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GUIDELINES

SAGES guidelines for the surgical treatment of esophageal achalasia

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Preamble

The guidelines for the surgical treatment of esophageal achalasia are a series of systematically developed statements to assist surgeon (and patient) decisions about the appropriate use of minimally invasive techniques for the treatment of achalasia in specific clinical circumstances. It addresses the indications, risks, benefits, outcomes, alternatives, and controversies of the procedures used to treat this condition. The statements included in this guideline are the product of a systematic review of published work on the topic, and the recommendations are explicitly linked to the supporting evidence. The strengths and weaknesses of the available evidence are highlighted, and expert opinion is sought where published evidence lacks depth.

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Disclaimer

Clinical practice guidelines are intended to indicate the best available approach to medical conditions as established by a systematic review of available data and expert opinion. The approach suggested may not necessarily be the only acceptable approach given the complexity of the healthcare environment. These guidelines are intended to be flexible, because the surgeon must always choose the approach best suited to the individual patient and variables in existence at the moment of decision. These guidelines are applicable to all physicians who are appropriately credentialed and address the clinical situation in question, regardless of specialty.

Guidelines are developed under the auspices of SAGES—the guidelines committee—and are approved by the Board of Governors. The recommendations of each guideline undergo multidisciplinary review and are considered valid at the time of production based on the data available. New developments in medical research and practice pertinent to each guideline are reviewed, and guidelines will be periodically updated.

Literature review method

A systematic literature search was performed on MEDLINE in October 2010. The search strategy was limited to adult English language articles and is shown in Fig. 1.

We identified 214 relevant articles. The abstracts were reviewed by four committee members (DS, WR, TMF, and GPK) and divided into the following categories:

(a) Randomized studies, meta-analyses, and systematic reviews

Fig. 1 Literature search strategy

Laparoscopic Heller's Myotomy
Medline
(October 2010)

Database: Ovid MEDLINE(R) <1950 to October Week 1 2010>
Search Strategy:
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1 Esophageal Achalasia/su [Surgery] (1485)
2 endoscopy/ or endoscopy, digestive system/ or endoscopy, gastrointestinal/ or gastroscopy/ or esophagoscopy/ or laparoscopy/ (95005)
3 thoracoscopy/ or thoracic surgery, video-assisted/ (5991)
4 exp Esophagus/su [Surgery] (6733)
5 (heller$ or myotom$ or esophagomyotom$ or esophagocardiomyotom$ or cardiomyot$).mp. [mp=title, original title, abstract, name of substance word, subject heading word] (3977)
6 4 and 5 (508)
7 1 and (2 or 3) (391)
8 4 and 5 and (2 or 3) (164)
9 7 or 8 (439)
10 *Esophageal Achalasia/su and (*endoscopy/ or *endoscopy, digestive system/ or *endoscopy, gastrointestinal/ or *gastroscopy/ or *esophagoscopy/ or *laparoscopy/ or (*thoracoscopy/ or *thoracic surgery, video-assisted/)) (212)
11 exp *Esophagus/su and 5 and (*endoscopy/ or *endoscopy, digestive system/ or *endoscopy, gastrointestinal/ or *gastroscopy/ or *esophagoscopy/ or *laparoscopy/ or (*thoracoscopy/ or *thoracic surgery, video-assisted/)) (64)
12 10 or 11 (235)
13 limit 12 to evidence based medicine reviews (0)
14 limit 12 to (meta analysis or randomized controlled trial) (3)
15 limit 12 to "review articles" (18)
16 12 not (14 or 15) (214)

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(b) Prospective studies
(c) Retrospective studies
(d) Case reports
(e) Review articles

Randomized controlled trials, meta-analyses, and systematic reviews were selected for further review along with prospective and retrospective studies that included at least 50 patients. Studies with smaller samples were considered when additional evidence was lacking. The most recent reviews also were included. All case reports, old reviews, and smaller studies were excluded. According to these exclusion criteria, 102 articles were selected for review. Whenever the available evidence from Level I studies was considered to be adequate, lower evidence level studies were not considered.

The reviewers graded the level of evidence and manually searched the bibliography of each article for additional articles that may have been missed during the original search. Additional relevant articles ($n = 25$) were obtained and included in the review for grading. A total of 127 graded articles relevant to this guideline were included in this review. To facilitate the review by multiple reviewers, these articles were divided into the following topics and distributed to the reviewers:

- Myotomy versus nonsurgical treatment
- Laparoscopic myotomy with or without fundoplication
- Technique (laparoscopic, open, robotic, thoracoscopic, other)
- Revisional surgery
- Predictors of success
- Outcome
- Epiphrenic diverticula
- Other articles

The recommendations included in this guideline were devised based on the reviewers' grading of all articles.

Levels of evidence

Both the quality of the evidence and the strength of the recommendation for each of the guidelines were assessed according to the GRADE system. There is a four-tiered system for quality of evidence (very low (⊕), low (⊕⊕), moderate (⊕⊕⊕), or high (⊕⊕⊕⊕)) and a two-tiered system for strength of recommendation (weak or strong) [1, 2].

Introduction

Achalasia is a rare primary motility disorder of the esophagus that affects one person in 100,000 per year and is characterized by the absence of esophageal peristalsis and incomplete relaxation of a frequently hypertensive

lower esophageal sphincter (LES) in response to swallowing [3].

The pathological changes seen in achalasia consist of myenteric inflammation with injury to and subsequent loss of ganglion cells and fibrosis of myenteric nerves [4]. There also is a significant reduction in the synthesis of nitric oxide and vasoactive intestinal polypeptide [5, 6]. The probable etiology of the disease is thought to be an autoimmune-mediated destruction of inhibitory neurons in response to an unknown insult in genetically susceptible individuals; however, a definite trigger has not been identified [7].

