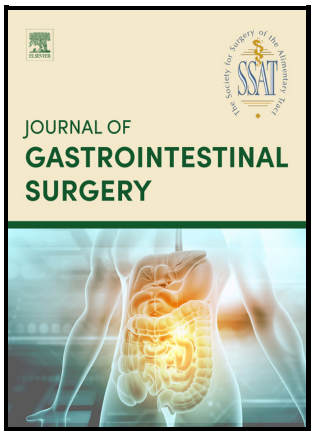

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THE ESOPHAGEAL PULL-DOWN TECHNIQUE IMPROVES THE OUTCOME OF LAPAROSCOPIC HELLER-DOR MYOTOMY IN END-STAGE ACHALASIA

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Abstract

BACKGROUND: Treatment of end-stage achalasia patients with a sigmoid-shaped esophagus is particularly challenging. A modified technique (pull-down) has been developed to straighten the esophageal axis, but only a limited number of studies on this topic are available in the literature. This study aimed to compare the outcome of patients who underwent the pull-down technique

(PDLHD) with that of patients who had a classical Heller-Dor (CLHD).

METHODS: All the patients with a radiological diagnosis of end-stage achalasia who underwent a laparoscopic myotomy (LHD) between 1995-2022 were considered eligible for the study. All of the patients underwent symptom score, barium-swallow, endoscopy and manometry tests before and after the procedure was carried out. Treatment failure was defined as the persistence or reoccurrence of an Eckardt score > 3 or the need for retreatment.

RESULTS: Of the 94 patients who were diagnosed with end-stage achalasia (M:F = 52:42), 60 were treated with CLHD and 34 with PDLHD. Two patients (2.1%), both belonging to the CLHD group, developed a squamous cell carcinoma (SCC) during the follow-up. The overall success of LHD was seen in 76/92 patients (82.6%). All the patients in both groups achieved a lower Eckardt score after surgery; there was a failure rate of 27.6% (16/58) in the CLHD group, as compared to 5.9% (2/34) of the PDLHD ($p<0.01$).

CONCLUSIONS: The findings of our study confirm that LHD is an effective treatment for end- stage achalasia patients, and the pull-down technique further improves the outcome in these patients so difficult to treat.

Keywords: achalasia; end-stage achalasia; sigmoid esophagus; Laparoscopic Heller-Dor

Background

Achalasia, defined as the absence of peristalsis associated to elevated integrated relaxation pressure (IRP) resulting from an incomplete relaxation of the low esophageal sphincter (LES),[1] is a rare neurodegenerative disease affecting esophageal motility. The Chicago Classification of motility disorders categorises patients' esophageal motility using metrics from high resolution manometry (HRM). Manometric findings, which quantify the intensity of the esophageal dysmotility, and radiological data, which assess the esophageal diameter above the LES, seem to interlink and evolve together during the progression of the disease towards its end-stage[2] when the esophagus develops a sigmoid shape and a diameter >6 cm.[3]

Since the disorder's pathogenesis is still unknown, its treatment is symptomatic and aims to disrupt the LES. Up to date, treatment is endoscopic with graded pneumatic dilations or endoscopic myotomy (POEM) or surgical, with laparoscopic Heller myotomy[3]. The laparoscopic Heller-Dor (LHD) myotomy, which provides satisfactory symptom improvement in 80% to 85% of patients as long as and even longer than 10 years after surgery,[4] is presently considered the most effective long-term treatment,

However, the efficacy of myotomy in treating end-stage achalasia[5] has not been entirely defined and, despite the reports of worse quality of life following esophagectomy [6,7] this is still considered a feasible surgical option in these patients[5]. A recent study has demonstrated that the LHD myotomy, and in particular the "pull-down" technique, is successful in approximately 70% of patients with radiological grade IV achalasia; these findings have however been confirmed by only a limited number of studies in the literature.[8]

The current study was therefore carried out to compare the outcome of the pull-down technique (PDLHD) with that of classical myotomy (CLHD) in patients with end-stage achalasia.

