Does transhiatal esophagectomy represent an efficient line of treatment for end-stage achalasia? a single-center study of the outcomes

Tarek A.O. Abouzeid[a], Reda S. Ezz[a], Hesham Elsawah[b], Ahmed A. Shoka[a]

[a]Department of General and UGI Surgery, College of Medicine, Ain-Shams University, [b]Department of Gastroenterology, Egypt Air Hospital, Cairo, Egypt

Correspondence to Tarek A.O. Abouzeid, MD, Department of General and UGI Surgery, College of Medicine, Ain-Shams University, Cairo 11566, Egypt. orcid.org/0000-0002-8875-336X. Tel: +20 100 311 4199; fax: 20 2683 0154; e-mail: tarekabouzeid@med.asu.edu.eg

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Background
Achalasia is a rare primary esophageal motility disease that could lead to a state of complete esophageal failure known as end-stage achalasia. The proposed treatment lines have been changed over the past few decades. Since it was described in 1976, the transhiatal esophagectomy (THE) has been evaluated in many esophageal disorders. However, there were scarce data regarding its effects on patients with end-stage achalasia.
Objective
In this prospective trial, we tried to spotlight on this mysterious disease and to unveil the real outcomes of THE in patients with an end-stage achalasia complicated with sigmoid changes regarding the efficacy and the complications.
Patients and methods
A prospective study had been conducted at Ain-Shams University Hospitals, Cairo, Egypt, between January 2018 and December 2019 on 17 consecutive patients who have been diagnosed with end-stage achalasia. Those patients were scheduled for THE. The dysphagia score was assessed preoperatively and at each postoperative follow-up visit along with the other relevant surgical data.
Results
In this series, there were 10 (58.8%) males and seven (41.1%) females, with a median age of 61.3 years, the mean duration of symptoms was 73.3 months (range, 32–135 months), and the mean preoperative dysphagia score was 3.0. One of our patients died owing to pneumonia on the 27th day postoperatively. Another patient was converted to the transthoracic approach owing to severe adhesions hindering the safe dissection. The general morbidity rate was 52.9%, including three (16.7%) cases of cervical leakage, two (11.7%) cases of bleeding, nine (52.9%) cases of pleural effusion, and four (23.5%) cases had surgical site infection. All these cases were managed conservatively, with no need to reoperate. There was one patient who had a transient vocal cord paresis that improved spontaneously after 6 months.
Conclusion
This prospective trial verified that THE is a safe and efficient surgical treatment with an acceptable rate of mortality and morbidity.

Keywords:
achalasia, end-stage achalasia, esophagectomy, sigmoid esophagus, transhiatal esophagectomy

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Introduction

Achalasia is a primary motility disorder characterized by esophageal body aperistalsis and impaired swallowing-induced lower esophageal sphincter (LES) relaxation with the evident upsurge of its resting pressure [1–4]. It is a rare disease, with an appraised annual incidence of 0.7–3 cases per 100 000 population [1,5]. The pathologic studies illustrate esophageal myenteric plexus dysfunction owing to loss of ganglion cells [2,6–8].

Overall, 5% of the untreated or improperly managed patients eventually develop end-stage achalasia, which is a state of esophageal failure in which the esophagus cannot push its contents downward with the resultant progressive dilatation and sigmoid changes [2,8]. It is characterized by a wide scale of esophageal symptoms [2], with periods of remission and sporadic exacerbation [9]. These symptoms include dysphagia, saliva, undigested food regurgitation, weight loss, respiratory symptoms (nocturnal cough, recurrent aspiration, and pneumonia), heartburn, and chest pain [5,6,10].

The high-resolution manometry (HRM) enables not only to detect the increased integrative relaxation

pressure and the pathognomonic aperistalsis but also to subclassify the disease into three clinically pertinent groups based on the contractility patterns [1,7]. Consequently, it is considered the gold standard investigating tool with the characteristic increased integrative relaxation pressure greater than 15 mmHg along with an obvious failure of the LES relaxation [2,9].

Throughout the ages, the cure of achalasia was the dream of physicians. The journey of treatment started with just a whalebone. With time, the therapeutic techniques were the target of scientific research and technological development. There is no convincing evidence that medical treatment with nitrates, calcium blockers, or phosphodiesterase inhibitors is effective [5]. Nowadays, the lines of treatment include pneumatic dilatation (PD), botulinum toxin injection (BTI), peroral endoscopic myotomy, Heller myotomy (HM), and esophagectomy [11]. The aim of the treatment is to mitigate symptoms and more importantly to improve emptying [3,12].

In 1913, while Dr. Ernst Heller [13] conducted the first myotomy, Dr. Franz Torek [14] in New York underwent the first esophageal resection. Since then, extensive research has been conducted around the world to evaluate and develop both operations.

In 1976, Professor Marc Orringer [15] announced the success of the new approach of transhiatal esophagectomy (THE). Studies were tickling from overseas aiming to evaluate, compare, and develop these surgical procedures. Accordingly, the treatment guidelines and algorithms have been subjected to major changes over the past few decades [1,5,11,16–18].

Albeit its initial excellent results in end-stage achalasia, HM leaves a nonfunctioning esophagus with a 10% risk of neoplastic changes [19–21]. Besides, transthoracic esophagectomy (TTE) is associated with a higher risk of respiratory complications [3]. This paved the way for THE to emerge as a curative line of treatment that obviates all these pitfalls. Nevertheless, there are scarce heterogeneous data in the literature exploring its effect on esophageal failure state.

In this context, we tried to evaluate the outcomes of THE as a surgical treatment for patients having end-stage of achalasia with sigmoid changes.

