# Treatment and surveillance strategies in achalasia: an update

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**Abstract** | Controversy exists with regard to the optimal treatment for achalasia and whether surveillance for early recognition of late complications is indicated. Currently, surgical myotomy and pneumatic dilation are the most effective treatments for patients with idiopathic achalasia, and a multicenter, randomized, international trial has confirmed similar efficacy of these treatments, at least in the short term. Clinical predictors of outcome, patient preferences and local expertise should be considered when making a decision on the most appropriate treatment option. Owing to a lack of long-term benefit, endoscopic botulinum toxin injection and medical therapies are reserved for patients of advanced age and those with clinically significant comorbidites. The value of new endoscopic, radiologic or surgical treatments, such as peroral endoscopic myotomy, esophageal stenting and robotic-assisted myotomy has not been fully established. Finally, long-term follow-up data in patients with achalasia support the notion that surveillance strategies might be beneficial after a disease duration of more than 10–15 years.

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## Introduction

Idiopathic achalasia is a rare primary motility disorder of the esophagus with an estimated incidence of 1 case per 100,000 of the general population.[1] The disease is characterized clinically by symptoms of dysphagia, regurgitation, weight loss and chest pain. These symptoms are primarily caused by incomplete relaxation of a frequently hypertensive lower esophageal sphincter (LES) and to some extent by a lack of peristalsis in the tubular esophagus. The diagnosis of achalasia is suspected clinically on the basis of the above symptoms and confirmed by diagnostic tests, such as a barium swallow, endoscopy, standard esophageal manometry or high-resolution esophageal manometry. Although the exact pathogenesis of the disease remains unclear, the apparent esophageal motor abnormalities are probably the result of autoimmune-mediated destruction of inhibitory neurons by an unknown, possibly viral, trigger in genetically susceptible individuals.[2,3] Since the underlying defect cannot be reversed, treatment of achalasia remains palliative with the goal to improve clinical symptoms and to restore quality of life. This goal can be achieved either by medical therapy or by more-invasive measures, such as surgical myotomy or pneumatic dilation. However, the efficacy of these treatment options varies and, even for the most effective treatments, no unanimous opinion exists as to which option should be preferred. In addition, surveillance strategies remain a matter of debate and only now are discussions emerging about whether surveillance for cancer, late complications and early recurrence of symptoms should be performed.

**Competing interests**
The authors declare no competing interests.

## Tools for diagnosis and monitoring

A number of diagnostic tools are available to confirm the suspicion of idiopathic achalasia, to guide treatment and to detect complications. The barium swallow is usually used as the first diagnostic test to facilitate diagnosis. Patients with achalasia typically show a smooth tapering of the distal esophagus, known as the 'birds beak', with proximal dilation of the esophagus and lack of peristalsis during fluoroscopy (Figure 1). A modification of this test, the timed barium swallow, may be preferred, since it has the additional advantage of quantifying esophageal emptying and can therefore be used as a simple and reproducible tool to assess outcomes after surgical or endoscopic treatment for the disease.[4,5] Other imaging studies, such as MRI, CT or transabdominal ultrasound can be used as an adjunct to the barium swallow to rule out neoplastic or infiltrative processes that can be the cause of pseudoachalasia, but these tests have no role in monitoring achalasia.[6,7]

In addition to the barium swallow, esophagogastroduodenoscopy (EGD) is an essential part of the initial work up, as it more reliably detects mucosal lesions that can cause pseudoachalasia. Furthermore, EGD might show esophageal dilation and retention of food or liquid in patients with achalasia, although it frequently reveals normal findings in those with an early stage of disease. EGD might be a valuable tool for the detection and treatment of late complications that can be a result of the disease itself (for example, megaesophagus or squamous cell carcinoma) or of successful treatment (for example, reflux esophagitis and peptic strictures).