Methods

All the consecutive patients with radiologically-diagnosed end-stage achalasia who underwent LHD myotomy at the Department of Surgery of the Padova University Medical Center between 1995 and 2022 were considered eligible for study inclusion. They were divided in two groups depending upon the type of LHD they received: the pull-down technique (PDLHD) or a classical

myotomy (CLHD).

Preoperative assessment

The patients' demographic and clinical data were collected prospectively in a dedicated database; moreover, relevant details regarding all of their previous treatments, including pharmacological, endoscopic or surgical ones, were recorded.

All the patients underwent the following tests before undergoing the myotomy:

- An endoscopy to rule out cardia malignancies and/or other esophageal diseases
- A barium swallow X-ray to assess the diameter and the shape of the esophagus permitting us to identify and thus classify the stage of achalasia[9,10]
- An esophageal manometry (Conventional or High-Resolution technique) to assess esophageal motility parameters and to classify the manometric pattern [1,11]

The Eckardt score (ES) was used to evaluate the patients' symptoms. [12]

Surgical technique

The CLHD was performed using the established technique[13]. The PDLHD technique differs from the classic one in connection to a few key passages. After freeing the lower esophageal attachments and circling the gastro-esophageal junction using a string, approximately 10 cm of the lower mediastinal esophagus is isolated upwards (Figure 1); two stitches are applied on either side of the esophageal wall, the esophagus is pulled down and the stitches are tied to the diaphragmatic pillars (Figure 2), thus verticalizing the organ's axis. Once these steps are performed, the Heller-Dor myotomy is

carried out (Figure 3).[8]

Postoperative assessment

After surgery, the center's postoperative protocol for these patients was followed; it includes:

- A barium swallow X-ray carried out one month after the procedure to evaluate the relaxation of the LES (Figure 4),
- A High-Resolution Manometry (HRM) and 24-hour pH monitoring test carried out 6 months after the procedure to assess the differences in esophageal motility patterns and the presence or absence of pathological acid exposure,
- An esophagogastroduodenoscopy (EGDS) carried out 12 months after the procedure and every 2 years thereafter to monitor the esophageal mucosa.

The patients' symptoms were scored with ES at every clinical examination carried out during the entire follow-up.

Treatment failure was defined as the persistence or recurrence of an ES > 3 or the need for retreatment such as pneumatic dilation or, in case of inefficacy, of redo-myotomy, POEM or esophagectomy, according to the patient's characteristics and the research group's experience.

Statistical analysis

Continuous data were expressed as medians and interquartile ranges (IQR), and categorical data as numbers and percentages. Comparisons were

performed using the Mann-Whitney test, the Chi Square test, and Fisher's test. A $p<0.05$ was considered statistically significant.

A professional data manager carried out the data analysis.

Results

Ninety-four patients (52 men and 42 women; median age = 53 years, IQR 61-40) underwent laparoscopic LHD during the study period: 60 underwent CLHD and 34 PDLHD. The patients' demographic and clinical data are summarized in Table 1.

There were no statistically significant differences between the two groups in terms of their sex and symptom scores, nor were there any statistically significant differences between the two groups in terms of the endoscopic treatments they had undergone before the operation (Pneumatic dilation, Botox injections, or both): 17/60 (28%) in the CLHD and 13/34 (38%) in the PDLHD ($p=0.36$). None of the patients had undergone a peroral endoscopic myotomy (POEM) before LHD.

The median symptom duration was longer for the PDLHD patients (144 months, IQR:72-240) with respect to the CLHD ones (24 months, IQR:25-120); the difference was statistically significant ($p<0.002$). The median pre-operative Eckardt Score was 5 for the PDLHD group (IQR:4-7) and 7 for the CLHD group (IQR:5-8) ($p<0.02$). Preoperatively all the patients in both groups were classified as manometric pattern I.

The surgical procedures were completed laparoscopically in all ~~of~~ the patients. There were 2 mucosal lesions, one in each group (p=n.s); both were detected and repaired intraoperatively without subsequent complications. The surgery times were

noticeably higher in the PDLDH group: 150 mins (IQR:40-175) versus 125 mins (IQR:110-150) in the CLHD group ($p<0.01$). No postoperative complications were noted during the hospital stay in any of the patients. The intraoperative and postoperative results are shown in Table 2.