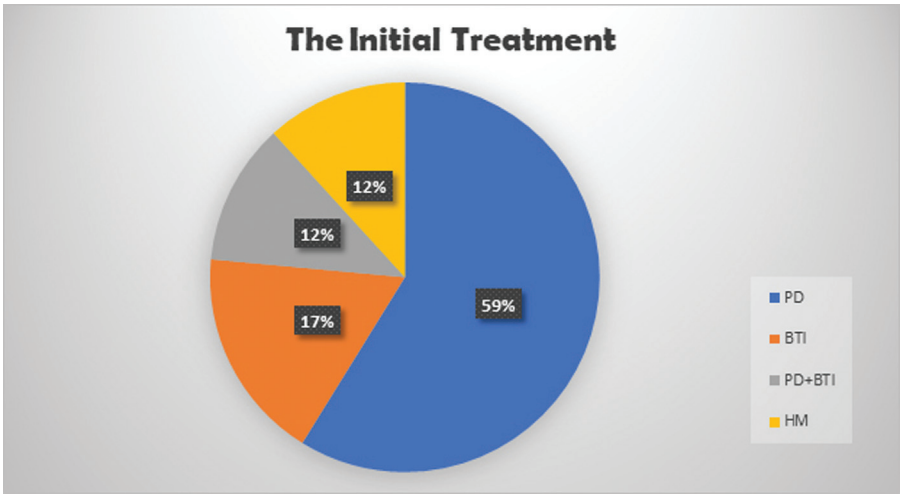
Patients and methods

Study design

Upon approval of the Institutional Review Board, a prospective trial had been conducted between January 2018 and December 2019 at Ain-Shams University Hospitals, Cairo, Egypt, on 17 consecutive patients who have been diagnosed with end-stage achalasia. This study has been conducted in accordance with the Code of Ethics of the World Medical Association for experiments involving humans.

The research criteria allow the inclusion of patients of either sex aged from 20 to 70 years irrespective of their ethnicity with an established diagnosis of end-stage achalasia complicated with sigmoidal changes after the failure of their initial treatment. The initial treatment of those patients is illustrated in Fig. 1. Failed initial treatment is defined as persistence or reappearance of symptoms after a period of initial improvement following either endoscopic (BTI, PD, and peroral

Figure 1



The initial treatment of patients.

endoscopic myotomy) or surgical (HM) intervention [5,12,19]. Exclusion criteria were psychiatric disorders, history of UGI malignancy, bleeding disorders, and those with a high operative risk (American Society of Anesthesiologists 4 and 5).

The diagnosis was based on some radiographic, manometric, and endoscopic criteria. Barium esophagram (Fig. 2) demonstrated proximal esophageal dilation, sigmoidal changes. The HRM (Fig. 3a and b) is the gold standard tool in the diagnosis. It shows esophageal body aperistalsis and incomplete relaxation of the LES with swallowing. In four patients, manometry could not be done owing to either patient intolerance or difficulty in positioning the probe in the roomy esophagus. The special technique for probe insertion includes placing it at the LES with an axial rotation to the right after a water swallow followed by deep inspiration. In addition, there is a failure rate of 30% to do HRM even with the aforementioned technique. The endoscopy was routinely done for all cases to confirm the diagnosis and to rule out the possibility of any neoplastic changes.

Preoperative preparation

The lung is the site of most of the esophagectomy-related complications; consequently, optimization of the preoperative pulmonary state is of utmost importance. Parenteral hydration was given for all patients along with repeated esophageal wash. Routine blood investigation, pulmonary function tests, and thorough cardiological evaluation were done for all patients. Computed tomography (CT) scan was requested if malignant pseudoachalasia is suspected. Patients were counseled about their diagnosis, results of investigations, and the possible outcomes of esophagectomy.

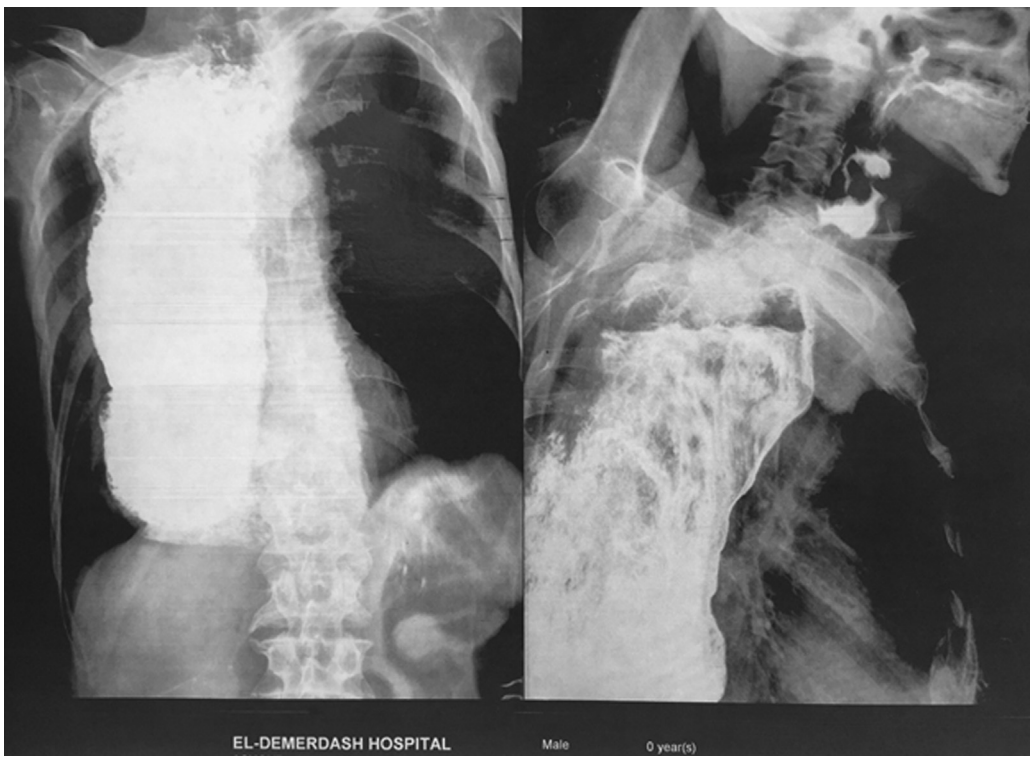
Taking into consideration that relief of symptoms is the most important treatment target, dysphagia score [12], as shown in Table 1, was used to evaluate the results of THE. The symptoms and their duration as well as the failed previous treatment (PD, BTI, or HM) were documented.

