Review Article

Esophagectomy for end-stage achalasia—is it too aggressive?

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Abstract: Achalasia is a progressively worsening primary motility disorder of the esophagus, characterised by a lack of peristalsis and impaired relaxation of the lower esophageal sphincter. The management of this disease aims to palliate symptoms by improving gastric emptying and reducing the pressure gradient. Nonetheless, approximately 5% of patients will progress to end-stage disease with the development of a massively dilated and tortuous megaesophagus. Esophagectomy for the treatment of end-stage achalasia remains a controversial topic and has been recommended as a last resort by the 2018 International Society for Diseases of the Esophagus guidelines. We describe a patient with end-stage achalasia who had exhausted conventional therapy and was successfully managed with an Ivor Lewis esophagectomy, followed by a review of current practice regarding the management of this difficult problem.

Keywords: End-stage achalasia; esophagectomy; megaesophagus; esophageal resection

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Introduction

Achalasia is a rare primary motility disorder of the esophagus. Degeneration of the inhibitory neurons of the myenteric plexus within the esophagus leads to the characteristic loss of peristalsis and impaired relaxation of the lower esophageal sphincter. The subsequent abnormal emptying of esophageal contents into the stomach and stasis leads to a constellation of symptoms including dysphagia, regurgitation, aspiration, heart burn, and chest pain (1,2). Patients will often present with radiological features of esophageal dilatation on contrast studies which can be further categorized according to Rezende's classification of Chagasic megaesophagus (*Figure 1*) (3).

The annual incidence of achalasia in South Australia has been estimated at 2.3 to 2.8 per 100,000 people (4). This is higher than the previously cited estimate of 0.5 to 1.6 per 100,000 that has been historically noted in studies throughout Europe, Asia, Canada and America. The management of this illness involves a multidisciplinary approach with endoscopic and surgical therapies which aim to palliate symptoms by improving gastrointestinal emptying and lowering the pressure gradient across the lower esophageal sphincter (5). Despite these treatments, 5% of patients with achalasia will progress to end-stage disease for which the management remains controversial (6).

The latest International Society for Diseases of the Esophagus (ISDE) guidelines released in 2018 state that management of recurrent symptoms should initially focus on less invasive treatments. In the instance that these methods fail, there should be progression to esophagectomy for management of end stage achalasia (7). In this report, we aim to review our own experience of end-stage achalasia by discussion of a representative case, review of the current literature, and discussion of our local results.

Case report

A 40-year-old male with type I achalasia was referred to our unit with progressively worsening dysphagia

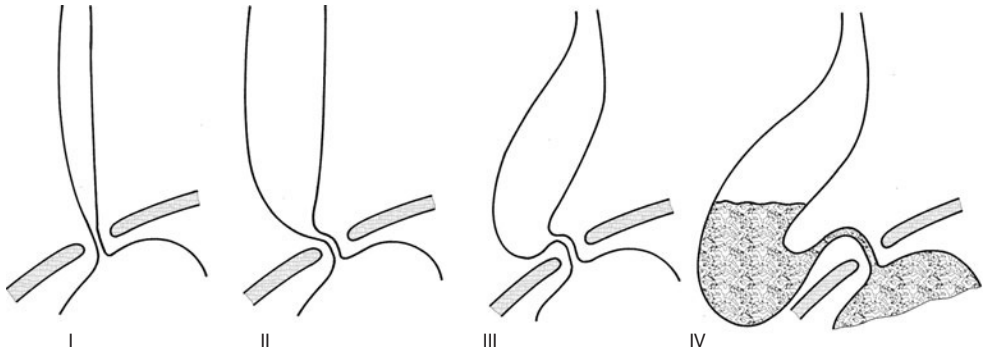

Figure 1 Illustrative representation of the progressive esophageal dilatation according to Rezende's classification of Chagasic megaesophagus with associated contrast retention.

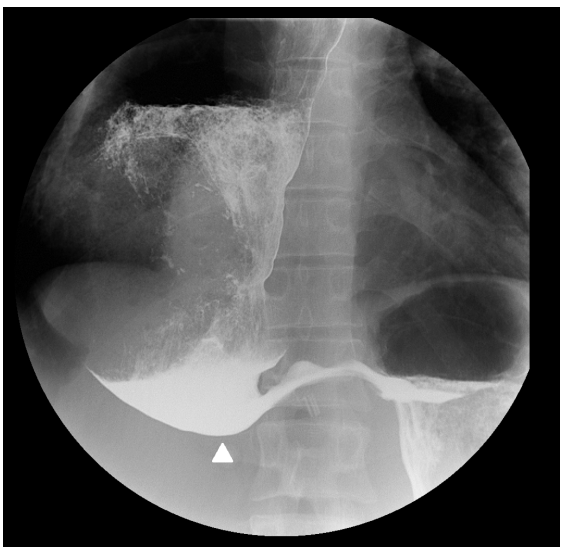

Figure 2 Barium swallow demonstrating a grossly dilated sigmoid esophagus with the presence of a 'sump' (arrowhead) at the level of the diaphragm; features consistent with end-stage achalasia.