Diagnosis and preoperative workup

Dysphagia with solids and liquids is the most common symptom of the disease, followed by regurgitation of undigested food, chest pain, weight loss, nocturnal cough, and heartburn. Although heartburn is the cardinal symptom of gastroesophageal reflux disease and is caused by irritation of the esophagus by refluxed gastric acid, in patients with achalasia, it might be explained by retention of acidic or noxious food contents or by lactate production from bacterial fermentation within the esophagus [6].

The clinical suspicion of achalasia should be confirmed by a barium esophagram showing smooth tapering of the lower esophagus leading to the closed LES, resembling a "bird's beak." Esophageal manometry establishes the diagnosis showing esophageal aperistalsis and insufficient LES relaxation with swallowing. All patients should undergo upper endoscopy to exclude pseudoachalasia arising from a tumor at the gastroesophageal junction [6]. For details on the diagnostic workup of achalasia, refer to the American Gastrointestinal Association guidelines [6].

Recommendation: Patients with suspected achalasia should undergo a barium esophagram, an upper endoscopy, and esophageal manometry to confirm the diagnosis (**+++**, **strong**).

Treatment options

Unfortunately, no current therapy can change the underlying pathology of achalasia, and all available treatment options are directed at the palliation of symptoms only.

Pharmacotherapy

The goal of pharmacotherapy for achalasia is the relief of the functional obstruction of the lower esophagus by relaxation of the lower LES. Smooth muscle relaxants, such as calcium channel blockers and long-acting nitrates, are effective in reducing LES pressure and temporally relieving dysphagia but do not improve LES relaxation or improve peristalsis [6]. Because the prolonged esophageal transit and delayed esophageal emptying that characterize achalasia make the absorption kinetics and effectiveness of orally administered medications unpredictable, these agents are used sublingually [8]; (e.g., nifedipine 10–30 mg sublingually 30–45 min before meals; isosorbide dinitrate 5 mg sublingually 10–15 min before a meal) [7]. These drugs decrease LES pressure by approximately 50% with the long-acting nitrates having a shorter time to maximum effect (3–27 min) and symptom improvement in 53–87% of achalasia patients compared with sublingual nifedipine (30–120 min and 0–75% symptom improvement, respectively) [6].

The main limitations of these agents are their short duration of action, incomplete symptom relief, and decreased efficacy during long-term use [6, 7]. In addition, side-effects, such as peripheral edema, headache, and hypotension, occur in up to 30% of patients [9] and further limit their use [10]. The use of the available pharmacologic agents is, therefore, limited to symptomatic relief of patients with very early disease with a nondilated esophagus or as a temporary measure for patients who are awaiting a more definite treatment option or are high risk for or refuse more invasive options [6, 11]. In addition, the use of some medications may be useful in the case of severe achalasia-related chest pain [11].

Recommendation: Pharmacotherapy plays a very limited role in the treatment of achalasic patients and should be used in very early stages of the disease, temporarily before more definitive treatments, or for patients who fail or are not candidates for other treatment modalities (**++++**, **strong**).

Botulinum toxin injections

Botulinum toxin is a potent neurotoxin that inhibits the release of acetylcholine at presynaptic terminals of motor neurons [12]. A single injection of botulinum toxin has been shown to be effective in approximately 85% of patients with achalasia, but its effect diminishes over time (50% at 6 months and 30% at 1 year) [9, 13, 14], and universal symptomatic relapse occurs at 2 years [15].This treatment effect can be maximized by repeat injections [16], but its long-term effectiveness remains limited. The best results of botulinum toxin have been achieved in older patients [17] who tend to have higher lower esophageal pressures than younger patients [18], patients with vigorous achalasia, and patients whose LES pressures do not exceed $\geq$50% of the upper limit of normal [14, 19]. In contrast, a lack of an initial symptomatic response and residual LES pressure $\geq$18 mmHg after botulinum toxin indicates

patients unlikely to respond to further treatment with botulinum toxin [20].

Reported complications of botulinum toxin injection are rare and include esophageal mucosal ulceration, pleural effusion, cardiac conduction defects, and mediastinitis [21, 22]. Two recent meta-analyses concluded that botulinum toxin injection in patients with achalasia had an excellent safety profile but was slightly less effective than pneumatic dilatation in the short-term and clearly inferior in the long-term [23, 24]. Of note, a randomized, controlled trial has shown that the two currently commercially available formulations of botulinum toxin are equally effective but need to be given in different dosages because of variable potency [25].

Botulinum toxin might be especially useful in very old patients or those with major comorbidities and poor operative risk because of its excellent safety profile [7].

Recommendation: Botulinum toxin injection can be administered safely, but its effectiveness is limited especially in the long-term. It should be reserved for patients who are poor candidates for other more effective treatment options, such as surgery or dilation (++++, **strong**).

Dilatation

Endoscopic dilatation is currently considered the most effective nonsurgical treatment for achalasia [3, 6]. Pneumatic dilators are preferred over rigid dilators for the management of achalasia, because they not only stretch but also produce rupture of the LES muscle fibers [26]. Several different pneumatic dilators are available currently with similar efficacy and safety, but comparative data are limited [7]. Using a graded approach with increasing diameters of the polyethylene balloon dilator from 3.0 to 4.0 cm, a 93% response rate has been achieved during a mean follow-up period of 4 years with a relatively low complication risk [27]. Both endoscopic and fluoroscopic guidance have been used effectively for the deployment of these balloons [28].

Varying definitions of success in the literature make analysis of the efficacy of dilatation difficult. Postdilatation, dysphagia-free rates (single or repeated) have been reported to range from 40–78% at 5 years to 12–58% at 15 years [29–31]. A single treatment with dilatation is adequate in only 13% of patients followed over this time interval [31]. While some authors have reported remission rates of up to 97% at 5 years and 93% at 10 years with on-demand repeat dilations [32], it is generally accepted that long-lasting treatment effects cannot be expected from such therapy [33]. Younger patients (<40 years) are less likely to achieve long-term clinical resolution than older patients [7, 33]. Other predictors of treatment failure with balloon dilation include the presence of pulmonary symptoms and failed response to the first or second initial dilations [29, 34, 35]. Some authors have recommended the routine use of manometry before and after intervention, because high initial LES pressures (e.g., >15–30 mmHg) or a reduction of LES pressure < 50% after the first dilation have been found to be predictors of poor outcomes [29, 35].