All the enrolled patients signed a preoperative written informed consent and were scheduled for THE. The preoperative demographic data (such as age and sex) and clinical data (such as the presenting symptoms and signs, and previous interventions) were documented.

Surgical technique

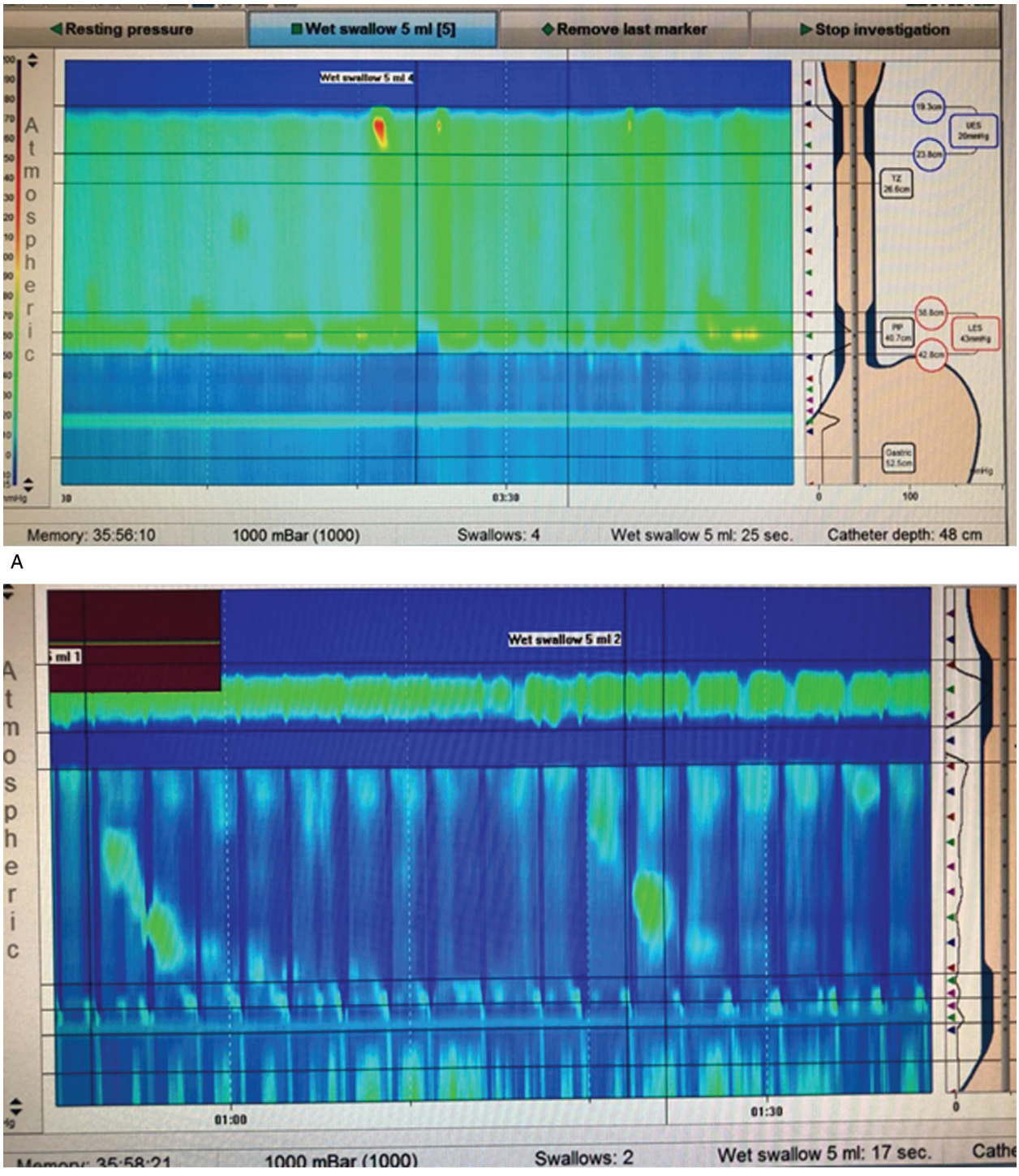
Awake fiberoptic intubation or rapid sequence induction in a semi-upright position is done to avoid aspiration. After induction of general anesthesia using a double-lumen endotracheal tube, the patient is put in

Figure 2



Barium esophagogram showing a sigmoid esophagus (anteroposterior and lateral views).

Figure 3



(a) HRM in end-stage achalasia. (b) HRM in end-stage achalasia. HRM, high-resolution manometry.

