines in the last decade (*Table 2*), aimed to provide an overview of the evolution of the treatment for esophageal achalasia, from the open to the minimally invasive approach.

The comparison of new and updated guidelines (*Table 3*) summarize the recent advancements and the evolution of achalasia therapy towards a better outcome, from Conventional Treatment to Peroral Endoscopic Myotomy (POEM).

The author's comment is, that in spite of searching the same database, the statements are not identical, surgeons still favor laparoscopic myotomy with partial fundoplication, and that may be a bias even in working groups designed to elaborate guidelines. Another interesting fact is, even using the same grading system – GRADE – for evaluating the quality of evidence, the results were different, but not in a manner that changes deeply the recommendations.

High-volume centers provide expertise and concentrate highly specialized surgeons in a specific domain. In the modern era, besides accumulating experience with the number of cases treated, concentrating the study in the same domain is of great benefit and requires time and ultra-specialization. Even in the EBM era, studies and guidelines addressed to the same disease might be biased by the characteristics of the working groups and release non-

Table 2. Comparison of guidelines

	SAGES (2011)			ACG (2013)			ISDE 2018		
	Statement	R	QE	Statement	R	QE	Statement	R	QE
Laparoscopic Myotomy (LM)	Treatment of choice	Strong	High	First intention treatment	Strong	Moderate	Chicago type I and II	Strong	Moderate
Fundoplication	Yes	Strong	High	First intention treatment	Strong	Moderate	Partial fundoplication	Strong	Moderate
Partial	Yes	Low	Weak	First intention treatment	Strong	Moderate	Partial fundoplication	Strong	Moderate
Trained surgeon/ high-volume center	Yes	Strong	High	Yes	Strong	Low	No evidence		
Pneumatic dilatation (PD)	Non-surgical patients	Strong	High	First intention treatment	Strong	Moderate	Graded PD is an effective treatment	Strong	Moderate
Botulinum toxin injection	Patients unfit for LM or PD	Strong	High	Patients unfit for LM or PD	Strong	Moderate	Patients unfit for LM or PD		
POEM	Further studies needed			No evidence			Effective therapy	Conditional	Very low

R = recommendation, QE = quality of evidence

Table 3. Comparison of new and updated guidelines

	SAGES (2021)			ACG (2020)			European Guidelines (2020)			Seoul 2019			ASGE 2020		
	Statement	R	QE	Statement	R	QE	Statement	R	QE	Statement	R	QE	Statement	R	QE
Laparoscopic Myotomy (LM)	Treatment of choice	Strong	High	First intention treatment	Strong	Moderate	Treatment of choice	Strong	High	First-line therapy	Weak	Moderate	Shared decision-making between the patient and Provider for type I and II	Strong	Moderate
Fundoplication	Yes	Strong	High	First intention	Strong	Moderate	Treatment of choice	Strong	High	First-line therapy	Strong	Low			
Partial	Yes	Low	Weak	First intention	Strong	Moderate	Treatment of choice	Strong	High	First-line therapy	Strong	Low			
Trained surgeon/high-volume center	Yes	Strong	High	Yes	Strong	Low	Yes	Strong	Moderate	No evidence	No evidence	No evidence	No evidence	No evidence	No evidence
Pneumatic dilatation (PD)	Refuse surgery/non-surgical patients	Strong	High	First intention treatment	Strong	Moderate	First intention treatment	Strong	High	Initial treatment	Strong	Moderate	In patients with failed initial myotomy	Weak	Low
Botulinum toxin injection	Patients unfit for LM or PD	Strong	High	Patients unfit for LM or PD	Strong	Moderate	Patients unfit for LM or PD	Conditional	Moderate	Patients unfit for LM or PD	Strong	Moderate	Unfit for other definitive	Strong	Moderate
POEM	First intention treatment for Type III achalasia	Strong	Moderate	Treatment of choice in Type III achalasia	Strong	Moderate	Effective treatment	Strong	High	More studies are required	Strong	Low	Type III achalasia	Weak	Low

R = recommendation, QE = quality of evidence

identical statements. But guidelines are the best we have at the moment and the surgeons should follow them in order to standardize the treatment in order to achieve the best results.

Conclusion

There are two main conclusions that can emerge from this study.

One is more general, and is related to the methodology of the studies. Faced with so many literature resources, a surgeon should spend a lot of time for individual research in order to reach the best answer and the best treatment for a certain case by himself. Guidelines can provide valuable information, but sometimes they are different. Literature should be monitored periodically by the working groups for new evidence and the guidelines updated in order to offer similar statements, otherwise, a physician could get confused.

The other conclusion is focused on the achalasia treatment options. POEM and LHM seem to be comparable to each other, and both may be more effective than PD, in the definitive treatment for patients with achalasia, while Botulinum toxin retains a role in those with poor life expectancy. Laparoscopic myotomy with partial fundoplication still remains the best option for treatment and preferred by most surgeons, but POEM seems to be a promising procedure, with outcomes comparable to conventional procedures.

Conflicts of Interests

The authors declare that they have no conflict of interest.

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