Complications of pneumatic esophageal dilatation include esophageal perforation, intramural hematoma, and gastroesophageal reflux. The most feared complication, esophageal perforation, occurred in 1.6% (range, 0.67–5.6%) of patients in a meta-analysis of 1,065 patients treated by experienced physicians [3, 27]. After balloon dilation, the damaged LES allows gastric contents to more easily reflux into the esophagus, and up to 40% of patients develop chronic active or ulcerating esophagitis after dilatation [32, 33, 36], although only 4% are symptomatic [37].

Recommendation: Among nonoperative treatment techniques, endoscopic dilation is the most effective for dysphagia relief in patients with achalasia but is associated with the highest risk of complications. It should be considered in selected patients who refuse surgery or are poor operative candidates (++++, **strong**).

Combination treatments

Botulinum toxin before pneumatic dilatation

Attempts have been made to increase the remission rates following pneumatic dilatation. One proposed technique is to inject with botulinum toxin before dilatation. This has been found to be ineffective [38].

Botulinum toxin after pneumatic dilatation

Patients in whom pneumatic dilatation has failed can be effectively treated with botulinum toxin. Up to 71% of such patients have symptom resolution at 6 months post-injection [12]. Rates of resolution of symptoms following botulinum toxin injections do not appear to be impacted by previous treatment using other modalities.

Other options

Esophageal stents

To prolong the beneficial effect of dilatation, some authors have recommended the use of expandable metal stents [39, 40]. Whereas the reported results on the effectiveness of the stents have been mixed, their use is clearly associated with high complication rates and even mortalities.

Recommendation: The use of esophageal stents cannot be recommended for the treatment of achalasia (++, **strong**).

Peroral endoscopic myotomy

Recently an endoscopic technique has been described for myotomy, and short-term outcomes have been reported in a small number of patients by Japanese investigators [41]. This technique is in its infancy, and further experience is needed before recommendations can be provided.

Surgical treatment of achalasia

The goal of surgery is to alleviate the distal esophageal obstruction by division of the circular muscle fibers comprising the LES. Myotomy can be accomplished via laparotomy, thoracotomy, and since the early 1990s, laparoscopically and thoracoscopically.

Brief description of myotomy technique

The esophagus is mobilized several centimeters into the mediastinum until there is enough room for the myotomy. The epiphrenic fat pad is excised from the anterior LES starting to the left of the anterior vagus nerve to create adequate room to perform the myotomy on the stomach. The anterior vagus nerve is dissected off the distal esophagus so that the myotomy can be taken high up the esophagus beneath the nerve. When there is a hiatus hernia, adequate mobilization of the esophagus to restore a normal intra-abdominal length is required, and the crura should be closed behind the esophagus making sure not to restrict the esophagus. Crural closure is typically performed after completion of the myotomy.

The myotomy is started on the esophagus just above the gastroesophageal junction. The surgeon and assistant each grasp one side of the esophagus and retract in opposite directions to provide better exposure and facilitate the myotomy. The esophageal muscle fibers are split and dissected laterally starting with the longitudinal fibers and entering the circular fibers until a small pocket is made between the circular fibers and the mucosa. The myotomy is continued up the esophagus for at least 4 cm and taken onto the stomach for approximately 2 cm. This dissection is tedious and should be done with care to avoid perforation of the esophageal mucosa. The change from esophageal to gastric muscle fibers can be seen as they change from a horizontal circular orientation to an oblique one and are more adhered to the mucosa. There also is bulging of the mucosa at the LES area. Injection of dilute epinephrine into the muscle before myotomy may be useful, because it minimizes bleeding and allows for better visualization of the mucosa [42].

The completeness of the myotomy should be checked at the end of the procedure. This can be done with an endoscope where the lower esophagus is inspected and complete division of the muscle is verified by identification of a wide open GE junction with no visible crossing muscle fibers. Any residual fibers can be divided as needed. Some authors have suggested the use of intraoperative manometry to assess the myotomy for completeness [43], but comparative data are lacking. The myotomy also can be assessed for perforation by placing it under a column of saline and inflating gently through the endoscope. When bubbles are seen, the area from where they emanate should be oversewn with 4–0 Vicryl, and the subsequent fundoplication should be used to cover the area. In the context of perforation, consideration also should be given to drain placement.

The most commonly used options for fundoplication after myotomy include an anterior Dor fundoplication or a posterior Toupet fundoplication. For the Dor fundoplication, the greater curvature of the stomach is pulled over the esophagus making sure it is redundant so as not to restrict the LES and is sutured to the crura where they meet anteriorly. Some surgeons also attach it to the edges of the myotomy to hold it open, and some attach the edges of the myotomy to the crura as well. When a Toupet fundoplication is used, the fundus is pulled behind the esophagus and attached to the left and right cut edges of the myotomy to keep it open. More detailed descriptions of these procedures can be found in textbooks of laparoscopic surgery.

Myotomy outcomes

After laparoscopic esophagomyotomy, symptomatic improvement has been reported in 89% of patients (range, 77–100) independent of whether a fundoplication was performed concurrently [3]. This improvement appears to be long lasting, as some studies have not shown differences between early and late dysphagia resolution rates [44]. Nevertheless, other better quality studies have shown that clinical deterioration occurs over long follow-up periods. Csendes et al. demonstrated in a randomized, controlled trial that while response rates were 95% at 5-year follow-up [45], the success rate was reduced to 75% after a mean follow-up of 15.8 years [46].