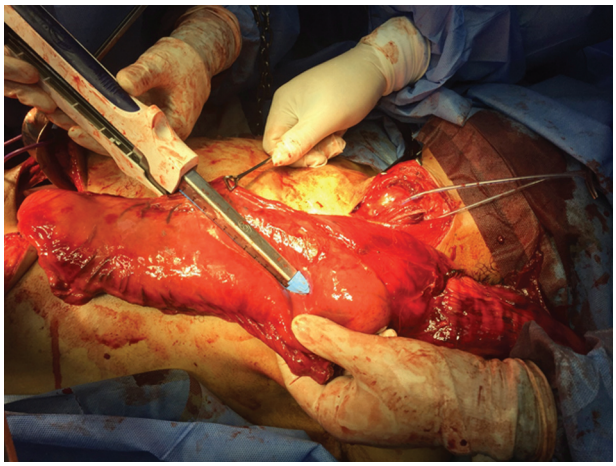
Table 1 Dysphagia score

Dysphagia	Score
No dysphagia	1
Difficulty with hard solids	2
Difficulty with soft solids	3
Difficulty with liquids	4
Cannot swallow saliva	5

a supine position. The cuff must be inflated before changing the position to the supine one.

The abdominal dissection is commenced at the gastroesophageal junction. We fashioned a greater curve-based gastric conduit (Fig. 4) in all cases. Successive stapling was done by the GIA, DST Series (Covidien, Autosuture, Mansfield, Massachusetts,

Figure 4



Fashioning of the gastric conduit using the GIA stapler.

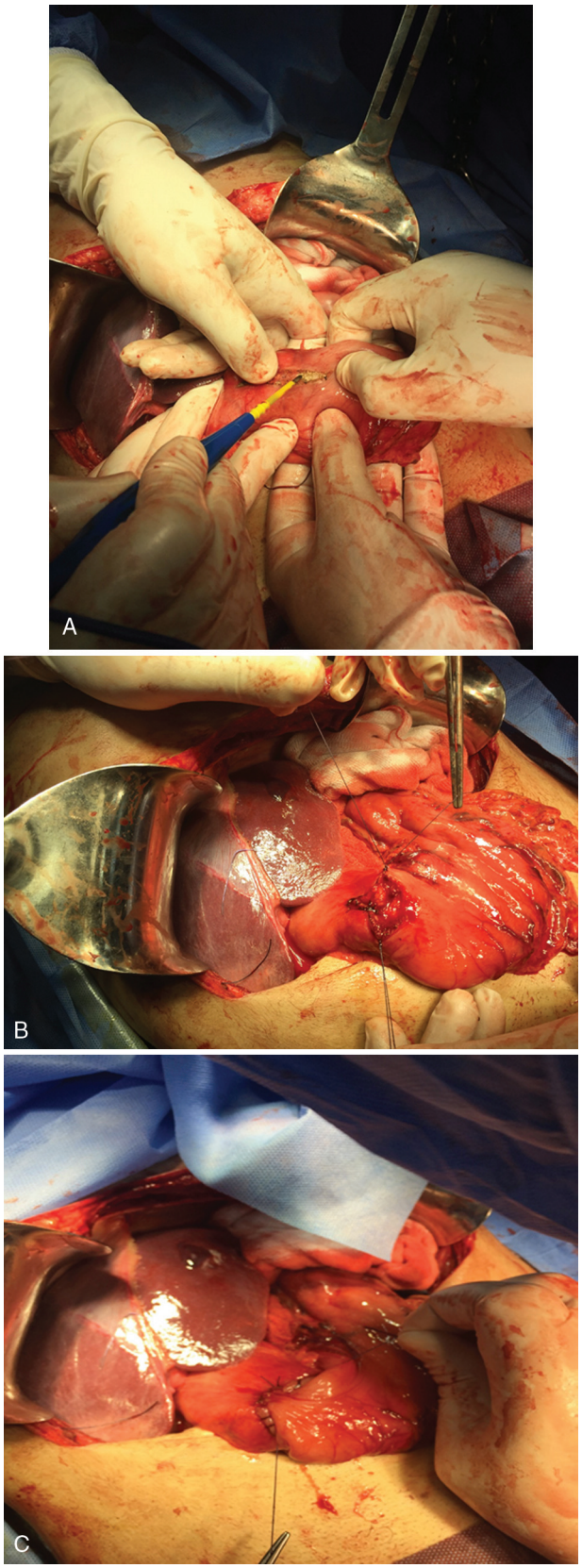
USA), with 60 mm reloads to create a tube of 3–4 cm in diameter. We avoided forming a tube narrower than 3 cm because it is not only considered very susceptible to ischemia and leakage but also makes an anastomosis with a dilated esophagus an exceedingly difficult step. Pyloroplasty (Fig. 5a–c) and a feeding jejunostomy were done as a routine step.

A sharp dissection under vision is used to safely separate the esophageal submucosa from the descending aorta, especially in patients who had a previous HM. A low threshold to convert to TTE could prevent inadvertent mediastinal structures injury during hazardous dissection. Therefore, one case was converted to and completed by a right thoracotomy.

The cervical phase started with an oblique incision over the left sternocleidomastoid muscle. A careful blunt dissection of the prevertebral fascia is done to avoid injury of the recurrent laryngeal nerve (RLN). Identification of the esophagus is done, along with complete dissection of the periesophageal tissues and adhesions. Encircling the mobilized esophagus with a small drain aids markedly in the upper thoracic dissection (Fig. 6a and b). We hereby ascertain the importance of the deflation of the ETT cuff at this stage to avoid any inadvertent injury of the carina and the resultant air leak and rapid desaturation.

