Data analyses and perspectives on laparoscopic surgery for esophageal achalasia

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Abstract

In general, the treatment methods for esophageal achalasia are largely classified into four groups, including drug therapy using nitrile or a calcium channel blocker, botulinum toxin injection, endoscopic therapy such as endoscopic balloon dilation, and surgery. Various studies have suggested that the most effective treatment of esophageal achalasia is surgical therapy. The basic concept of this surgical therapy has not changed since Heller proposed esophageal myotomy for the purpose of resolution of lower esophageal obstruction for the first time in 1913, but the most common approach has changed from open-chest surgery to laparoscopic surgery. Currently, the laparoscopic surgery has been the procedure of choice for the treatment of esophageal achalasia. During the process of the transition from open-chest surgery to laparotomy, to thoracoscopic surgery, and to laparoscopic surgery, the necessity of combining antireflux surgery has been recognized. There is some debate as to which type of antireflux surgery should be selected. The Toupet fundoplication may be the most effective in prevention of postoperative antireflux, but many medical institutions have selected the Dor fundoplication which covers the mucosal surface exposed by myotomy. Recently, a new endoscopic approach, peroral endoscopic myotomy (POEM), has received attention. Future studies should examine the long-term outcomes and whether POEM becomes the gold standard for the treatment of esophageal achalasia.

Key words: Esophageal achalasia; Surgery; Treatment; Review; Laparoscopy

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Core tip: Esophageal achalasia is the most common primary esophageal motility disorder and the major symptoms are dysphagia, vomiting, and chest pain. Various studies have suggested that the most effective...
treatment of esophageal achalasia is surgical therapy and the basic concept of surgical therapy has not changed since Heller proposed esophageal myotomy for the purpose of resolution of lower esophageal obstruction. However, the most common approach has changed from open-chest surgery to laparoscopic surgery. This article reviews the outcomes of surgical procedures for esophageal achalasia from various viewpoints and discusses the problems and prospects of laparoscopic surgery for esophageal achalasia.

INTRODUCTION

Esophageal achalasia is the most common primary esophageal motility disorder and is historically characterized by lack of the Auerbach’s nerve plexus\(^\text{[5]}\). It causes loss of esophageal peristalsis and/or a lack of lower esophageal sphincter relaxation during swallowing, which results in esophageal obstruction\(^\text{[6-8]}\). The major symptoms are dysphagia, vomiting, and chest pain\(^\text{[5]}\). There are neither racial nor gender differences in its incidence, according to epidemiologic studies. The disease is quite rare with a frequency of approximately 1 in 0.1 million\(^\text{[6,7]}\). The pathogenesis of esophageal achalasia has not been elucidated, and the pathogenic mechanism is not understood. At the moment, the goal of treatment is not complete resolution of the disease, but rather symptomatic improvement that may significantly affect the patients’ quality of life (QOL). The treatment methods are largely classified into four groups, drug therapy using nitrite or a calcium channel blocker, botulinum toxin injection, endoscopic balloon dilation, and surgery\(^\text{[8]}\). Esophageal myotomy was the first surgery that was proposed by Heller in 1913. Thereafter, a combination with cardioplasty was adapted to prevent reflux esophagitis, which was sometimes induced by the myotomy\(^\text{[9,10]}\). Currently, laparoscopic myotomy has been widely performed as a standard treatment approach in many institutions, because it is minimally invasive, achieves esthetic results, and has a defined surgical area\(^\text{[7,8,11-14]}\). The objective response rate by surgery is good, ranging from 88% to 97%\(^\text{[15-20]}\). There are some reports on the long-term outcome\(^\text{[21-23]}\), which have demonstrated the safety and effectiveness of the procedure.

This article reviews the outcomes of surgical procedures for esophageal achalasia from various viewpoints and discusses the problems and prospects of laparoscopic surgery for esophageal achalasia.