Finally, esophageal manometry remains the gold standard for the diagnosis of achalasia and the procedure typically shows three cardinal features of the

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**Key points**

- There is controversy with regard to the optimal treatment for and surveillance of achalasia
- The most effective treatment modalities for achalsia are pneumatic dilation and surgical myotomy
- Comparative studies show equal efficacy of pneumatic dilation and surgical myotomy in the short term
- Patients undergoing pneumatic dilation require more frequent re-interventions than patients undergoing surgical myotomy
- Surveillance may lead to early recognition of cancer or late complications and should be considered after a disease duration of >10–15 years

disease: aperistalsis of the smooth muscle portion of the esophagus, incomplete LES relaxation and, frequently, an increased LES pressure. On the basis of conventional esophageal manometry readings, some authors have discussed manometric variants of achalasia, such as high-amplitude contractions (known as vigorous achalasia), the occasional occurrence of peristaltic waves or almost complete LES relaxation in the presence of aperistalsis.[8] Another subclassification system for achalasia that may have therapeutic implications was put forward after the introduction of high-resoluton manometry (HRM). Pandolfino *et al.* described three distinct variants of achalasia (Figure 2): type I representing classic achalasia with minimal esophageal contractility and low intraesophageal pressure, type II representing absent peristalsis and panesophageal pressure elevations, and type III representing lumen-obliterating esophageal spasm. In the study by Pandolfino *et al.*, patients with type II achalasia had the best overall treatment response, whereas patients with type III achalasia responded poorly to all types of therapy.[9] These findings were recently confirmed in patients with achalasia undergoing surgical treatment with Heller myotomy plus Dor fundoplication.[10] Independent of such clinical subtypes, a post-interventional LES pressure of <10 mmHg was shown to predict a favorable long-term treatment response and standard manometry is, therefore, still routinely used to monitor treatment success in patients with achalasia at many European centers.[11,12]

## Treatment options

Although progress has been made in our understanding of the pathophysiology of achalasia, treatment options remain strictly palliative. Current treatments aim to reduce distal esophageal obstruction, facilitate esophageal emptying (preventing stasis of food) and improve dilation of the esophagus. Such improvements will, in turn, lead to symptomatic relief of dysphagia and regurgitation, as well as weight gain. However, none of the available therapies has convincingly been shown to abolish the symptom of chest pain,[13] although a small study published in 2010 suggested that surgical myotomy may benefit some patients with this symptom.[14] Established treatments include pharmacologic and endoscopic therapies, but the most-effective treatments are pneumatic dilation and surgical myotomy.

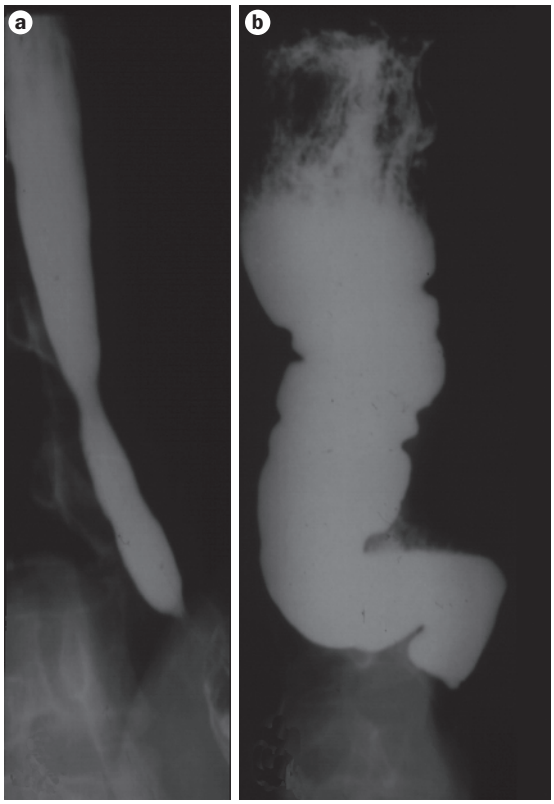


**Figure 1** | Radiographic images of two patients with achalasia after a barium swallow. **a** | Early achalasia. **b** | Advanced achalasia with megaesophagus.

### Pharmacologic treatment

Oral pharmacological therapy is the least effective of the available treatment options for achalasia. Such therapy is aimed at reducing LES pressure via smooth muscle relaxation, thereby facilitating esophageal emptying. Calcium-channel blockers and long-acting nitrates have been most commonly used, but are considered temporary measures at best.[15] These short-acting drugs are given sublingually before meals. In order to account for differences in pharmacokinetics, nifedipine is given 30–45 min before meals and at bedtime, whereas isosorbide dinitrate is given 10–15 min before meals.[16] The phosphodiesterase-5 inhibitor, sildenafil, has been found to lower LES tone and residual pressure as well as contraction amplitude in patients with achalasia, but comparative studies are not available.[17] The main limitations of these agents are their short duration of action, limited clinical efficacy and the frequent occurrence of adverse effects. The use of such therapy is, therefore, mainly reserved for patients who cannot tolerate more-invasive interventions or as a bridge to a more-definite therapeutic option.[18]