The mediastinal dissection now could be performed from up and down (Figs 7 and 8) till the esophagus becomes completely freed from the surrounding (Figs 9 and 10a, b). Usually, we do proceed slowly in this critical step because we consider it the conversion-determining step. In other words, failure to progress safely means an inevitable thoracotomy. This could be

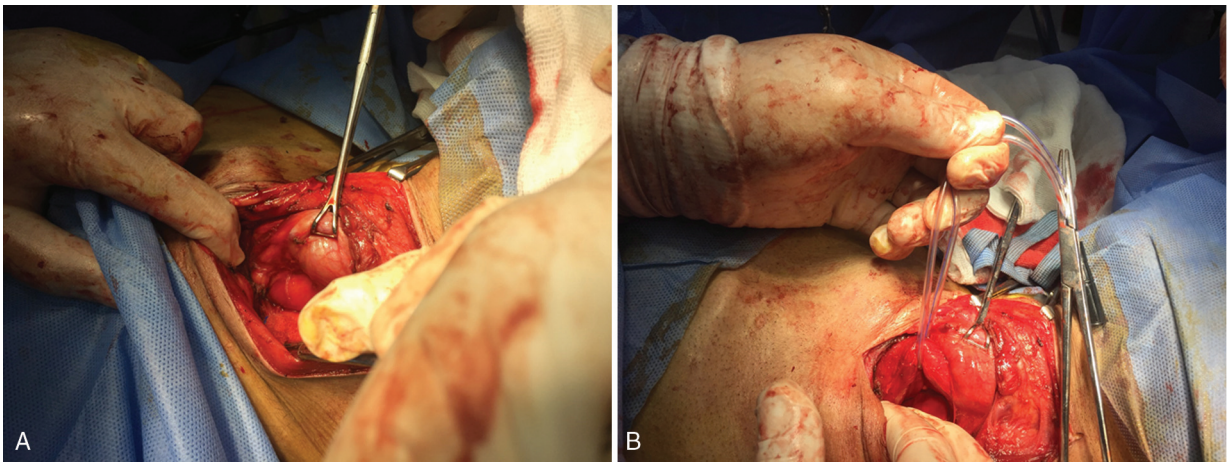
Figure 5



(a) Pyloroplasty. (b) Pyloroplasty. (c) Pyloroplasty.

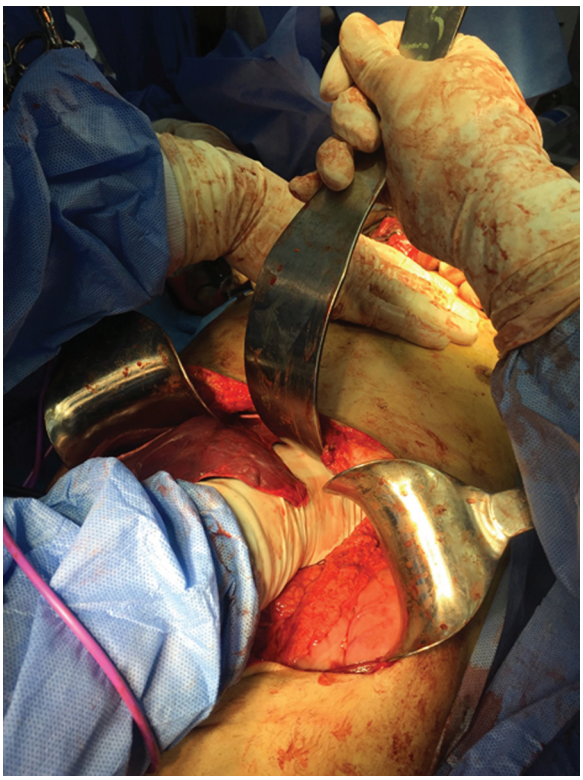
attributed to two main obstacles: the first one is the altered anatomy that makes the esophagus deviated to the right side with a high chance of right

Figure 6



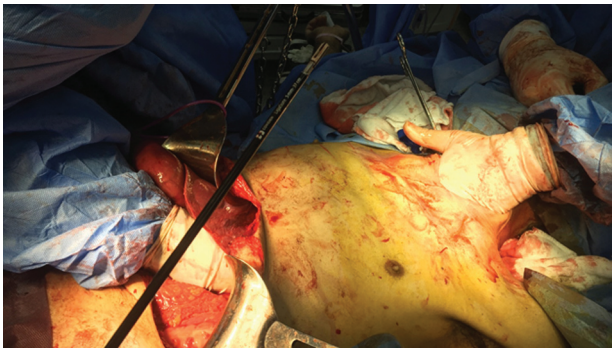
(a) Cervical dissection and mobilization of the esophagus. (b) Cervical dissection and mobilization of the esophagus.

Figure 7



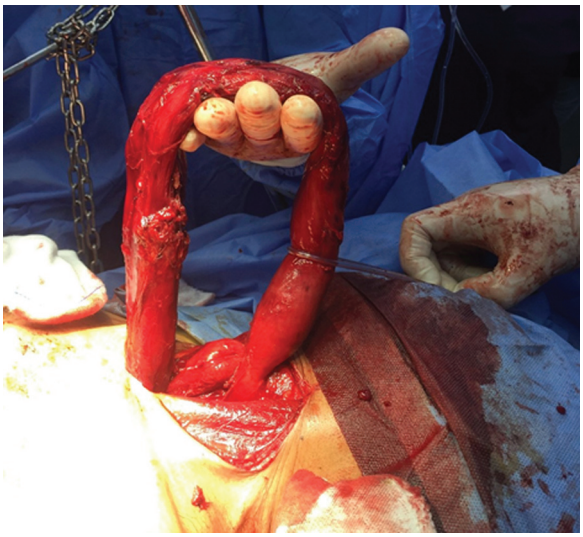
Transhiatal dissection.