CHANGES IN SURGICAL PROCEDURES

FOR ESOPHAGEAL ACHALASIA OVER TIME

Open surgery

Lower esophageal myotomy via left thoracotomy for the purpose of improvement of esophageal clearance was first reported by Heller. Heller’s approach involved two incisions of approximately 8-cm made on the anterior and posterior esophageal walls to relieve the esophageal obstruction. The approach was modified by Williams et al\(^\text{[24]}\) and the currently used long myotomy with anterior fundoplication was established. While the open-chest surgery was widely used, myotomy via laparotomy was also performed in order to avoid the complicated surgical procedures and postoperative wound pain of open-chest surgery. Abir et al\(^\text{[25]}\) who studied 18 articles regarding Heller myotomy reported that the response rate in 2680 patients was 83% and concluded that the procedure was very effective. However, since Heller myotomy required myotomy of the gastroesophageal junction to prevent antireflux, there was a risk of postoperative gastroesophageal reflux disease (GERD). They reported that the overall incidence of postoperative GERD was 12.3%, but 11 of the 18 articles on surgical treatment of esophageal achalasia reported combination of myotomy with laparoscopic antireflux surgery (LARS). The occurrence of postoperative GERD in patients with antireflux surgery was lower than those in patients without antireflux surgery (10% vs 16%). These findings suggested that laparotomic myotomy should be performed along with antireflux surgery.

Minimally invasive surgery

Successful laparoscopic cholecystectomy was first reported in 1987. Since then, the surgical procedures for various pathologies have changed from open-chest surgery to laparoscopic surgery. This trend was also observed in the treatment of esophageal achalasia. Laparoscopic procedures have been rapidly adopted due to its minimally invasive nature and better visualization of the surgical area, compared with open-chest surgery and laparotomy. The procedure was performed using the left thoracic approach similar to that of open-chest surgery. Pellegrini et al\(^\text{[26]}\) reported that 14 of 17 patients (82%) were satisfied with the surgical outcome that was comparable with that obtained after thoracotomy. The major advantage of thorascoscopic surgery is that long myotomy can be applied to the cranial esophagus. This approach does not require mobilization of the paraesophageal membrane, but it is difficult to reach the anterior wall of the gastric cardia, and an incision cannot reach the oblique muscle due to this lack of sufficient myotomy onto the cardia. Therefore, this approach will not damage the antireflux mechanism and be less likely
to cause postoperative reflux esophagitis. However, there are still risks of persistence or relapse of the obstruction sensation of the esophagus[26-28]. Thus, thoracoscopic surgery cases are limited in number whereas laparoscopic surgery is widely used.

Laparoscopic surgery was first reported by Shimi et al[29] in 1991. Since then, there are many successful reports not only on the short-term results but also on the long-term surgical outcomes[30,31]. The operating time and duration of postoperative hospital stay are shorter, and the symptomatic improvement is greater by laparoscopic surgery, when compared with thoracoscopic surgery[32].

**COMPARISON OF SURGICAL RESULTS BY APPROACH**

**Open method vs minimally invasive surgery**

Transthoracic approaches include open-chest surgery and thoracoscopic surgery. A retrospective study conducted by Kesler et al[33] which compared thoracoscopic myotomy and open-chest myotomy reported that the operating time and intraoperative blood loss were significantly decreased in the thoracoscopic myotomy group (P < 0.05, respectively). In addition, the patients in thoracoscopic myotomy was experiencing a shorter hospitalization, which was due to earlier resumption of oral nutrition, earlier removal of chest tube, and less requirement of postoperative analgesic agents. Those results indicated that intra-and post-operative results were better in the patients undergoing thoracoscopic surgery than that in those undergoing open-chest surgery. Furthermore, a study on the long-term outcomes by Pellegrini et al[34] showed relief of dysphagia seen in 88% of patients and 66% of patients had regained their original weight. The open-chest surgery was replaced with thoracoscopic surgery due to the minimally invasive closed-chest approach.

The transabdominal approach was also converted to laparoscopic surgery over time in the institutions which performed laparotomic myotomy. Ancona et al[35] performed a retrospective study on 17 patients undergoing the laparoscopic Heller-Dor procedure and 17 background-matched patients undergoing laparotomic surgery, and reported that the operating time was longer in the laparoscopic surgery group than that in the other group (178 min vs 125 min). In addition, the duration of the postoperative hospital stay and time to reintegrate into society were significantly decreased with the laparoscopic surgery (P < 0.0001, respectively). However this study were consisted with short-term examination, and the analysis in long-term were expected. The above-mentioned findings suggested that laparoscopic surgery was more effective than the transabdominal approach as a treatment for esophageal achalasia. Currently, laparoscopic surgery is a gold standard for treatment of esophageal achalasia. And we are not able to find any shortcoming in laparoscopic surgery for esophageal achalasia without lengthening of operating time if the patients have no contraindication of laparoscopic surgery.