The median follow-up time of the whole population was 61 months (IQR: 22-110); concerning the two groups, it was 78 months (IQR:61-119) in the CLHD and 37 months (IQR:20-105) in the PDLHD group ($p=0.04$). During the follow-up, two patients (2.1%) in the CLHD group developed a squamous cell carcinoma (SCC) of the distal esophagus, thus they were removed from the follow up when analyzing the results of the operation.

All the patients in both groups had an improvement in their Eckardt score after surgery with respect to their preoperative one, as seen in Table 2 ($p=0.002$). Excluding the two patients who had the SCC, the success of LHD was seen in 76/92 patients (82.6%).

The failure rates were 27.6% (16/58) after the CLHD and 5.9% (2/34) after the PDLHD ($p<0.01$). Fifteen of the patients who complained about persistent dysphagia underwent single or multiple Rigiflex dilations; all of them reported symptom relief. Three patients complaining about dysphagia refused additional operative treatments, two of these were able to control their symptoms by occasionally assuming oral medications; none agreed to undergo further pH monitoring after surgery.

The persisting failures underwent additional treatment: three of them underwent redo-myotomy, one underwent POEM, and one ultimately required esophagectomy.

Amongst the patients who adhered to all of the post-operative follow-up examinations, an abnormal acid exposure time during pH monitoring was detected in 2 patients in the PDLDH and in 6 in the CLHD one (p= n.s.).

Discussion

Despite the development of reliable diagnostic tools[1] and ongoing research focusing on its pathophysiology, esophageal achalasia is a rare disorder whose treatment remains fundamentally symptomatic. According to recent studies examining large cohorts of achalasia patients, pre-operative manometric patterns and the presence or absence of a sigmoid esophagus represent the strongest predictors of outcome in terms of symptom relief[4,14]. These data confirm the importance of a detailed pre-treatment work-up to define the patient's radiological grade [9,10] and manometric pattern [1,11].

In the event of a late diagnosis (in approximately 5% of achalasia patients) or when therapies are unsuccessful, the disease can progress to the end-stage phase, in which case the esophagus acquires a sigmoid shape and an augmented diameter (> 6 cm)[14]. The use of esophagectomy to treat late stage disease continues to be a debated practice and mostly reported in case series [15] in view of the fact that patients need to be fit and because of the high morbidity and increased mortality [3] associated to the operation. According to a recent study which identified worse quality of life in patients subjected to esophagectomy with respect to those undergoing LHD, it should be offered only in cases of high risk of cancerization, due to chronic stasis inflammation in a dilated esophagus [7].

We strongly believe that LHD should be the first therapy offered to end stage patients. In fact, the findings from a recent study carried out at our center demonstrated that LHD is a safe and effective

treatment also for end-stage achalasia[8]. Our findings confirmed the results of Patti et al, Sweet et all, and Mineo et al [9,16,17]: in fact more than 70% of the patients with stage IV disease studied at our

center reported symptom relief without major complications or mortality, well comparable, albeit slightly lower, to those obtained with the same treatment in earlier stages [8].

The present study, with a larger number of patients and longer follow-up, "reinforces" this conclusion demonstrating a success rate > 82% of LHD in end-stage achalasia patients.

In the previous study, we also described a modified LHD technique initially outlined by Faccani et al.[18] The case series they reported included 33 patients with end-stage achalasia; 15 underwent a classic LHD (CLHD) and 18 a pull-down technique during laparoscopic Heller-Dor. PDLHD straightens the esophagus by applying two stitches on either side of the organ; after the stitches are tied to the diaphragmatic pillars, the surgeon goes on to carry out the rest of the LHD. The clinical and radiological results demonstrated that PDLHD is more effective than CLHD. We need to bear in mind however that although the study was characterized by a long follow-up (78 months), it included only a few patients [18].

In our previous study recently published, we described our initial experience with PDLHD for end- stage achalasia patients, but since the focus of that study was not to compare CLHD and the pull- down technique, we were not able to

draw any conclusions.