Figure 8



Combined mediastinal dissection from up and down.

Figure 9

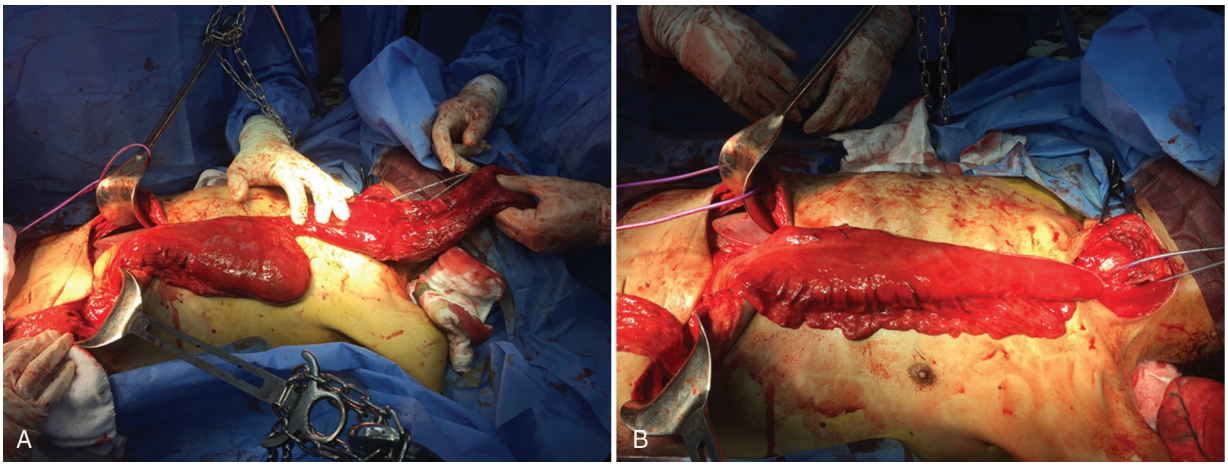


The mobilized esophagus.

pneumothorax. The second obstacle is the altered pathology in the form of hypertrophied esophageal vessels that could add to the difficulty and morbidity of the procedure.

Removal of the specimen was accomplished (Fig. 11). The delivery of the neo-esophagus to the neck in the right orientation is a tricky step. This could be facilitated by the Mousseau-Barbin tube (Fig. 12). However, if this tube is not available, we do not rely solely on the presence of the greater curve at the patient's left side but we recommend passing hands to rule out any 360-degree torsion of the tube. The

Figure 10



(a) After complete dissection. (b) The conduit after completed dissection and removal of the specimen.

Figure 11

The final specimen showing the aganglionic segment.

Figure 12

The Mousseau-Barbin tube.

conduit was placed in the posterior mediastinum in all the cases. Regarding the anastomosis, we did it via a linear stapler with a closure of the stapler entry site with Vicryl 2-0. A nasogastric tube and cervical drains were put as usual.

Postoperative care

A gastrografin swallow was routinely requested on the seventh postoperative day. If there is no leak, fluid intake is commenced. All patients were instructed to abide by regular follow-up after 2 weeks and then at 1, 3, 6, 9, and 12 months postoperatively. In each follow-up visit, full history was taken, and meticulous clinical assessment was performed.

The postoperative dysphagia score was assessed at each visit. The other relevant surgical and radiological data such as the intraoperative and postoperative complications, length of stay, and clinical outcomes

were documented in a standard Excel sheet for Windows and were verified checking for its statistical significance.

Statistical analyses

The standard descriptive statistics were used to analyze the demographic, clinical, and surgical data. The quantitative variables with a normal distribution were expressed as mean±SD, whereas the qualitative data with binary variables were expressed as frequency and percentage and were analyzed with Fisher's exact test.

Given the importance of dysphagia improvement in the evaluation of the curative effect of THE, we have used the logistic regression analysis longitudinally of the single readings. To unveil the real effect of THE on the weight over the follow-up period, statistical slopes for weight change were generated and were compared by the one-sample *t* test checking for their statistical relevance. The *P* value was calculated and documented.

The operative variables such as intraoperative complications, conversion of transhiatal approach to thoracotomy, and whether the operation was elective or urgent were documented. Similarly, the postoperative variables include complications, blood transfusion, and hospital lengths of stay were also documented. The statistical analyses were conducted using the statistical package for social sciences, version 22 software package (SPSS Inc., Chicago, Illinois, USA). The significance level was set to 0.05.

Results

During the defined period of study, 17 patients had undergone THE for end-stage achalasia. Among them, there were 10 (58.8%) males and seven (41.1%) females, with a median age of 61.3 years (range, 41–68 years). The presenting symptoms are shown in Table 2. The mean duration of symptoms was 73.3 months (range, 32–135 months). The mean preoperative dysphagia score was 3.0.

The endoscopic approaches (PD, BTI, or both) were done in 15 (88.2%) cases before being referred to our unit, whereas HM was performed in two (11.7%) cases (Fig. 1). The average length of stay was 12.1 days (range, 8–23 days).

One (5.8%) patient had an intraoperative conversion to TTE because of dense adhesions between the esophageal submucosa and the aorta, hindering the progression of safe dissection. In this series, we have one (5.8%) deceased patient. The morbidity rate was 52.9%. The encountered complications are illustrated in Table 3.