It also has been suggested that the clinical outcome is dependent on the stage of the disease before the surgery, with stage IV disease patients responding only 50% of the time compared with 90% for stage I–III patients [47]. On the other hand, postoperative reflux has been described to occur in 8.8% (range, 0–44) of patients who received a fundoplication compared with 31.5% (range, 11–60) of those who did not after myotomy, respectively

($P = 0.001$). These findings held true whether reflux assessment was based on patient symptoms or pH monitoring [3]. Importantly, long-term studies have reported that 92% of patients with poor outcomes resulted from complications of severe reflux disease and not from incomplete myotomy [46].

With regard to surgery-related complications, esophageal perforation during surgery has been reported to occur on average in 6.9% (range, 0–33) of patients but with clinical consequences in only 0.7% (range, 0–3%) of patients [3]. In one series of 222 patients, inadvertent esophagotomy occurred in 16 (7.2%), resulting in longer hospitalization but not different postoperative symptomatology [48].

Postoperative complications have been reported in 6.3% (range, 0–35%) of patients, and only 3 (0.1% incidence) mortalities were found in a recent meta-analysis of >3,000 patients [3]. Reoperation rates have been demonstrated to be <5% [44, 49]. One study found the reasons of laparoscopic myotomy failure to be incomplete myotomy (33%), myotomy fibrosis (27%), fundoplication disruption (13%), too tight fundoplication (7%), and a combination of myotomy fibrosis and incomplete myotomy (20%) [50].

Patient quality of life has been demonstrated to be significantly improved after myotomy in several studies [51–54], and patient satisfaction rates with surgery have consistently been reported to exceed 80–90% [44, 47].

The effect of surgical myotomy on chest pain continues to be debated, and patients should be aware that this symptom might not improve after either pneumatic dilation or surgery [55].

Recommendation: Laparoscopic myotomy can be performed safely and with minimal morbidity in appropriately selected patients by appropriately trained surgeons and leads to dysphagia control and improved quality of life in the majority of patients (++++, **strong**). A relatively small proportion of patients, however, will experience recurrent symptoms in the long term that are often associated with postoperative reflux.

Effect of previous endoscopic treatments on myotomy outcomes

Preoperative endoscopic therapies have been associated with greater likelihood for persistent or recurrent severe symptoms and need for additional treatments (19.5% vs. 10.1%) [56]. Previous esophageal surgery for achalasia also has been associated with poorer functional results after laparoscopic esophagomyotomy [57]. Furthermore, several studies have suggested an increased risk for intraoperative complications during esophagomyotomy after prior endoscopic intervention. Reported intraoperative esophageal perforation rates have ranged from 7.8% to 28% after previous endoscopic treatment (botulinum toxin or balloon) versus lower rates in patients without prior endoscopic treatment (range, 0–6%; Table 1) [58–60].

In contrast, other studies found no association between preoperative endoscopic treatment and intraoperative perforations [57], and some authors have reported no difference in the degree of surgical difficulty [61]. In addition, several authors also have reported similar patient outcomes after myotomy even after previous failed pneumatic dilation or Botulinum toxin injections [33, 62]. Surgery after botulinum toxin injections has been suggested to be more difficult because of a marked fibrotic reaction that can develop at the gastroesophageal junction that obliterates surgical planes [61, 63–65]. Nevertheless, some authors have reported similar outcomes in this situation to those of a primary procedure [66, 67]. In fact, surgical complication rates are thought to be more dependent on surgeon experience and the incidence of previous esophageal surgery than on previous botulinum toxin injection or previous pneumatic dilatation [57].

Recommendation: Previous endoscopic treatment for achalasia may be associated with higher myotomy morbidity, but the literature is inconclusive. A careful approach by an experienced team is advisable (++, **strong**).

Myotomy versus endoscopic treatment

The only randomized, controlled trial available to date with long-term follow-up that compared myotomy with 180° Dor fundoplication to pneumatic dilation with a Mosher bag demonstrated good response for 95% versus 65% of patients, respectively, at a 5-year follow-up period [45]. This study is the best available evidence to date, although it has been criticized because the technique used in delivering pneumatic dilation may have lead to suboptimal results. Another recent single-center, randomized, controlled trial that compared laparoscopic cardiomyotomy with partial Toupet fundoplication to pneumatic dilation in patients with newly diagnosed achalasia also showed significantly fewer treatment failures in the surgical arm after 12 months [68].

Furthermore, according to three recent meta-analyses that have mainly considered retrospective cohort studies, current evidence suggests that surgical myotomy is superior to pneumatic dilation (Table 2) [3, 24, 50]. In addition, one study [69] demonstrated that the probability for reintervention (i.e., repeated pneumatic dilation, surgical myotomy, or esophagectomy) during a period of 10 years was significantly smaller in the myotomy group (26%) versus the pneumatic dilation group (56%).

A multicenter, randomized trial found similar 6-month dysphagia response rates for patients treated by laparoscopic

Table 1 Intraoperative esophageal perforation rates of patients with and without prior treatment

Type of endoscopic treatment	Perforations		Reference
	Prior endoscopic treatment	No prior endoscopic treatment	
Pneumatic dilatation or botulinum toxin	7.8% ($N = 154$)	3.6% ($N = 55$)	[56]
Pneumatic dilatation or botulinum toxin	25% ($N = 13$)	6% ($N = 14$)	[127]
Pneumatic dilatation or botulinum toxin	12.5% ($N = 32$)	5% ($N = 60$)	[128]
Pneumatic dilatation	28% ($N = 14$)	0% ($N = 7$)	[59]
Botulinum toxin	13.3% ($N = 15$)	2.4% ($N = 42$)	[65]

Table 2 Achalasia outcome comparison based on treatment (adapted from the meta-analysis by Campos et al. [3])