Given the encouraging results obtained, however, and since "*those who do not evolve are destined to extinction*", we decided to start performing PDLHD as the treatment of choice for end-stage disease. So, in the present study we aimed to compare the outcome of PDLHD with that of CLHD for stage IV achalasia patients. An improvement of symptoms was observed in both groups during the postoperative evaluation, confirming once again that LHD is safe and effective in treating end-stage achalasia in more than 80% of patients. Our study also demonstrated the clinical advantage of PDLHD with respect to CLHD given the significantly fewer cases of failures. In our clinical practice the first approach in patient who complain persistence or recurrence of symptoms is pneumatic dilation.[4] We know that this procedure might be considered as a necessary complementary treatment, even more if patients are severely non-responders like the end-stage ones. So far, literature is lacking well-defined criteria of failure, but thanks to our previous experience on the matter we believe that using the "need for retreatment" criterion could be the most objective way to evaluate a real failure of the surgical treatment.[4,8,11]

Considering the data available for this study, fewer patients from the PDLHD experienced the need of a further retreatment other than PD (POEM, redo-myotomy, esophagectomy). Although the surgery duration times were slightly higher for PDLHD, it did not require more technical skills nor was it associated to more complications, remaining thus a viable surgical alternative.

Judging from the results of our study, only 8 patients experienced abnormal acid exposure at the pH- monitoring testing. No statistically significant difference was found in the distribution of these conditions between the two groups studied. These data suggested that the hiatus approach of the "pull-

down" technique does not increase incidence of postoperative gastroesophageal reflux. The CLHD demands anterior mediastinal dissection only, thus a hiatal treatment is not necessary. The PDLHD technique demands a circumferential dissection of the esophagus but the two to three stitches applied between on either side of the esophageal wall and the pillars, provide closure of the hiatus. Moreover, we performed this technique in an esophagus larger than 6 cm, and a hiatoplasty could compress the gullet creating an hyatrogenic outflow obstruction.

The symptom relief even over a long period does not eliminate the pathological substrate of achalasia. The disease can still lead to an increased risk of neoplastic degeneration during its progression, even if the condition is not considered a precancerous one. The progression towards an increased risk of cancer in patients with achalasia derives from the chronic inflammatory response to food stasis, which can lead to dysplasia and in some cases to squamous cancerous degeneration (SCC). Post-operative GERD may also be the cause of the less frequent Adenocarcinomas. Evidence of an increased risk of developing esophageal cancer, both SCC and adenocarcinoma, has been described by studies examining large cohorts of patients [19,20]. In the patients with sigmoid-shape esophagus we studied here, (2.1%) developed a SCC. One of them refused to undergo periodical endoscopies. As far as we are concerned, an endoscopy every 2 years after surgery can effectively exclude the possibility of long-term complications and neoplastic degeneration.[4]

This study has some limitations that need to be considered. Firstly, it is a retrospective, non- randomized study. Secondly, there are differences in time window and different follow-up between the two groups: the PDLHD group

has been followed for fewer months, and the differences in follow up will never be fully eliminated, unless we assume the possibility of a balance between the groups later in time; also, this type of technique has been performed only by the most expert surgeons of our team, thus eliminating possible biases in surgeons' expertise in the PDLHD group. Further studies with longer follow-up and larger cohort of patients are needed to confirm the results of the pull-down technique.

Conclusions

The study findings indicate that LHD is an effective treatment for end-stage achalasia patients. We therefore believe that PDLHD should be the first surgical option offered to these patients before esophagectomy is taken into consideration. This approach allows to avoid esophagectomy in more than 4 patients out of 5 with end stage disease. Finally, the pull-down technique during LHD further improves the outcome of this difficult condition to treat.

Conflicts of interest

All authors declare that they have no conflicts of interest.