### Endoscopic treatment

Strictly speaking, botulinum toxin injection into the LES is a pharmacologic treatment, but it requires upper endoscopy for its application. Botulinum toxin is a potent neurotoxin that leads to blockade of the release of acetylcholine from excitatory motor neurons. When

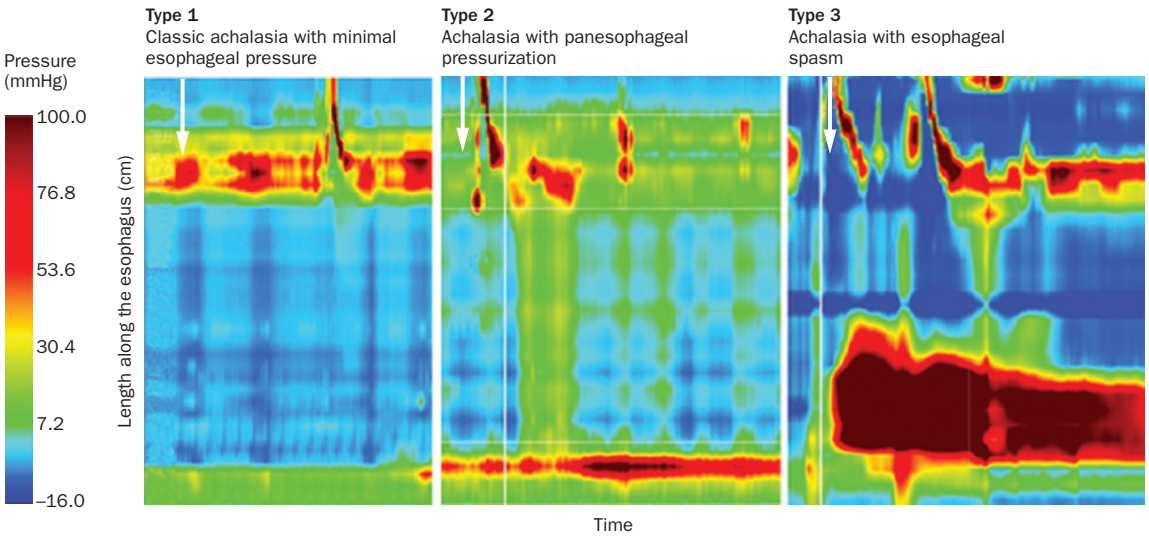


**Figure 2** | High-resolution manometry of the esophagus showing three different types of achalasia. White arrows indicate swallows. Courtesy of H. D. Allescher, Garmisch-Partenkirchen, Germany.

injected into the LES, botulinum toxin lowers the resting pressure by >50%, thereby facilitating esophageal emptying.[15] Pasricha *et al.* were able to demonstrate that this treatment can lead to impressive symptomatic improvement and improved esophageal emptying in about two-thirds of patients at 1-year follow-up.[19] However, subsequent studies have shown that response rates are not durable and symptomatic relapse occurs in more than 50% of patients after 1 year and is nearly universal after 2 years.[20,21] One randomized, controlled study showed that the two commercially available formulations of botulinum toxin (Botox®, Allergan, Irvine, CA, USA and Dysport®, Ipsen, Milan, Italy) are equally effective but need to be given in different doses, because of their variable potency. The effect of Botox® might be improved, with a repeated injection of 100 IU 1 month after the first injection,[22] although <20% of patients who lack of an initial response will have success after a second injection.[23] The best treatment response to botulinum toxin injection can be expected in patients with vigorous achalasia, patients of advanced age and those who have an LES pressure that does not exceed ≥50% of the upper limit of normal. In summary, botulinum toxin injection seems to be an effective treatment in the short term, but it has clearly been shown to be inferior to pneumatic dilation or surgery in a number of comparative studies.[24–26] This treatment is, therefore, best reserved for patients of advanced age and those with significant comorbidities.