Treatment modality	*n*	Follow-up (months)	Antireflux procedure	Symptom improvement	Postop GERD	Complications
Botulinum toxin injection	315	18 (6–30)	NA	41% (10–55)	NR	NR
Endoscopic balloon dilation	1798	34 (6–111)	NA	59% (33–89)[a]	Up to 45%[b]	1.6%
Laparoscopic myotomy	3086	36 (8–83)	81%	89%[†] (77–100)	15%[†] (0–60)	6.4%
Thoracoscopic myotomy	211	36 (12–72)	0%	78%[†] (31–94)	28%[†] (15–60)	10%
Transabdominal myotomy (open)	732	87 (8–190)	81%	84% (48–100)	12% (0–39)	6.4%
Transthoracic myotomy (open)	842	102 (57–172)	27%	83% (64–97)	25% (4–66)	4.7%

NA not applicable, *NR* not reported

[†] $P < 0.05$

[a] Refers to symptoms present at longest reported follow-up after first dilation

[b] GERD after dilation has not been measured and reported consistently; the incidence reported is from a few studies that have assessed GERD symptoms 4 years after dilation

esophagomyotomy (82%) or two botulinum toxin injections a month apart (66%) [70]; however, after 2 years, 87.5% of surgical patients versus 34% of botulinum toxin patients were free of symptoms [70].

A decision analysis estimating 10-year outcomes after laparoscopic esophagomyotomy with partial fundoplication, pneumatic dilatation, botulinum toxin injection, and thoracoscopic Heller myotomy found the longest quality-adjusted survival after laparoscopic therapy, although differences were small. The study concluded that decisions among therapies depend on the relative importance placed by patients and physicians on primary efficacy, risk, and durability [71].

This study also indicated that surgical expertise should be taken into consideration, as pneumatic dilatation became the favored strategy when dysphagia response after laparoscopic surgery was below 89.7% and operative mortality was greater than 0.7%. In addition, the authors also noted that the probability of reflux after pneumatic dilatation should be less than 19% [71].

Recommendation: Laparoscopic myotomy with partial fundoplication provides superior and longer-lasting symptom relief with low morbidity for patients with achalasia compared with other treatment modalities and should be considered the procedure of choice to treat achalasia (++++, **strong**).

Type of surgical approach

Five different technical approaches have been described for the accomplishment of myotomy in achalasia patients: open transabdominal, open transthoracic, thoracoscopic, laparoscopic, and the robotic approach. A recent systematic review and meta-analysis of the available literature on the surgical approach to myotomy compared the percent symptom improvement and incidence of postoperative gastroesophageal reflux (GER) among the first four approaches (Table 2) [3]. Accordingly, the open abdominal ($n = 732$) and transthoracic ($n = 842$) myotomy led to similar symptom improvement (84.5% vs. 83.3%, respectively; $P =$ not significant), but after the transabdominal approach, patients had half the incidence of GER compared with the transthoracic approach (12% vs. 24.6%; $P = 0.13$). The lack of statistical significance for this result is likely a consequence of an inadequate sample size. The comparison of the laparoscopic ($n = 3{,}086$) with the thoracoscopic ($n = 211$) myotomy revealed better symptom improvement (89.3% vs. 77.6%; $P < 0.05$) and lower

incidence of postoperative GER (28.3% vs. 14.9%; $P < 0.05$) after the laparoscopic approach. Furthermore, the laparoscopic approach was as effective as the open transabdominal and the open transthoracic approach but was associated with a lower postoperative GER incidence compared with the open transthoracic but not the open transabdominal approach. No differences were found in perioperative complications. Laparoscopic myotomy also has been found to be associated with shorter hospital stays, less blood loss, less narcotic use, less pulmonary dysfunction, and shorter return to regular activities compared with open myotomy [72–76]. Given the advantages of the minimally invasive approach, most procedures are currently being performed laparoscopically. Of note, when the procedure is performed thoracoscopically, a fundoplication is rarely created which likely explains the higher incidence of postoperative GER. In addition, the requirement for dual lumen intubation with deflation of the left lung during thoracoscopic myotomy can add complexity and potential complications to the case. It is important to note that the results of the meta-analysis are derived from observational studies, and no randomized trials exist that compare the various techniques. Overall, the laparoscopic esophagomyotomy with partial fundoplication appears to have evolved into the surgical procedure of choice [3, 26, 77].

With regard to robotic myotomy, a retrospective multicenter trial suggested decreased esophageal mucosal perforations with the use of the robot (0% vs. 16% with conventional laparoscopy; $P < 0.05$) with similar patient outcomes and equal operative times after the learning curve [78]. Another publication also found a lower rate of esophageal perforations and better quality of life based on the Short Form (SF-36) Health Status Questionnaire and a disease-specific gastroesophageal reflux disease activity index (GRACI) scores in the robotically treated patients [79]. A very recent meta-analysis of the efficacy of robotic abdominal surgery that included three studies relevant to myotomy also concluded that the risk of perforation is lower with robotic assistance [80]. It should be noted, however, that the lower perforation rate of robotic myotomy may be subject to bias, because most authors compare their results with laparoscopic myotomy cases performed earlier in their learning curve.

Recommendations: Transabdominal is superior to transthoracic esophageal myotomy due to improved postoperative reflux control by the addition of an antireflux procedure, performed only when the myotomy is done transabdominally. Laparoscopic myotomy offers advantages regarding postoperative pain, length of stay, and morbidity compared with open myotomy. The laparoscopic approach also allows routine incorporation of an antireflux procedure after myotomy and is associated with the lowest patient morbidity, and therefore, is the procedure of choice for the surgical treatment of achalasia in most patients (+++, **strong**).

Compared with laparoscopy, robotic assistance has been demonstrated to decrease the rate of intraoperative esophageal mucosal perforations (++, **weak**), but no clear differences in postoperative morbidity, symptom relief, or long-term outcomes have been described. Further study is necessary to better establish the role of robotic myotomy.

Role of fundoplication after myotomy

The role of a simultaneous fundoplication after esophagomyotomy has been debated for several years. Several authors have suggested that a fundoplication is not needed after myotomy, because it does not confer a significant benefit to patients and may increase the risk for dysphagia [81–85]. Others have argued that it is beneficial due to decreasing the incidence of postoperative GER [86–89].