and regurgitation. He had undergone a laparoscopic cardiomyotomy and Dor fundoplication 4 years prior with symptom recurrence after approximately 12 months. He was initially treated by the original surgical team with four pneumatic dilatations with each providing only temporary control. At the time of referral, he was tolerating soft foods, with a stable BMI of 25. Other relevant co-morbidities included Type 1 diabetes mellitus which was increasingly difficult to control, and gastroparesis.

Initial investigations included esophageal manometry, barium swallow showing sump formation at the lower end and a dilated esophagus, and endoscopy. The decision was made to perform a diagnostic laparoscopy, with take-down of the original Dor fundoplication and possible redo cardiomyotomy. At surgery, a mal-positioned anterior fundoplication was found where the body of the stomach (rather than the fundus) had been inadvertently used to perform the wrap. Subsequently, there had been a band across the cardiomyotomy, causing gastro-esophageal obstruction. The patient initially reported improvement of his symptoms, but at follow-up 6 months later, reported worsening symptoms of dysphagia and regurgitation. A repeat endoscopy was performed showing copious amounts of fluid and food in the dilated esophagus despite a 48-hour fast. Fortuitously, the patient was intubated for the endoscopy to prevent aspiration. A barium swallow was also repeated showing end-stage achalasia (*Figure 2*). The patient agreed to proceed to an esophagectomy following discussion with a prior patient of the authors' who had undergone esophagectomy for end-stage achalasia in 2016 with an excellent result.

An Ivor-Lewis esophagectomy and feeding jejunostomy was performed through an anterolateral thoracotomy and upper midline abdominal incision. The esophagus was mobilised and divided with a gastric pull-up and hand-sewn anastomosis performed. A pyloroplasty was performed and a feeding jejunostomy was inserted along with a routine chest drain. The intra-operative blood loss was approximately 500 mL. The post-operative period was complicated by lung atelectasis, elevated blood glucose levels, and a transient pyloric obstruction managed conservatively. The total length of stay was 14 days; 6 of which were in a high dependency unit.

Histopathology of the resected specimen showed patchy lymphoplasmacytic inflammatory injury in the myenteric

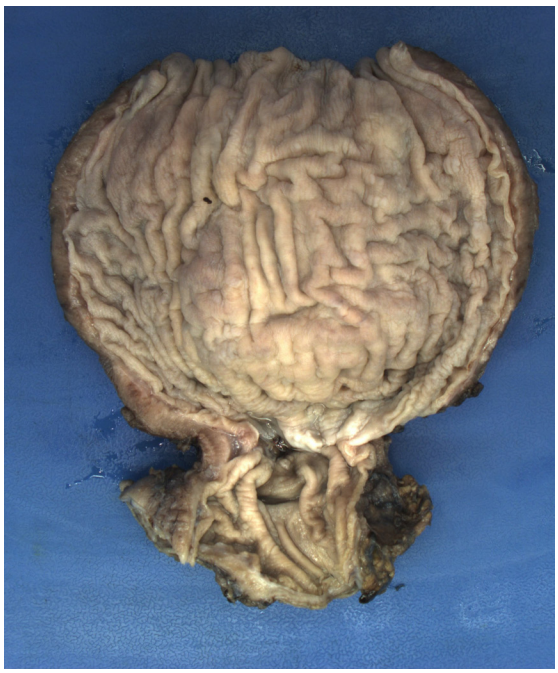

Figure 3 Esophagectomy specimen following Ivor-Lewis esophagectomy showing a dilated megaesophagus, and proximal stomach (courtesy of Drs. Nick Rodgers and Jurgen Stahl, Clinpath Pathology, Mile End, South Australia).

plexus with no definite ganglion cells detected (*Figure 3*). At 3 months, the patient reported no dysphagia, no regurgitation, and a normal diet. His weight had increased, and he reported being satisfied with the outcome of surgery.

Literature review

An extensive literature search was conducted of MEDLINE, Embase, Cochrane and ClinicalKey databases using the search terms "achalasia", "end-stage achalasia", "esophagectomy" and "esophageal resection" with "AND" and "OR". English-written papers published between 1970 to 2019 were included. Abstracts and case reports of less than 5 patients were excluded.