**Thoracoscopic surgery vs laparoscopic surgery**

Since laparoscopic surgery involves minimal invasiveness and yields a similar response rate as compared to that of the open-chest method, minimally invasive surgery has been used as the first-line therapy. Ramacciato et al[36] performed a case controlled study to compare the results of thoracoscopic myotomy with laparoscopic myotomy in 16 patients with thoracoscopic surgery group and in 17 patients with laparoscopic surgery (with Dor) group. The results indicated that the operating time and duration of postoperative hospital stay were significantly decreased in the laparoscopic surgery group (P = 0.0001 in both), and the frequency of persistence and relapse of a sensation of postoperative obstruction in the esophagus was significantly greater in the thoracoscopic surgery group (38% vs 6%, P = 0.04). However this study was not enough for analyzing postoperative GERD including pH-metry, and further examination was expected. Patti et al[37] investigated 8-year experience for minimally invasive surgery for esophageal achalasia and they indicated that the laparoscopic surgery is the better choice for this disease.

**PROBLEMS ASSOCIATED WITH LARS AFTER ESOPHAGEAL MYOTOMY**

**Laparoscopic myotomy only vs laparoscopic myotomy with fundoplication**

The majority of the previous studies reached the consensus that laparoscopic surgery was the most suitable surgical procedure for esophageal achalasia[38]. One of the advantages of the transabdominal approach is that myotomy can be sufficiently extended to the gastric side, but the approach may induce postoperative gastroesophageal reflux. Several studies have been performed to validate whether laparoscopic myotomy alone or in combination therapy with antireflux surgery should be performed (Table 1)[39]. The observation period ranged from 6 to 96 mo but the postoperative improvement in the loss of the obstructive sensation was good, ranging from 70% to 100%. Thus, all of the studies showed no significant difference in symptomatic improvement between the groups. Nevertheless, the incidence of postoperative GERD symptoms tended to be higher when laparoscopic myotomy was performed alone, which suggested that cardioplasty was essential for prevention of gastroesophageal reflux.
**Table 1** Comparison of surgical outcomes between laparoscopic Heller myotomy vs laparoscopic myotomy with fundoplication

| Author        | Year | Study design | Samples | Procedure                  | Follow up (mo) | Success | Postop-GERD |
|---------------|------|--------------|---------|----------------------------|----------------|---------|-------------|
| Campos et al. | 2009 | Meta-analysis| 579     | myotomy only               | NA             | 90%     | 31%         |
|               |      |              | 2507    | myotomy + fundoplication   | NA             | 90%     | 9%          |
| Falkenback et al | 2003 | RCT          | 10      | myotomy only               | 96             | 70%     | 13%         |
|               |      |              | 10      | myotomy + fundoplication   | 96             | 70%     | 0.1%        |
| Richards et al | 2004 | RCT          | 21      | myotomy only               | 6              | 100%    | 47.6%       |
|               |      |              | 22      | myotomy + fundoplication   | 6              | 95.5%   | 9.1%        |
| Simić et al.  | 2010 | RCT          | 22      | myotomy only               | 36             | 100%    | 9.1%        |
|               |      |              | 62      | myotomy + fundoplication   | 36             | 91.7%   | 9.7%        |
| Finley et al. | 2007 | Retrospective| 24      | myotomy only               | 12             | 100%    | NA          |
|               |      |              | 71      | myotomy + fundoplication   | 12             | 98.6%   | NA          |

NA: Not available; GERD: Gastroesophageal reflux disease; RCT: Retrospective cohort study.