Nevertheless, the recent meta-analysis by Campos et al. that reviewed 39 observational studies reporting on 3,086 patients after laparoscopic myotomy shed some light on this controversy. They found that even though the rate of symptom improvement after myotomy was not influenced by the addition of fundoplication, the incidence of postoperative GER symptoms was clearly higher when no fundoplication was performed (31.5% vs. 8.8%; $P = 0.001$). Furthermore, the analysis of the subset of articles that reported objective data (24-hour pH monitoring) corroborated these findings showing 41.5% abnormal reflux when no fundoplication was added compared with 14.5% when one was performed ($P = 0.01$) [3].

One randomized, double-blind trial on this issue ($n = 43$) reported that at 6-month follow-up, 47.6% of patients who did not have fundoplication had objective evidence of GER and median distal esophageal acid exposure time of 4.9% compared with 9.1% and 0.4% of patients who underwent a Dor fundoplication ($P < 0.01$ for both comparisons) [90]. Given that dysphagia scores and postoperative LES pressures were similar between the groups, the authors concluded that esophagomyotomy with Dor fundoplication was superior to esophagomyotomy alone [90]. Importantly, a randomized, controlled trial by Csendes and colleagues reported that poor outcomes 15.8 years after myotomy were the result of severe reflux disease and not of incomplete myotomy in 92% of patients [46].

The type of fundoplication has been subject to debate. An anterior 180° Dor fundoplication, a posterior 270° Toupet fundoplication, and a loose Nissen fundoplication have all been proposed. In a randomized, controlled trial, laparoscopic myotomy with Dor fundoplication was equally as effective as a myotomy with "floppy" Nissen fundoplication in controlling reflux, but dysphagia rates

were significantly higher in the latter group (2.8% vs. 15%, respectively; $P < 0.001$), leading the authors to conclude that the Dor fundoplication is the preferred method for GER control after myotomy [91]. This article had few patients and a short follow-up time.

A recent multicenter, randomized, controlled trial that compared myotomy outcomes after Dor ($n = 49$) versus Toupet ($n = 36$) fundoplication found that at 6-month follow-up of 47% of patients, no significant differences existed between the two groups in regards to dysphagia improvement and reflux control [92] Nevertheless, the Dor fundoplication was associated with a higher percentage of patients with abnormal reflux than the Toupet fundoplication, but this difference did not reach statistical significance due to the small sample size. Longer follow-up data and higher % patient follow-up from this trial may provide more robust evidence for the superiority of Toupet fundoplication. Importantly, the evidence from the antireflux surgery literature suggests that Toupet fundoplication may be superior to Dor fundoplication for the long-term control of reflux [93–95]. It should be noted, however, that the Dor fundoplication may have some advantages, because it leads to less disruption of the hiatal anatomy, allows coverage of the esophageal mucosa with the fundus, which is especially important if a perforation has occurred, and is a quicker and easier procedure compared with a Toupet fundoplication [96].

It should be noted that because myotomy is less likely to relieve dysphagia in patients with extremely dilated sigmoid esophagus, some experts omit fundoplication after myotomy, fearing that the related increase in pressure will be associated with persistent dysphagia in this patient population. Limited evidence exists to support or refute this approach.

Recommendations: Patients who undergo a myotomy also should have a fundoplication to prevent postoperative reflux and minimize treatment failures (++++, **strong**).

The optimal type of fundoplication is debated (posterior vs. anterior), but partial fundoplication should be favored over total fundoplication, because it is associated with decreased dysphagia rates and similar reflux control (++, **weak**). Additional evidence is needed to determine which partial fundoplication provides the best reflux control after myotomy.

Length of myotomy

The recommended length of the myotomy has ranged between 4–8 cm on the esophagus and 0.5 to 2 cm on the stomach [45, 97, 98]. Symptomatic improvement and lower esophageal resting pressures have been found to be similar (mean, 10–12 mmHg) when the myotomy is within this range. Unfortunately, this evidence comes from studies that did not directly compare short versus long myotomies, and therefore an evidence-based recommendation is difficult. Nevertheless, since one of the most important postoperative outcomes is dysphagia resolution, a longer myotomy may be more appropriate.

Recommendation: The length of the esophageal myotomy should be at least 4 cm on the esophagus and 1–2 cm on the stomach (+, **weak**).

Hiatal dissection and hiatus hernia repair during myotomy

Repair of the hiatus is not advocated by all surgeons due to concerns of increased dysphagia rates by a hiatus repair that may be too tight. Some have argued that not repairing the hiatus may lead to a higher rate of reflux, which may exacerbate postoperative recurrence of dysphagia [99]. Others have argued that the dissection of the hiatus should be limited by leaving the lateral and posterior phrenoesophageal attachments intact, as this measure minimizes postoperative reflux independent of the addition of a Dor fundoplication [100]. Unfortunately, there are no high-quality studies that address this issue, but it appears plausible that the hiatus should be approximated when necessary, emphasizing that it not be made too tight.

Predictors of successful outcomes after myotomy

Several studies have investigated preoperative factors that predict poor outcome after surgical myotomy. Such factors include severe preoperative dysphagia, low preoperative LES pressures (<30–35 mmHg), progressive esophageal body dilation with flask type or sigmoid esophagus (stage IV disease), and balloon dilation or botulinum toxin injections before myotomy [101–103]. In one series, patients with LES pressure >35 mmHg were 20 times more likely to achieve "excellent" dysphagia relief compared with those with LES pressure ≤35 mmHg [77]. Another study showed that patients with stage I-III disease on preoperative evaluation had 90% satisfactory clinical outcome that was maintained during long-term follow-up, whereas patients with stage IV disease responded only 50% of the time and even the responders demonstrated symptom deterioration over time [47]. On the other hand, other studies have shown treatment responses even in (selected) patients with dilated esophageal bodies or sigmoid esophagus [33, 104, 105]. In addition, the rate of improvement after myotomy even in patients with a normotensive or hypotensive LES has been reported to be similar to those with a hypertensive LES in some other studies [106]. Another prospective case-control study of 29 patients who underwent laparoscopic esophagomyotomies with Dor

fundoplication found functional outcomes were related to the extent of reduction in esophageal width after surgery [107]. Patients with BMI $\geq$ 30 have been reported to be more likely to have choking and vomiting before myotomy and to suffer heartburn episodes after myotomy. Nevertheless, in the same study, achalasia symptom improvement was not affected by preoperative BMI [108].