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Figure legend

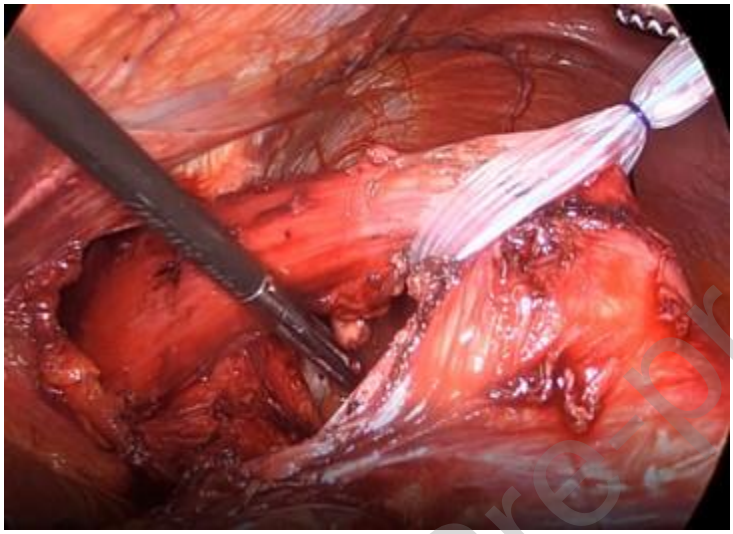

Figure 1. The pull-down technique: the esophagus is isolated from the pillars and the dissection is extended about 10 cm in the mediastinum to take the esophagus in the abdomen thus verticalizing the organ's axis.

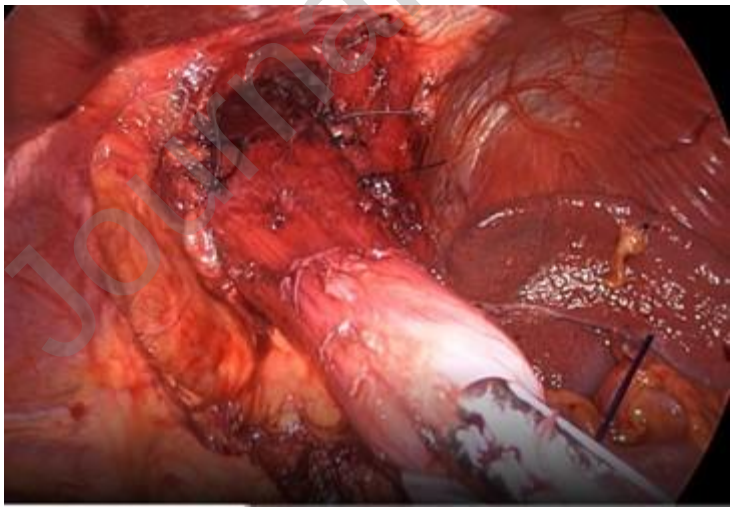

Figure 2. The surgeon applies two or more stitches on each side of the esophageal wall to anchor it to the pillars and to stabilize the straightening.

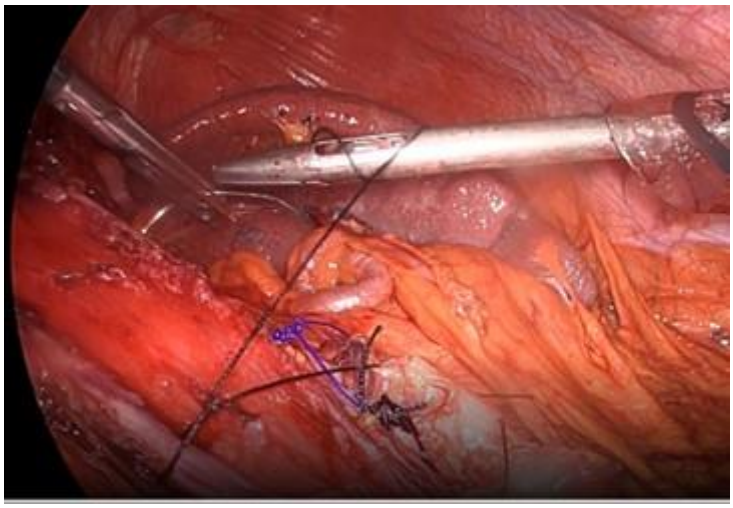

Figure 3. The Dor procedure is carried out without fixing the wrap to the pillars.