**Laparoscopic myotomy with Dor fundoplication vs laparoscopic myotomy with other types of fundoplication**

A combination of laparoscopic myotomy and antireflux surgery may be desirable for treatment of esophageal achalasia, but it is still controversial which type of antireflux surgery should be performed. Many institutions in the world seem to select the Dor fundoplication, but the Nissen fundoplication and the Toupet fundoplication have also been performed. Previous studies mainly compared the Dor fundoplication with other types of fundoplications (Table 2)[38-43]. All types of antireflux surgery showed similar symptomatic improvements and a high response rate, but the incidence rate of postoperative GERD was slightly greater in the patients undergoing the Dor fundoplication. However, there was no statistically significant difference.

The 2012 guidelines of the Society of American Gastrointestinal and Endoscopic Surgeons[44] also strongly recommended a combination of laparoscopic myotomy with antireflux surgery. However, the guidelines declined to say which type of antireflux surgery should be performed but they did state that circumferential fundoplication should be avoided because of the risk of persistence and relapse of the postoperative obstructive sensation of the esophagus. In general, the previous studies indicated that the Toupet fundoplication had a slightly higher antireflux result, but there was no definite conclusion. There was a report that diverticula developed in the esophageal myotomy site when esophageal myotomy using the Toupet fundoplication was not sufficiently extended to the gastric side[45], which suggested that the Dor fundoplication which completely wraps the exposed mucosa should be performed.

### COMPARISON BETWEEN SURGICAL PROCEDURES AND OTHER FUNDOPPLICATION APPROACHES

**Esophageal myotomy vs PD**

Endoscopic balloon dilation is an effective treatment for esophageal achalasia[46,47]. The procedure was proposed by Vantrappen et al[46] in 1971 for the first time, and the response rate is currently 80%-90%[48]. However, a long-term follow-up study indicated that 60% of the patients had relapse and needed radiation[49]. Furthermore, the incidence of esophageal perforation after the procedure was not high, ranging from 0.5% to 5%, but 50% or more of these patients with perforations required emergency surgery. These patients are at the greatest disadvantages for this procedure[50,51]. In cases where patients had a previous history of balloon dilation, scar formation and other tissue injury that possibly occurred during the recovery process from submucosal hemorrhage may cause detachment and myotomy of the esophagus in the abdomen[52-54]. We studied whether a history of dilation influences surgical outcome and reported that there was no difference between those with and without previous Parkinson’s disease (PD) in the operating time, perioperative blood loss, incidence rate of mucosal perforation during myotomy, and rate of postoperative symptomatic improvement[46].

There are many studies comparing the therapeutic effects of PD and laparoscopic myotomy, and Table 3 shows representative studies[55-59]. The duration of observation ranged from 3 mo to 5 years, and the rate of symptomatic improvement was greater with laparoscopic surgery, which indicated that laparoscopic surgery was strongly recommended to the patients with esophageal achalasia.

**Esophageal myotomy vs botulinum toxin injection**

The botulinum toxin inhibits release of acetylcholine from nerve terminals. Injection of botulinum toxin into the lower esophageal sphincter of patients with esophageal achalasia enables muscle relaxation and eases the passage of food into the esophagus. Since a significant symptomatic improvement was observed in patients with esophageal achalasia on short-term outcome in a placebo-controlled trial for one week, the therapy in now an effective treatment for esophageal achalasia[60]. However, the persistence of the therapeutic effect varied depending on the patient. A long-term study indicated that the response...
rate of patients undergoing botulinum toxin injection was approximately 65%. The relatively greater effect was observed in elderly patients and in patients with an advanced type of esophageal achalasia, and the effect lasted approximately 1.3 years. Zaninotto et al performed a randomized controlled trial in 80 patients with esophageal achalasia to compare the therapeutic effects of laparoscopic myotomy and botulinum toxin injection. The results demonstrated that laparoscopic myotomy was safer, and the 6-mo post-treatment evaluation showed that the response rate was greater in laparoscopic myotomy compared with that in botulinum toxin injection (82% vs 66%, P < 0.05). Another evaluation after 2 years showed that the symptomatic improvement effect was seen in 87.5% of the laparoscopic myotomy group and in 34% of the botulinum toxin injection group. The long-term outcome of botulinum toxin injection was not successful enough, similar to dilation therapy, but the injection therapy may be effective in treating the patients who are not a candidate for either dilation or surgical procedures due to reduced activities of daily living (ADL).