Whereas a variety of preoperative patient and disease characteristics have been suggested to predict myotomy outcomes, the literature is inconsistent, and further study is needed to better define such predictors. Although the existing evidence should be taken into consideration before myotomy, its limitations do not allow for firm recommendations.

Treatment options after failed myotomy

Patients in whom myotomy has failed can be effectively treated with botulinum toxin. Up to 71% of such patients can have symptom resolution at 1 year postinjection [12]. These rates of resolution are similar to primary treatment with botulinum toxin.

On the other hand, pneumatic dilatation has been used rarely as salvage therapy following failed myotomy because of fears of increased perforation rates. A small study reported this treatment to be safe but with limited effectiveness in less than half of patients [109].

Small series of redo laparoscopic interventions have been reported. Reported outcomes have been good or excellent [110, 111]. Another study reported a higher dysphagia resolution rate after redo myotomy (4/5 patients) versus pneumatic dilation (1/6 patients) for failed primary myotomy [112].

When patients experience refractory symptoms despite appropriate treatment, subtotal esophageal resection with gastric pull-up is a viable treatment option. Although such therapy is extremely invasive and associated with a high postoperative morbidity, favorable long-term results with significant improvement of symptoms can be achieved, even if endoscopic therapy or surgical myotomy have persistently remained unsuccessful [113].

Recommendations: Endoscopic botulinum toxin treatment can be applied safely and with equal effectiveness before or after myotomy (++, **weak**), but endoscopic balloon dilation after myotomy is currently considered hazardous by most experts and should be avoided (++, **weak**).

Repeat myotomy may be superior to endoscopic treatment and should be undertaken by experienced surgeons (++, **strong**).

Esophagectomy should be considered in appropriately selected patients after myotomy failure (+, **weak**).

Epiphrenic diverticula

Epiphrenic diverticula (ED) are outpouchings of the esophagus that are usually located in the distal 10 cm of the esophagus and have an estimated prevalence of 0.015%. The size of most diverticula has been reported to range between 3 and 8 cm when first detected. They are typically classified as pulsion diverticula, because they are thought to result from increased intraluminal pressure within the esophagus. The wall of the diverticulum is comprised of the mucosal and submucosal layer herniating through the muscle layers of the esophagus.

ED can be congenital or acquired. Many authors believe that they are caused by primary esophageal motility disorders such as achalasia [114]. Our review of the literature has identified approximately 343 cases of ED. Of these, 244 patients (71%) had documented primary esophageal motility disorders. Other presumed etiologies include the presence of hiatus hernias, esophageal leiomyomas, or prior fundoplications as sources of a mechanical obstruction leading the development of diverticula [115].

ED often are discovered incidentally during upper endoscopy performed for unrelated causes [116]. Although the majority of epiphrenic diverticula are asymptomatic, some may present with dysphagia, odynophagia, regurgitation of undigested food, chest pain, heartburn, or aspiration. There are several case reports of carcinoma arising in ED with an estimated incidence of 0.3–3% [117, 118]. Symptomatic diverticula are usually best characterized by a barium esophagogram. Upper endoscopy can be used as a method for surveillance for neoplasia.

The treatment of ED is debated. Some authors recommend only treatment of symptomatic diverticula and those larger than 2 cm [119]. Other indications for diverticulectomy are fistulae, perforation, inflammation, and pulmonary complications. Although there is a very small risk of carcinoma in an esophageal diverticulum, the potential morbidity of a postoperative complication precludes most surgeons from operating on small and asymptomatic ED. Minimally invasive techniques and stapling technology have helped decrease postoperative morbidity and may have lowered the threshold for operation.

Transabdominal, transthoracic, open, laparoscopic, and thoracoscopic approaches have been described for the treatment of ED. Although there is evidence that all approaches can be performed safely, no large studies have compared one approach with the other.

Whereas diverticulectomy alone has been advocated by some authors [120], others emphasize the importance of esophageal myotomy given the link of the disease with achalasia [121]. Valentini and colleagues argue that lack of or incomplete myotomy increases the risk of a recurrent diverticulum [122]. Selective myotomy has been advocated

by some surgeons based on the status of the LES on preoperative manometry; accordingly myotomy is not suggested for patients who have a normally relaxing LES to prevent potential reflux complications that can occur after myotomy even with the addition of a fundoplication [123]. Black et al. recommend the addition of a fundoplication after myotomy to minimize postoperative reflux and its associated complications [99]. Some surgeons have even suggested that the addition of an antireflux procedure may not only prevent reflux but also help prevent leakage from the diverticulectomy staple line [119]. Others have argued against a full fundoplication citing the possibility of an increased recurrence rate of ED due to the increased pressure zone caused by the fundoplication distal to the diverticulectomy [90, 124] as well as increased leak rates [125]. Some authors have advised that a coexisting hiatus hernia not be repaired to minimize the risk of diverticulum recurrence through possible mechanical obstruction related to closure of the hiatus [115].

Intraoperative endoscopy is recommended by many experts, because it may be useful in guiding the completeness of the myotomy and the diverticulectomy, preventing esophageal narrowing, and detecting leaks intraoperatively [126].

Only one death has been reported among 343 patients who were treated for ED (0.3%). Twenty-three (6.7%) leaks have been reported, and nine (2.6%) patients required reoperation. The others were successfully treated with drains.