## Pneumatic dilation

Pneumatic dilation has been used for more than half a century and is currently considered the most effective nonsurgical treatment option for achalasia.[24] A graded approach of serial esophageal dilations (3.0 cm, 3.5 cm and 4.0 cm) with the low-compliance Rigiflex® balloon system (Microvasive, Natick, MA, USA), aided by an endoscopically placed guidewire with subsequent fluoroscopic monitoring of the balloon position, is the standard procedure used by most experts. However, dilation protocol and follow-up varies among different investigators in the US and Europe. Although some authors have used single dilations with success,[11,27] serial dilations performed on consecutive days or a few weeks apart with balloon sizes ranging from 3 cm to 4 cm have been advocated by others.[12,28–31] In order to avoid radiation exposure, some centers monitor balloon position by direct endoscopic observation.[32,33] Immediately following dilation, radiologic esophagograms with water-soluble contrast agents (for example, Gastrografin®, Schering-Plough, Berlin, Germany) are frequently performed to rule out perforation. However, it remains questionable whether this test is needed in the absence of symptoms that are suggestive of a perforation. Many centers now even perform pneumatic dilation on an outpatient basis and discharge patients after an extended observation period (at least 4–6 h) if there are no signs of complications.[34–36]

The success of pneumatic dilation can be monitored symptomatically, but additional objective criteria are useful to predict treatment responses. European centers, including our own, commonly use esophageal manometry for follow-up and regard a postdilation LES pressure of <10–15 mmHg as a favorable predictor of long-term treatment success.[12,37] In the US, treatment results are more commonly assessed by determining esophageal emptying with a timed barium swallow. In a 2009 study of patients with achalasia who underwent pneumatic dilation, patients who had <50% improvement over baseline in the height of the barium column after 1 min had a 40% risk of treatment failure.[5]

Using the described graded pneumatic dilation protocols, good or excellent symptomatic responses can be achieved in 75–85% of patients who undergo such intervention.[38] A review of 24 studies published up to 2009 showed that success rates of 74%, 80% and 90% were achieved when balloon sizes of 3.0 cm, 3.5 cm and 4.0 cm were used, respectively.[39] However, such favorable results are mainly based on studies with relatively

short or intermediate observation periods. If patients are observed for more than 10 years, only 40–60% will remain asymptomatic after a single pneumatic dilation.[27,28,35] Many clinicians, therefore, now perform repeated on-demand pneumatic dilations and achieve successful long-term treatment results in ≥90% of patients.[12,31] A possible disadvantage of repeated pneumatic dilations is the patients' frequent exposure to potentially serious complications, such as esophageal perforation, intramural hematoma or aspiration, and the uncertain durability of symptom-free intervals between dilations.[40,41]

To optimize pneumatic dilation therapy further the issue must be raised as to whether subgroups of patients exist who respond more favorably to this type of treatment. In fact, patients who are older than 40 years generally have a better outcome following dilation than those who are younger.[37] By contrast, a wide esophagus, pulmonary symptoms, the use of small balloon sizes, an incomplete obliteration of the balloon waist during the procedure or a failed response to one or two dilations have all been shown to predict a poor treatment response.[11,30,37,42–44] In addition, manometric findings that predict a poor outcome are a high postdilation LES pressure (for example, >15 mmHg), a reduction in LES pressure of <50% after the first dilation and type I and III patterns of achalasia on HRM.[9,11,42–44] Poor esophageal emptying on a timed barium swallow is another negative predictor of treatment success. Timed barium swallow seems to be the favored follow-up examination in the US, probably because of better patient tolerability, but it has the disadvantage of radiation exposure and is therefore infrequently used in Europe.

### Surgical treatment

Surgical myotomy was inaugurated by Ernst Heller, a German surgeon, almost a century ago.[45] With the advent of minimally invasive laparoscopic approaches, this therapy has evolved to become one of the most effective treatment strategies to date.[24,46,47] Surgical myotomy involves a longitudinal incision of the internal and external muscular layers of the esophagus and is nowadays most effectively performed by a transabdominal laparoscopic approach.[47] The incision in the area of the LES must be extended 5–7 cm proximally and at least 2–3 cm distally into the stomach to cut the gastric sling fibers. Only careful adherence to this protocol will significantly reduce LES pressure.[48] In order to avoid long-term reflux complications, the procedure is usually combined with a partial anterior Dor fundoplication or posterior Toupet fundoplication.[47,49] Partial fundoplication is preferred to 360° Nissen fundoplication because it results in significantly lower postoperative dysphagia rates (2.8% versus 15%, $P = 0.001$).[50] A 2004 randomized controlled trial has shown that reflux symptoms can be reduced from 47.6% to 9.1% by adding a Dor fundoplication to conventional laparoscopic myotomy.[51]