Discussion

Achalasia is the consequence of T-cell mediated destruction of the myenteric plexus within the wall of the esophagus, with associated fibrous replacement (8). The precise etiology remains unclear. However, it is hypothesised to be multifactorial involving immunological and genetic factors (9). If left untreated, achalasia can lead to the progressive and irreversible elongation, dilatation, and loss of functionality of the esophagus (10). As a result, the diagnostic radiological feature of end-stage disease is a massively dilated and tortuous esophagus, usually greater than 6cm, known metaphorically as 'sigmoid esophagus' (11). The key finding on a contrast swallow, performed by an experienced radiologist, is the formation of a 'sump' in the lower esophagus, leading to pooling of fluid and food (*Figure 2*).

Further deterioration of function can then lead to significant morbidity including malnutrition, pulmonary complications from repeated aspiration, and chronic severe oesophagitis (12). Moreover, some authors have noted a 3 to 10% risk of developing esophageal squamous cell cancer due to the stasis of gastric contents inducing squamous hyperplasia with papillomatosis and basal cell hyperplasia (13,14). A recent meta-analysis in 2017 by Tustumi *et al.* also calculated an absolute risk increase of 18 cases per 100,000 per year for developing esophageal adenocarcinoma in patients with achalasia (15).

Management of end stage achalasia is challenging with many patients having undergone multiple failed therapeutic procedures. There is significant debate about the approach to patients with end-stage achalasia, but there is no doubt that each individual case requires thorough evaluation with repeat endoscopy, manometry, and contrast swallow to ascertain the potential cause of failure, and the appearance of the esophagus. Some of the various etiologies include inadequate myotomy (in particular, a myotomy which does not extend 2 to 3 cm onto the stomach), a tight or mal-positioned partial fundoplication, inappropriate hiatal repair, reflux esophagitis resulting in a peptic stricture, or development of a lower esophageal or junctional cancer (16).

The ISDE guidelines provide some advice on this matter. First, they recommended that failed pneumatic dilatations should undergo a cardiomyotomy, either laparoscopic or endoscopic (i.e., per oral endoscopic myotomy). Second, if there is recurrent achalasia despite a laparoscopic Heller's myotomy, pneumatic dilatation is advised. Third, if a peroral endoscopic myotomy fails to alleviate symptoms, the patient should undergo either a laparoscopic myotomy or pneumatic dilation. In the event that each of these strategies fail, or there is radiological progression to end-stage achalasia (*Figure 1*), the guidelines indicate that esophagectomy should be performed. Unfortunately, these recommendations are of low-grade evidence which reflects the absence of high-quality research and lack of consensus

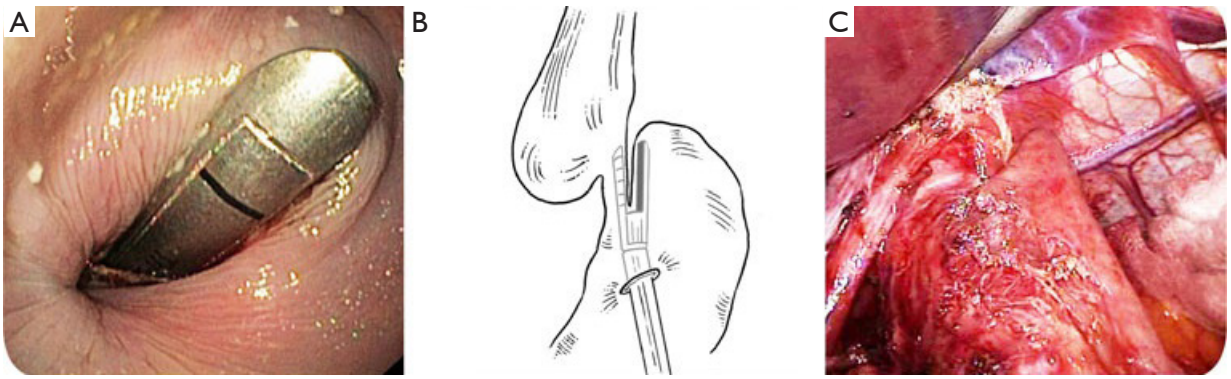

Figure 4 Endoscopic view of the bottom jaw of the laparoscopic angulated staple gun into the esophagus (A). Optimal position of the gastrostomy, 4 cm below the gastroesophageal junction (B). Laparoscopic view of the stapler placement in the esophagus and fundus simultaneously (C) (reprinted by permission from Springer Nature: Springer, *Journal of Gastrointestinal Surgery*, "Laparoscopic Stapled Cardioplasty for End-Stage Achalasia", Griffiths *et al.*, Copyright 2012).

amongst authors (7).