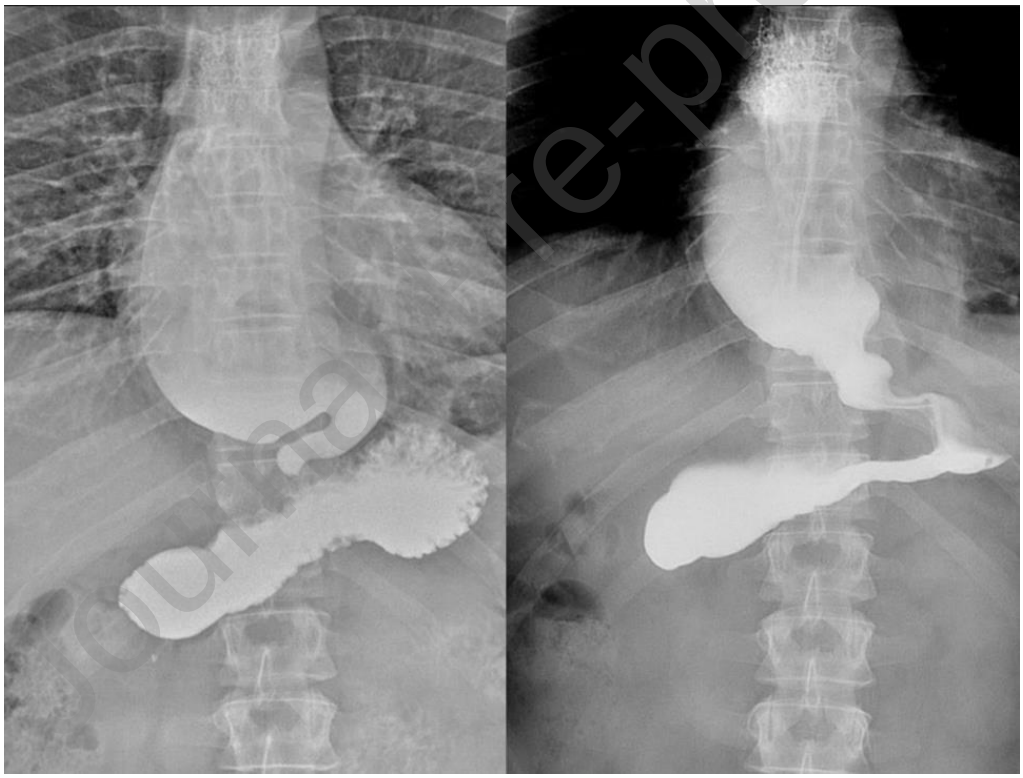

Figure 4. Pre- and post-operative barium swallows using the pull-down technique.

Table 1. Demographic and clinical data

	Classic LHD (n = 60)	Pull-down LHD (n = 34)	p-value

Age; years *	50 (39-57)	56 (43-63)	**0.03**
Sex; M:F	32:28	20:14	0.76
Previous treatment; n (%)	17/60 (28%)	13/34 (38%)	0.28
Symptoms duration; months *	60 (24-120)	144 (72-240)	**0.002**
Preoperatory Eckardt score; n *	7 (5-8)	5 (4-7)	0.10

*Data are expressed as median (IQR)

Table 2. Intraoperative and Postoperative data

	Classic LHD	**Pull-down LHD**	**p-value**
Surgery duration; minutes *	125 (110-150)	150 (140-175)	**0.006**
Mucosal lesions; n (%)	1 (2%)	1 (3%)	0.99
Follow-up; months *	78 (61-119)	37 (20-105)	**0.04**
Postoperative Eckardt score; n *	1 (0-2)	0 (0-0)	**0.002**
Failure; n (%)	16/58 (27.5%)	2/34 (5.9%)	**0.03**
Primary retreatment; n (%)			
Pneumatic dilation	13 (81%)	2(100%)	
None	3 (19%)	0	
Secondary retreatment; n			
POEM	0	1	
Redo-myotomy	3	0	
Esophagectomy	1	0	

*Data are expressed as median (IQR)