Good or excellent long-term symptomatic response rates can be achieved in approximately 75–85% of patients undergoing surgical myotomy,[52–55] with most clinical experts citing the upper range of this spectrum.[1,34] However, it should be noted that there is a substantial learning curve in performing laparoscopic myotomy, and the best results are likely to be achieved in centers of excellence with extensive experience.[56] Surgical myotomy can also be successfully performed after failed pneumatic dilation or botulinum toxin injection procedures.[40,57] However, it has been suggested by some that such procedures, especially the latter one, might result in worse surgical outcomes, possibly owing to substantial scarring.[58–61] Other predictors of poor surgical outcome have been defined and include severe preoperative dysphagia, progressive esophageal enlargement, and low preoperative LES pressures (<30–35 mmHg). Although advanced age is frequently viewed as an obstacle to surgery, mostly because of the increased frequency of clinically significant comorbidities, a 2010 study suggests that laparoscopic myotomy can achieve excellent outcomes in patients >60 years of age.[62] The introduction of real-time, intraoperative manometry[63,64] and robotic-assisted myotomy[65,66] may further improve postoperative outcomes, but these methods are not widely established.

Surgical myotomy is the treatment of choice if pneumatic dilations have repeatedly failed to improve symptoms.[67] Repeat surgery also remains a valid option if the initial myotomy does not result in sufficient symptomatic improvement. In such instances, a repeat myotomy performed at an opposite location to the initial intervention (for example, posterior instead of anterior) can achieve the same results as a successful primary procedure.[68] Although less effective, repeat pneumatic dilation could be considered as alternative to repeat surgery if the initial surgical procedure has failed, especially if the operative risk is high or if patients are reluctant to have further surgical interventions.[69] Finally, it should be noted that subtotal esophagectomy remains an option for patients who do not respond to any of the above therapeutic measures. Although some authors have reported favorable results with surgical myotomy in patients with substantial esophageal enlargement,[70] positive outcomes are not generally achieved in such patients and esophagectomy may become necessary. Admittedly, esophagectomy is an extremely invasive therapy with high postoperative morbidity and mortality; however, favorable long-term results with significant symptomatic improvement can be achieved, even if multiple other therapeutic measures have failed.[71,72]

### Pneumatic dilation versus surgical myotomy

As outlined above, pneumatic dilation and surgical myotomy are the most effective treatment options available. Three meta-analyses published in the English and Chinese literature in the past 15 years have favored surgery as the best treatment to achieve long-term success.[24,47,73] However, these analyses mostly included retrospective studies of different sizes and quality and did not consistently report on the use of on-demand pneumatic dilation. Although repeat interventions occur more frequently in patients who receive pneumatic dilation than in those undergoing surgery,[74] both procedures might have similar efficacy if on-demand

pneumatic dilations are performed for symptomatic recurrence and if patients for whom pneumatic dilation fails are referred early to surgery.[12,31,75] Without prospective, randomized, controlled trials of appropriate size and duration, a clear superiority of one treatment option over the other cannot be conclusively demonstrated. Until recently, only one such trial by Csendes *et al.* existed, which compared surgical myotomy plus Dor fundoplication with pneumatic dilation using a Mosher bag.[76] This study showed superior results in the surgical group after a 5-year follow-up period. Good symptomatic response rates were seen in 95% and 65% of patients in the surgical and pneumatic dilation groups, respectively. However, this study has been criticized because of the potential for technique-related inferiority in the pneumatic dilation group that may have lead to an underestimation of its effect. In addition, a recent long-term follow-up of the same patient group has shown that the results of surgery were less favorable after more than 15 years of observation, with only 75% of patients reporting persistent symptomatic relief.[77] In 2011, the results of another large multinational study are expected to be published. In this investigation, 94 patients were randomly assigned to pneumatic dilation with Rigiflex® (3.0 cm and 3.5 cm) and 104 patients to laparoscopic myotomy.[78] Patients with recurrent symptoms in the Rigiflex® group were allowed to undergo repeat treatment on demand up to a maximum of three series of pneumatic dilations. Both treatments had comparable treatment success at 2 years, with 92% and 87% of patients achieving symptomatic relief with pneumatic dilation and laparoscopic myotomy, respectively. Although age was not a predictor of overall success for either treatment, patients younger than 40 years of age presented more often with recurrent symptoms that required repeat pneumatic dilation. Whether these impressive results can be maintained in the long term is questionable but, at least in the short term, pneumatic dilation and surgical myotomy seem to have equal efficacy provided that patients undergoing pneumatic dilation are willing to have such therapy repeatedly performed.