The early results at the second-week follow-up visit were encouraging in terms of dysphagia improvement (Table 4). The mean preoperative dysphagia score was three which was dropped to a mean of one at the second-week visit and plateaued till the end of the follow-up period. A total of 14 cases had complete resolution of dysphagia, two cases improved, and one case had persistent dysphagia. The mean postoperative weight after 1 year was 68.4 kg (range, 56.9–85.1 kg). It significantly increased in comparison to mean preoperative weight of 59.8 kg (range, 48.9–80.3 kg) (*P*=0.039).

Discussion

Because of negligence or improper treatment and through unknown pathophysiologic mechanisms over around 15 years, the esophagus progressively dilates and acquires sigmoid angulations with the resultant state of end-stage achalasia.

Taking into consideration the pathophysiologic background including the esophageal aperistalsis and despite the palliative nature of myotomy, it has been tried to be used for those experiencing the decompensated

Table 2 The presenting symptoms with their percentage

Presenting symptoms	*n* (%)
Dysphagia	17 (100)
Regurgitation	15 (88.2)
Recurrent cough	10 (58.8)
Vomiting	6 (35.2)
Chest pain	5 (29.4)
Weight loss	8 (47)

Table 3 The complications and their percentage

Complication	*n* (%)
Bleeding	2 (11.7)
Cervical leakage	3 (16.7)
Pleural effusion	9 (52.9)
Vocal cord paresis	1 (5.8)
Surgical site infection	4 (23.5)

Table 4 Dysphagia improvement in other trials

References	Improvement of dysphagia
Devaney *et al.* [39]	95% free
Miller *et al.* [40]	91.4% free
Banbury *et al.* [10]	87% improved
Orringer and Stirling [48]	96% free
Peters *et al.* [49]	93% free

esophagus. Surprisingly, it has shown excellent results in terms of dysphagia resolution.

Since the early 1990s, many studies [22–29] have shown excellent outcomes of HM in patients with end-stage achalasia with sigmoid changes. These outcomes are not only subjective in terms of dysphagia resolution but also objective such as decreased esophageal width and improved emptying dynamics [30].

Furthermore, some recent studies [24,30] have concluded that the outcomes of Laparoscopic Heller Myotomy (LHM) in patients with sigmoid megaesophagus are similar to those without a dilated esophagus. In other words, the final results of LHM are not related to the preoperative esophageal diameter. Eldaif and colleagues [19] confirmed the aforementioned results in their retrospective study on 272 patients with LHM over 11 years in Atlanta by subdividing their patients into three groups according to their esophageal diameter. On the contrary, Banbury *et al*. [10] observed that patients with a smaller esophageal diameter are more prone to dysphagia, reflux, and regurgitation after esophagectomy. Other studies [31,32] have concluded that HM is less effective for end-stage esophageal dilatation.

Given all these trials, the guidelines for the treatment of end-stage achalasia have been changed over the past four decades from considering esophagectomy as a first-line treatment in 1988 [33] to reserve it as a last option in the ISDE guidelines and the Multidisciplinary European Guidelines [1,5,10,33].

Despite the initial excellent results of HM in the sigmoid esophagus, the disadvantages and the limitations are also evident. The first disadvantage is the limited durability of the results. Iqbal *et al.* [34] reported that up to 20% of HM patients need another intervention later on in their life. Moreover, the initial results have deteriorated over 10 years [35–37]. This is similar to the observation of Loviscek *et al*. [4].

In a review of their own experience over a mean follow-up of 11.2 years, Jeansonne *et al.* [38] drew a different picture. Only 6% of their cases experienced severe dysphagia at 10 years compared with 43% before the operation, which could imply a durable characteristic to the LHM.

It is worth pointing out that HM does not completely improve esophageal emptying, which is another disadvantage. Hence, we could expect that there is some degree of stasis with the resultant sequelae of esophagitis, erosions, ulceration, bleeding, fistulization, and perforation [8,39]. Therefore, HM leaves a functionless esophagus that is linked to an increased risk of malignancy by 10% [19]. This is supported by many trials that documented an incidental finding of cancer in the esophageal specimen [10,12,39,40].

Another pertinent disadvantage is that HM could lead to extensive adhesions between the submucosa and the descending aorta or the lung, which in turn could make the dissection in any next intervention more hazardous and ultimately carry a risk of bleeding, air leak, or perforation. In addition, the myotomy could compromise the gastric blood supply, making any trial of a remyotomy and rewrapping more and more difficult [37]. Therefore, the choice of the procedure for patients with sigmoid esophagus is still controversial.

Esophagectomy and reconstruction is the only curative treatment modality because it can correct and counteract all achalasia-related anatomical and pathological changes. Given the apparent similarities between primary achalasia and Chagas disease, Latin American surgeons have good experience dealing with megaesophagus [41]. Professor Pinotti *et al*. [42] in their study of 122 patients reported a mortality of 4.2%, with a 95% complete resolution of symptoms, which implies the safety and efficacy of THE in end-stage decompensated esophagus.

Despite there being some degree of consensus regarding the place of esophagectomy in the treatment algorithm of end-stage achalasia, some concerns have been raised regarding the approach of the operation [43]. Some prospective studies and meta-analyses [6,40,44] tried to identify the best approach of esophageal resection by comparing TTE and THE. These studies support the notion that TTE is linked to a greater incidence of lymphatic leakage, respiratory complications, and wound complications. On the contrary, THE was associated with a higher risk of leakage, bleeding, and RLN injury.