Our local institution has also looked at another option for end-stage achalasia: a laparoscopic cardioplasty. This operation was based on the treatment for a Zenker's diverticulum, where a stapler is used to divide the common wall between the dilated esophagus and stomach, thereby divided the lower esophageal sphincter and optimizing drainage into the stomach (*Figure 4*). Unfortunately, our later results published in 2016 showed that most patients failed this approach due to ongoing dysphagia or unremitting reflux necessitating esophagectomy (17,18).

We believe that esophagectomy is a reasonable and appropriate option for patients with end-stage achalasia. This view is supported by many others, particularly in the setting of significant dilatation of the esophagus, and formation of a sump at the lower end (19,20). There are those who disagree, and still advocate less aggressive measures if possible (21,22). Our local experience includes 12 documented cases of patients with end-stage achalasia who have progressed to esophagectomy following either laparoscopic cardiomyotomy, or pneumatic balloon dilatation, or a combination of both. The patient in our case report had previously undergone a laparoscopic cardiomyotomy with anterior fundoplication and multiple subsequent pneumatic dilatations for management of recurrent dysphagia and regurgitation.

Esophagectomy for management of end-stage achalasia can be technically challenging with several pathological changes distorting the anatomy within the pleural and abdominal cavities. Deviation of the megaesophagus into the right chest is common, increasing the risk of pleural and tracheal injury (23). Second, the increased vascularity of hypertrophied esophageal muscle in achalasia necessitates meticulous care to ensure haemostasis of the mediastinal vessels (16). Several studies have documented cases of slow mediastinal bleeding requiring reoperation within 24 hours (13,16,23,24). Third, prior surgery at the hiatus can cause adhesions and scarring of the lower esophagus and proximal stomach. As a result, adhesions to the adjacent aorta and left lung can complicate a transhiatal mobilisation, and adhesions in the abdomen can shorten the gastric conduit, sometimes obviating an anastomosis in the neck (16).

Our preferred approach is an Ivor-Lewis esophagectomy with an open thoracotomy, and laparotomy, either synchronous or as a 2-stage procedure, for the reasons listed above. A 3-stage procedure, with a thoracoscopic approach in the chest, has also been performed in our institution. However, this approach is only possible if (I) the original myotomy was done via the abdomen, and not via the chest (to avoid adhesions between the myotomy and the lung), and (II) an anterior partial fundoplication was performed at the original procedure, not a posterior fundoplication (Toupet or Nissen) which can limit the length of the gastric conduit. We always perform a pyloromyotomy or pyloroplasty to help with gastric emptying, and we prefer a handsewn anastomosis due to the dilated esophageal lumen, which is too wide for a stapler anvil.

Open transthoracic (13,25-27), open transhiatal (11,16,20,23,24,28), and laparoscopic transhiatal (29,30) are three of the most common operations used for resection in this patient population, with much controversy regarding which is the superior approach.

Miller *et al.* report that transhiatal esophageal resection was associated with increased morbidity and mortality and should only be reserved for patients who have had multiple prior operations due to the increased bleeding risk (20). In contrast, Orringer and co-workers state that a transhiatal approach was the most reliable technique and could be performed safely with a good level of morbidity (24). Furthermore, a left sided thoracoabdominal approach has been advocated by Hsu *et al.* as it provided an excellent operative field with less dissection needed of the intrathoracic esophagus and easier mobilisation of the wrapped esophagogastric junction (27).

We have had no immediate mortalities in our series, and our morbidity rate is 50%. Several studies have cited morbidity rates ranging from up to 50% (30) and mortality from 0% (11,24-29) to 9% (30). Post-operative complications including pneumonia, anastomotic leak, bleeding, chylothorax, and wound infection have all been reported (16). Anastomotic leaks were noted in the post-operative period in 4% (24) to 18% (30) of the population. These values have potentially been overstated given the lower incidence of this disease resulting in smaller sample sizes. Furthermore, the average length of stay for our patients was 20 days, which is comparable to other publications (11,13,16,20,23,24,26-30).

In summary, esophagectomy is a viable and safe option to manage end-stage achalasia. Our representative case study reported a considerable improvement in his symptoms and quality of life and wishes he had undergone esophagectomy much sooner. We are in the process of obtaining ethics to retrospectively contact all 12 patients to assess their current quality of life, and gastrointestinal function, and these results will be published in the coming year. Nevertheless, our anecdotal findings echo the outcomes observed in previous studies, which suggests that esophageal resection is not as aggressive a measure as previously believed!

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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