### Current and future developments

New endoscopic techniques have been described for the treatment of achalasia. These techniques primarily include peroral endoscopic myotomy (POEM) and esophageal stenting. In 2010, the results of a Japanese study and an American study of the POEM procedure were published.[79,80] In all 18 cases the procedure was performed by use of a peroral cap-fitted endoscopic approach under general anesthesia and with positive pressure ventilation.[79,80] This approach involves endoscopic dissection of the esophageal submucosal space with $CO_2$ insufflation to gain access to LES muscle fibers. The semicircumferent dissection starts approximately 6–13 cm proximal to the esophagogastric junction and is extended 2 cm into the stomach. Circular muscle bundles are then dissected, leaving the longitudinal muscle layer intact. In the uncontrolled Japanese study, the authors demonstrated significant improvement of dysphagia and LES pressure after intervention, although the mean postinterventional LES pressure was still high at 20 mmHg.[79] Although the authors promoted this procedure as a less invasive and more permanent approach than surgical myotomy, POEM requires general anesthesia, has suboptimal results for lowering LES pressure compared with surgery, has not been shown to be permanent, and is not less time consuming than a laparoscopic surgical approach. In addition, although the authors encountered no specific complications during follow-up, pneumoperitoneum occurred in one patient and asymptomatic pneumomediastinum was common after the procedure. Surprisingly, no infectious complications occurred with this procedure, but the number of patients reported is too small to exclude such complications.

Another novel therapeutic approach is temporary esophageal stenting. A group of Chinese investigators has published multiple reports on what seems to be the same group of patients with achalasia who were followed up for a period of 13 years after undergoing this procedure.[81–84] These investigators radiologically placed partially covered, self-expanding metal stents (SEMS) with a diameter of 20 mm, 25 mm or 30 mm in unsedated patients with achalasia and removed these stents endoscopically after 3–7 days. The authors showed that after more than 10 years the best results were obtained in patients treated with 30 mm SEMS. 83–92% of these patients achieved clinical remission compared with 0% of patients treated with pneumatic dilation. However, multiple problems exist with this study including repetitive publications with differing results and suboptimal pneumatic dilation techniques. In addition, multiple complications occurred such as stent migration, bleeding, chest pain and gastroesophageal reflux,[83] rendering this treatment experimental at best.

## Surveillance

Patients with achalasia should undergo a clinical follow up for a number of reasons. First, treatment success needs to be documented by objective parameters. Second, regular follow-up enables the clinician to detect symptomatic recurrences at an early stage and, third, endoscopic surveillance has the potential for early recognition of late complications, such as esophageal squamous cell cancer, megaesophagus or reflux esophagitis.

Objective evaluation of treatment success should be performed early after the initial intervention. At our center, to avoid misinterpretation of success by immediate treatment effects, such as intramural hematoma, we preferentially perform these studies 4 weeks after therapy. However, some centers assess treatment success by esophageal manometry intraoperatively[63,64] or immediately after pneumatic dilation.[12] In a very ambitious approach, Hulselmans *et al.*[12] even performed serial pneumatic dilations with daily esophageal manometry over 1–3 days to achieve and assess their manometric treatment goal. A postdilation LES resting pressure of <10–15 mmHg is generally considered to be predictive of a good long-term response.[12,37] Similarly, a >50% improvement over baseline in the height of the barium

**Table 1** | Clinical scoring system for achalasia (Eckardt score)

| Score | Symptom | | | |
|---|---|---|---|---|
| | Weight loss (kg) | Dysphagia | Retrosternal pain | Regurgitation |
| 0 | None | None | None | None |
| 1 | <5 | Occasional | Occasional | Occasional |
| 2 | 5–10 | Daily | Daily | Daily |
| 3 | >10 | Each meal | Each meal | Each meal |

**Table 2** | Clinical staging of achalasia

| Stage | Eckardt score* | Clinical Implication |
|---|---|---|
| 0 | 0–1 | Remission |
| I | 2–3 | Remission |
| II | 4–6 | Treatment failure |
| III | >6 | Treatment failure |

*See Table 1 for details regarding the Eckardt score. Permission obtained from Elsevier Ltd © Eckardt V. F. *et al*. *Gastroenterology* **103**, 1732–1738 (1992).