Regarding the safety of THE, Banbury *et al.* [10] analyzed the results of 32 THE operations at the Cleveland Clinic. There were five intraoperative conversions to TTE, with no reoperations for hemorrhage. Durable dysphagia improvement and the constant postoperative weight were evident in their long-term follow-up. Likewise, Devaney *et al.* [39] from the University of Michigan reported their experience on 93

esophagectomies (TTE and THE), with a 2% mortality and 30% major complication rates. Six operations were converted to a thoracotomy, and two patients required an urgent thoracotomy for hemorrhage.

Esophagectomy in advanced esophageal motility disorders led to marked functional improvement as concluded by Gockel *et al.* [44] in their small series of eight patients (six THE and two TTE). They considered THE as the preferred procedure because of its documented low morbidity. However, in their meta-analysis of 1307 patients, Aiolfi *et al.* [6] from the University of Milan failed to identify any conclusive evidence to support the use of one approach of esophageal resection. Hence, they left the choice of the surgical approach to the surgeon's preference.

The average length of stay was 12.1 days (compared to 12.5 days reported by Devaney and colleagues). In this trial, 14 patients had a dysphagia score of one, two patients had a score of two, whereas only one patient had a score of three, which is the same as his preoperative score (Table 4). This patient was 37-year-old male, with a 5.5-year history of achalasia. He had three sessions of PD before being referred to our unit. His postoperative UGI was essentially normal along with a normal barium study. It stands to reason that the statistical data have shown significant improvement of dysphagia, denoting the curative effect of THE on end-stage achalasia.

Banbury *et al.* [10] documented a 7% rate of persistent dysphagia. They postulated that these patients have a disordered perception of swallowing. Additionally, they found that a younger age at operation and a shorter duration of disease are linked to a higher possibility of developing worsening dysphagia after the operation. In this study, a significant weight change (P=0.039) could be noted in contrast to the findings reported by Banbury *et al.* [10].

Perioperative mortality

Esophagectomy is an ultra-major operation; therefore, there is a concern regarding the morbidity and mortality rates. In this study, there was one case of mortality (5.8%) for a 67-year-old male. He had a cervical leakage, which was managed conservatively. However, he developed severe pneumonia and died owing to it on the 27th postoperative day. This rate is comparable with other studies (1–5%) [40,42,45] (Table 5).

Perioperative morbidity

The general morbidity rate was 52.9%, which is in range with other published trials [6,10,40] (Table 5). In one of the largest published meta-analyses (Aiolfi 1), the general complication rate was 50%.

Despite the major difficulties that are usually encountered during esophagectomy for achalasia, the general complication rate is the same as that for cancer. This denotes that achalasia-related anatomical and physiological changes have no effect on the general morbidity rate [6,39,46–50].

It seems that increased age and associated comorbidities, particularly kidney diseases, are predictive of mortality after esophagectomy as advocated by a recent multivariate analysis [11]. This supports the current concept of offering esophagectomy for those with younger age with no or minimal comorbidities [5,46,47].

In this study, three (17.6%) patients experienced cervical leakage and were diagnosed by clinical suspicion. The diagnosis was supported by a contrast study and CT scan, and they were managed by conservative treatment, which was successful. This

Table 6 The leakage rate in other studies

References	Leakage rate (%)
Devaney *et al.* [39]	10
Miller *et al.* [40]	5.4
Banbury *et al.* [10]	13
Orringer and Stirling [48]	4
Schuchert *et al.* [12]	16.7

Table 5 The perioperative morbidity and mortality in other comparable studies

References	Year	No	Follow-up	Morbidity (%)	Mortality (%)	Dysphagia (%)
Orringer and Stirling[48]	1989	26	30	19	0	4
Pinotti *et al.* [42]	1991	242	60	19	4.9	5
Banbury *et al.* [10]	1999	32	43	69	0	28
Devaney *et al.* [39]	2001	87	38	30	2	5
Gockel *et al.* [44]	2004	6	44	25	0	0
Crema *et al.* [50]	2009	60	6–118	20	0	0

rate is comparable with that published by other clinical trials [10,12,39,40,48] (Table 6).

Herein, we report that four patients out of 17 developed atrial fibrillation during their stay in the ICU. Chemical cardioversion was given after exclusion of ischemia by an ECG.

The achalasia literature settles that up to 21% of patients develop pneumonia [6,17]. In this study, two (11.7%) patients experienced pneumonia. One of them died and the other one recovered after a long course of intravenous antibiotics. This relatively high figure could be attributed to the preoperative chronic lung damage from repetitive aspiration.

As might be expected, nine (52.9%) patients had pleural effusion. Despite the difficulty confirming it, the THE is linked to an exceedingly high incidence, which is documented to be up to 76% [9].

One (5.8%) of our patients developed transient vocal cord palsy which was diagnosed by an indirect laryngoscopy and completely improved over a 6-month period. Different studies [9,39] observed a similar trend, with up to 20% of patients developing it.

Some precautions during the cervical dissection are suggested to decrease the possibility of RLN injury such as to use the bipolar cautery rather than the monopolar one, and to avoid putting any retractor beneath the plane of the deep fascia.

The limitation of this single-institution study includes the small number of cases and the short-term follow-up. Further studies with long-term follow-up should address this issue to reveal the durability effect of THE.

Conclusion

Achalasia is a rare challenging disease that is best diagnosed by HRM. It constitutes a unique example in the surgical science for which the curative surgical treatment is postponed till the exhaustion of other palliative lines.

This trial yielded further details that confirm the efficiency and safety of THE for patients with end-stage achalasia and imply with the scarce present knowledge.

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Conflicts of interest

There are no conflicts of interest.

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