**Esophageal myotomy vs per oral endoscopic myotomy**

Recently, a new treatment for esophageal achalasia, per oral endoscopic myotomy (POEM), has been introduced and has received attention. The method is an adaptation of the natural orifice transluminal endoscopic surgery (NOTES) in the mediastinum, and has come to use in a small number of medical institutions. This method is based on a lower esophageal sphincter (LES) myotomy in a porcine survival model which was performed for the first time in 2007. POEM is quite novel and only a few comparative studies on the short-term outcome have been completed. Table 4 shows representative results. There was no difference in the operating time and in the incidence of perforation between the two groups, but the incidence of postoperative GERD symptoms was slightly greater in the POEM group. Furthermore, Teitelbaum et al performed the gastroesophageal junction distensibility measurements with a functional lumen imaging probe during laparoscopic myotomy with either cardioplasty or POEM on 25 patients with esophageal achalasia, and obtained similar results.

The long-term outcome of the new treatment method should be evaluated, but the short-term outcome was excellent, and the procedure was less invasive than laparoscopic surgery. Also in terms of a better esthetic outcome, the new procedure may have a higher potential. Future studies should evaluate the incidence of postoperative GERD and the therapeutic effects.

**PROBLEMS AND PROSPECTS OF LAPAROSCOPIC SURGERY**

Laparoscopic surgery for esophageal achalasia provides greater symptomatic improvement but some patients have a poor outcome. Such poor response...
to laparoscopic surgery may mainly be caused by the surgeon’s lack of technical skills, including insufficient esophageal myotomy, an overtight wrap, a loose wrap, and development of postoperative reflux esophagitis due to absence of cardioplasty\(^{(69,70)}\). Some studies have been performed to detect potential factors relating to the patients’ background and pathology. Iqbal et al\(^{(71)}\) compared 67 patients whose symptoms were improved and 15 patients whose symptom were not improved, and reported that the effect of surgery was more beneficial in patients with a short disease duration and in patients without a previous history of botox injection. Torquati et al\(^{(72)}\) performed a comparison study in 200 patients undergoing laparoscopic Heller myotomy, including 170 responders and 30 non-responders. The preoperative manometry showed that the LES pressure was significantly greater in the responders than that in the non-responders, and the patients with a LES pressure > 35 mmHg had more than 21 times the likelihood to achieve excellent dysphagia relief after myotomy as compared with those with a LES pressure ≤ 35 mmHg when the cutoff value was set at 35 mmHg for the LES pressure.

Patients who did not go into complete remission after the primary surgery or those who suffered from a relapse during the follow-up received the redo surgery at some medical institutions (Table 5)\(^{(71,73-76)}\). The rate of mucosal perforation was relatively high, ranging from 4.7% to 30%, but the patient satisfaction was 40% to 90%, which suggested that the redo surgery might need to be performed in highly experienced medical institutions for the purpose of QOL improvement.

High resolution manometry (HRM), which was recently introduced, is equipped with strong diagnostic capabilities in esophageal dysmotility. The pathology of esophageal achalasia is classified into Types I to III based on the level of esophageal motility. Several studies evaluated the treatment outcome by Type, and the analysis found that Type II had the greatest therapeutic response, followed by Type I and then Type III\(^{(77,78)}\). Salvador et al\(^{(79)}\) reported that the response of myotomy to esophageal achalasia Type I, II, and III was 85.4%, 95.3%, and 69.4%, respectively. According to the above-mentioned findings, treatment of Type III esophageal achalasia should be further studied and include a new treatment approach.