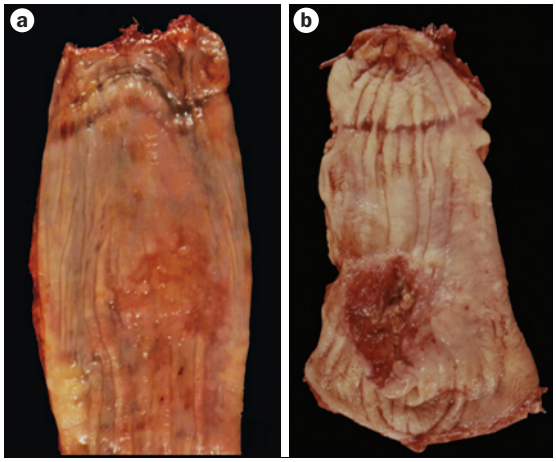


**Figure 3** | Esophageal resection specimens from patients with achalasia who developed esophageal cancer. **a** | Early squamous cell esophageal cancer detected during surveillance 14 years after diagnosis of achalasia. The patient is alive >20 years after esophagectomy. **b** | Advanced squamous cell esophageal cancer detected after recurrence of symptoms 20 years after diagnosis of achalasia. The patient died 2 years after esophagectomy.

column 1 min after timed barium swallow is a favorable predictor of treatment success if it occurs in concordance with symptomatic clinical improvement.[4,85] If these particular parameters of therapeutic success cannot be achieved by serial pneumatic dilations, many specialist will refer patients with such early treatment failure to surgery.[12,44,75]

Once clinical remission is achieved by subjective and objective criteria, most patients will have sufficient symptomatic improvement for several years, although on-demand treatments might become necessary. In our experience, many patients with achalasia will regard even a minor symptomatic improvement as a major relief from prolonged suffering, being unaware how much improvement could be achieved in reality.[86] The performance of a structured interview, therefore, seems of utmost importance during follow-up. Several scoring systems have been introduced that enable patients and physicians to better grade clinical response.[87] We use a simple scoring system, frequently referred to as the Eckardt Score, to grade the four major symptoms of achalasia (that is, dysphagia, regurgitation, retrosternal pain and weight loss) (Table 1 and 2).[37] This scoring system can be useful to monitor the clinical course of disease at regular follow-up intervals (for example, every 2 years) and to objectively assess treatment outcomes or the need for further interventions. Other clinicians prefer to periodically perform radiologic or manometric studies in order to recognize deterioration of disease at an early stage.[88,89]

Finally, surveillance might have a role in the detection or prevention of long-term complications. Up to 10% of all patients with long-standing achalasia (more than 10 years after first diagnosis) develop progressive enlargement of the esophagus, which can lead to a sigmoid-shaped esophagus and/or megaesophagus (Figure 1).[90] This complication more frequently develops in patients who remain ineffectively treated for years. If these morphological changes are only recognized at an advanced stage, esophageal resection may be the only remaining therapeutic option. In addition, there are accumulating data that the risk of esophageal squamous cell carcinoma (Figure 3) is substantially increased in patients with long-standing achalasia.[91–96] A 2010 prospective, long-term study of patients with long-standing achalasia who underwent regular surveillance at 3-year intervals found a hazard ratio of 28 for developing esophageal squamous cell carcinoma.[97] In this study, cancers occurred at a mean age of 71 years (24 years after the onset of symptoms and 11 years after diagnosis of achalasia). Although only 13% of patients who developed cancer had a survival benefit from surveillance, the authors suggested that such a strategy should be considered in patients with long-standing disease. A final long-term complication that requires careful attention is the development of clinically significant GERD, which occurs in up to 25% of patients with achalasia who are followed up for >30 years.[77] GERD-related findings range from reflux esophagitis and peptic strictures to Barrett esophagus, which in rare instances may progress to esophageal adenocarcinoma.[77,98] Although the latest American Society of Gastrointestinal Endoscopy guidelines correctly state that there are still "insufficient data to support routine endoscopic (cancer) surveillance for patients with achalasia",[99] overall such an approach might be beneficial if one considers that cancer is not the only late complication of this disease.[100] Most experts, therefore, now favor some form of endoscopic surveillance in patients with achalasia if the disease has been present for more than 10–15 years.[1,88,100,101] However, further studies are urgently needed to determine whether optimized surveillance strategies with defined intervals and improved endoscopic techniques will improve overall outcomes.