The rarity and incidental presentation of ED make it a disease that is difficult to study. The available literature is comprised of retrospective studies that report on small case series (rarely exceeding 30–40 cases), and no comparative studies exist. The lack of high-quality data (which may be impossible to accrue for such a rare disease) make it very difficult to provide firm recommendations about the appropriate treatment of this disease.

Recommendations: Epiphrenic diverticula should be treated surgically when symptomatic. Given their frequent association with achalasia, esophageal manometry should be pursued to confirm the diagnosis of achalasia when they are identified. A myotomy at the opposite side of the diverticulum that goes beyond the distal extent of the diverticulum should be performed when achalasia is present. In this situation, concomitant diverticulectomy may be indicated based on the size of the diverticulum. When diverticula are not resected, endoscopic surveillance is advised. The optimal approach for their treatment needs further study, and surgeons should be aware of the relatively high incidence of postoperative leaks (+, **weak**).

Limitations of the available literature

The achalasia literature is limited due to the rarity of the disease. Consequently, few, small, controlled trials are available, and most studies are retrospective in nature with significant heterogeneity among them and increased risk for publication bias and other confounding factors. In addition, reporting of outcomes varies significantly as does the follow-up period, which generally tends to be short making it difficult to combine and compare such data. Finally, the majority of the studies do not report details on the expertise of their surgeons, and most have been conducted in single institutions making the generalization of their findings difficult. Based on these limitations of the literature, firm recommendations are difficult.

Summary of recommendations

1. *Diagnostic workup*: Patients with suspected achalasia should undergo a barium esophagram, an upper endoscopy, and esophageal manometry to confirm the diagnosis (+++, **strong**).
2. *Use of pharmacotherapy:* Pharmacotherapy plays a very limited role in the treatment of patients with achalasia and can be used in very early stages of the disease, temporarily before more definitive treatments, or for patients who fail or are not candidates for other treatment modalities (++++, **strong**).
3. *Use of botulinum toxin*: Botulinum toxin injection can be administered safely, but its effectiveness is limited especially in the long term. It should be reserved for patients who are poor candidates for other more effective treatment options such as surgery or dilation (++++, **strong**).
4. *Endoscopic dilation*: Among nonoperative treatment techniques endoscopic dilation is the most effective for dysphagia relief in patients with achalasia but also is associated with the highest risk of complications. It should be considered in selected patients who refuse surgery or are poor operative candidates (++++, **strong**).
5. *Use of esophageal stents*: The use of esophageal stents cannot be recommended for the treatment of achalasia (++, **strong**).
6. *Surgical treatment*: Laparoscopic myotomy can be performed safely and with minimal morbidity in appropriately selected patients and by appropriately trained surgeons and leads to dysphagia control and improved quality of life in the majority of patients (++++, **strong**). A relatively small proportion of patients, however, will experience recurrent

symptoms in the long term often associated with postoperative reflux.

7. *Effect of prior endoscopic treatments on myotomy outcomes*: Previous endoscopic treatment for achalasia may be associated with higher myotomy morbidity, but the literature is inconclusive. A careful approach by an experienced team is advisable (++, **strong**).
8. *Surgery versus other treatment modalities*: Laparoscopic myotomy with partial fundoplication provides superior and longer-lasting symptom relief with low morbidity for patients with achalasia compared with other treatment modalities and should be considered the procedure of choice to treat achalasia (++++, **strong**).
9. *Type of surgical approach*: Transabdominal is superior to transthoracic esophageal myotomy due to improved postoperative reflux control by the addition of an antireflux procedure, performed only when the myotomy is done transabdominally. Laparoscopic myotomy offers advantages regarding postoperative pain, length of stay, and morbidity compared with open myotomy. The laparoscopic approach also allows routine incorporation of an antireflux procedure after myotomy and is associated with the lowest patient morbidity and, therefore, is the procedure of choice for the surgical treatment of achalasia in most patients (+++, **strong**). Compared with laparoscopy, robotic assistance has been demonstrated to decrease the rate of intraoperative esophageal mucosal perforations (++, **weak**), but no clear differences in postoperative morbidity, symptom relief, or long-term outcomes have been described. Further study is necessary to better establish the role of robotic myotomy.
10. *Role of fundoplication*: Patients who undergo a myotomy also should have a fundoplication to prevent postoperative reflux and minimize treatment failures (++++, **strong**). The optimal type of fundoplication is debated (posterior vs. anterior), but partial fundoplication should be favored over total fundoplication, because it is associated with decreased dysphagia rates and similar reflux control (++, **weak**). Additional evidence is needed to determine which partial fundoplication provides the best reflux control after myotomy.
11. *Length of myotomy*: The length of the esophageal myotomy should be at least 4 cm on the esophagus and 1–2 cm on the stomach (+, **weak**).
12. *Treatment options after failed myotomy*: Endoscopic botulinum toxin treatment can be applied safely and with equal effectiveness before or after myotomy (++, **weak**), but endoscopic balloon dilation after myotomy is currently considered hazardous by most experts (++, **weak**). Repeat myotomy may be superior to endoscopic treatment and should be undertaken by experienced surgeons (++, **strong**). Esophagectomy should be considered in appropriately selected patients after myotomy failure (+, **weak**).
13. *Epiphrenic diverticula*: Epiphrenic diverticula should be repaired surgically when symptomatic. Given their frequent association with achalasia, an esophageal manometry should be pursued to confirm the diagnosis of achalasia when they are identified. A myotomy at the opposite side of the diverticulum that goes beyond the distal extent of the diverticulum should be performed when achalasia is present. In this situation, concomitant diverticulectomy may be indicated based on the size of the diverticulum. When the diverticula are not resected, endoscopic surveillance is advised. The optimal approach for their treatment needs further study, and surgeons should be aware of the relatively high incidence of postoperative leaks (+, **weak**).

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Appendix

This document was prepared and revised by the SAGES Guidelines Committee:

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