As to laparoscopic surgery for esophageal achalasia, a single incision and reduced port surgery focusing on the esthetic aspect\(^{(80)}\) has widely been used, especially in high volume centers (Table 6)\(^{(81,82)}\). According to the report by Ross et al\(^{(83)}\), many studies

### Table 4 Comparison of surgical outcomes between laparoscopic Heller myotomy vs peroral endoscopic myotomy (%)

| Author          | Year | Study design | Samples | Procedure | Follow up (d) | OP time (min) | Major complication (perforation) | Postop-GERD |
|-----------------|------|--------------|---------|------------|---------------|---------------|----------------------------------|-------------|
| Hungness et al\(^{(66)}\) | 2013 | Retrospective | 55      | myotomy   | 42            | 125           | 1 (2)                            | NA          |
| Ujiki et al\(^{(67)}\) | 2013 | Case control | 21      | myotomy   | 164           | 154.5         | 1 (4.8)                          | 4 (19)      |

Symptomatic GERD or PPI required. NA: Not available; GERD: Gastroesophageal reflux disease; POEM: Peroral endoscopic myotomy; OP: Operation.

### Table 5 Surgical outcomes of reoperation for patients with achalasia

| Author          | Year | Samples | Approach (primary) | Approach (re-do) | Mucosal injury | Re-revision | Satisfaction |
|-----------------|------|---------|-------------------|-----------------|---------------|-------------|--------------|
| Iqbal et al\(^{(71)}\) | 2006 | 15      | 10: Laparoscopy   | 15: Laparoscopy  | 30%           | 20%         | 40%-89%      |
| Rakita et al\(^{(72)}\) | 2007 | 12      | 13: Abdominal     | 13: Abdominal    | 15.8%         | 10.5%       | 50%          |
| Grotenhuis et al\(^{(73)}\) | 2007 | 19      | 7: Laparoscopy    | 26: Laparoscopy  | 4.7%          | 9.3%        | 79%          |
| Lovisek et al\(^{(74)}\) | 2013 | 43      | 20: Thoracic      | 23: Thoracic     | 30%           | NA          | 90%          |
| Omura et al\(^{(75)}\) | 2012 | 10      | 3: Thoracotomy    | 2: Thoracotomy   | 30%           | NA          | 90%          |

NA: Not available.
reported that the learning curve of the laparoscopic surgery was 20 operations, but it might be easier to master the technique if the surgeons have had prior experience with conventional laparoscopic Heller myotomy (Lap-Heller). According to reports by two high volume centers that treat esophageal achalasia, the symptomatic improvement rate was similar to that by conventional methods, and no patients were converted to lap-Heller, which suggested that the outcome was sufficiently acceptable. In the future, younger patients and female patients with esophageal achalasia may prefer laparoscopic surgery, and such a surgical procedure will likely be widely used.

In general, esophageal achalasia is considered as a premalignant condition for esophageal squamous cell carcinoma, and the risk of developing the cancer might be 140-times greater than that in the general population\cite{84}. Esophageal achalasia might be caused by either saburra in the esophagus due to decreased clearance of the lower esophagus or chronic exposure of saliva to the esophageal mucosa\cite{84,85}. Some patients developed esophageal squamous cell carcinoma during the long follow-up after surgery\cite{86,87}. Therefore, even after the symptoms are improved by surgery, follow-up by periodic upper gastrointestinal endoscopy is required.

**CONCLUSION**

Since laparoscopic Heller myotomy was reported by Heller as the first-line surgical therapy for esophageal achalasia, myotomy has been modified in various ways for the last 100 years. At the moment, there is no room for doubt that laparoscopic myotomy has become the gold standard for treatment of achalasia throughout the world. However, the current surgical therapy does not provide a complete resolution of esophageal achalasia. The therapy achieves successful symptomatic relief but there is still a need for more improvement. It is expected that measures against the technical problems that have been pointed out by the previous studies lead to the development of a new approach. Additionally, further studies might provide guidelines for treatment based on various factors.

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**Table 6** Surgical outcomes of reduced port surgery for patients with achalasia

| Author          | Year | Samples | Procedure               | Follow up (mo) | OP time (min) | Mucosal injury | Conversion to laparotomy | Satisfaction |
|-----------------|------|---------|-------------------------|----------------|---------------|----------------|--------------------------|--------------|
| Barry et al     | 2011 | 66      | Myotomy                 | NA             | 117           | 3%             | 0%                       | 94%          |
| O’Neill et al   | 2001 | 24      | Myotomy with anterior fundoplication | 8              | 230           | 13%            | 0%                       | 90%          |

NA: Not available; OP: Operation.
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