**Table 3** | Predictors of treatment outcome in patients with achalasia

| Treatment option | Positive predictors | Negative predictors |
|---|---|---|
| Botulinum toxin injection | Vigorous achalasia<br>Advanced age | High initial LES pressure<br>Lack of response to first treatment |
| Pneumatic dilation | Age >40 years<br>Type II pattern of achalasia on HRM<br>Early disease<br>Postinterventional LES pressure <10 mmHg<br>>50% improvement over baseline in barium column height 1 min after initiation of a timed barium swallow | Male gender<br>Incomplete obliteration of the balloon waist or small balloon size (<30 mm)<br>High postdilation LES pressure<br>Type I or type III patterns of achalasia on HRM<br>Features of advanced disease (e.g. an enlarged esophagus)*<br>Postinterventional LES pressure >10–15 mmHg<br><50% improvement over baseline in barium column height 1 min after initiation of a timed barium swallow |
| Surgical myotomy | Age <40 years<br>Type II pattern of achalasia on HRM<br>Early disease<br>Postinterventional LES pressure <10 mmHg<br>>50% improvement over baseline in barium column height 1 min after initiation of a timed barium swallow | Severe preoperative dysphagia<br>Low initial LES pressure<br>Prior endoscopic treatment (primarily botox injection)<br>Type I or type III patterns of achalasia on HRM<br>Features of advanced disease (e.g. an enlarged esophagus)*<br>Postinterventional LES pressure >10–15 mmHg<br><50% improvement over baseline in barium column height 1 min after initiation of a timed barium swallow |

*A negative predictor in most studies. Abbreviations: HRM, high-resolution manometry; LES, lower esophageal sphincter.

## Conclusions

Despite several advances in the understanding of the pathophysiology of achalasia, treatment remains palliative as the neuronal defect of the disease seems to be irreversible. Treatment goals are, therefore, the palliation of symptoms by disruption of the LES and the prevention of long-term complications. Currently, the most effective treatment options are graded pneumatic dilation with on demand repeat dilation and laparoscopic Heller myotomy with partial fundoplication. Although both treatments seem to have similar efficacy in the short-term, the durability of surgical myotomy makes it the favored approach in young patients and in those who want to avoid frequent repeat intervention.

Owing to a limited long-term efficacy, endoscopic botulinum toxin injection and medical therapies are mostly reserved for patients with significant comorbidities, or they are used as a bridge until more definitive treatment can be performed. Predictors of treatment response have been well defined and should be considered when one therapeutic option is chosen over another (Table 3). In addition, patient preferences and local expertise are major factors that determine treatment choices. Therapeutic success should be monitored by documented improvement of clinical symptoms, ideally by using a clinical scoring system. In addition, esophageal manometry or a timed barium swallow should be performed a few weeks after therapeutic intervention to document adequate treatment response. Whether new treatment approaches, such as peroral endoscopic myotomy, esophageal stenting, or robotic-assisted myotomy will find a place in the treatment of achalasia remains to be shown by future investigations.

Surveillance of patients with achalasia remains a matter of debate. During the first 10–15 years after initial diagnosis and treatment, patients should be monitored for symptomatic relapses (for example, every 1–2 years), although some experts also perform occasional objective testing. Some form of endoscopic surveillance after 10–15 years of disease duration might be beneficial because of the increased risk of cancer and other delayed complications. However, further studies are needed to determine how frequently such surveillance should be performed and whether it will be cost effective.

### Review criteria

A PubMed (MEDLINE) database search was performed using the following search terms: "achalasia", "esophageal myotomy", "pneumatic dilation", "complications of achalasia". The search was not limited by year of publication. With one exception, only articles published in full length were considered. In addition, relevant articles that were mentioned in key manuscripts were reviewed.


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**Author contributions**

A. J. Eckardt contributed to all aspects of the article. V. F. Eckardt made a substantial contribution to the discussion of content and the review/editing of the manuscript before submission.