Comparison of treatment outcomes of endoscope-guided pneumatic dilation and laparoscopic Heller myotomy

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Abstract The debate on which is the better choice between laparoscopic Heller myotomy (LHM) and endoscopic pneumatic dilation (PD) for esophageal achalasia has been ongoing for decades. This study aims to compare the results of endoscope-guided PD and LHM in 42 patients with achalasia between May 1996 and August 2011. Twenty-one patients who had received PD and 21 who had received LHM were enrolled. The cumulative remission rate was analyzed using the Kaplan–Meier method with the assessment of symptom scores between grades before and after PD or LHM done at 6 weeks, 6 months, 1 year, and then every year thereafter. Possible confounding factors related to the remissions were analyzed by Cox’s proportional hazard model. For PD, the cumulative remission rates were 81.0% (1 year), 76.2% (2), 66.7% (3), 61.9% (4), and 47.6% (5). For LHM, the cumulative remission rates were 90.5% every year from the 1st to the 5th. The LHM patients had significantly better remission rates than the PD patients (p = 0.033, by log-rank test). The LHM group had a longer hospital stay than the PD group [median (interquartile range): 8 (6.5–10) days vs. 3 (2–3) days, p < 0.001] and had more reflux complications (52.4% vs. 19.0%, p = 0.024). No perforation occurred in either group. In conclusion, the 5-year cumulative effectiveness of LHM is better than that of PD despite the association of LHM with more reflux events (52.4%).

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Introduction

Achalasia is the primary motility dysfunction of the esophagus with the selective loss of inhibitory neurons of the myenteric plexus, which produces vasoactive intestinal polypeptides, nitric oxide, and inflammatory infiltrates and is thereby responsible for abnormal lower esophageal sphincter (LES) dysfunction. This results in the unopposed excitation of the LES and in the dysfunction or failure of the LES to relax in response to each swallow [1–6]. Dysphagia to both liquid and solid foods is the most commonly encountered symptom.

The currently available therapeutic options aim at loosening the LES and hence at relaxing it and relieving the obstruction of the esophagus [3]. Laparoscopic Heller myotomy (LHM) and pneumatic dilation (PD) are still the key treatment options, despite the introduction of peroral endoscopic myotomy (POEM) and laparoendoscopic single-site Heller myotomy with anterior fundoplication. Adding to the already ongoing debates on the superiority between PD and LHM, the first multiple-center randomized controlled 2-year follow-up research conducted by the European Achalasia Trial group indicated that LHM is not superior to PD [7]. However, publications on the satisfactory long-term success of laparoscopic surgical outcomes continue to emerge. Up to now, controversy surrounds the choice of LHM as the primary treatment for achalasia or as second-line treatment following failure of nonsurgical intervention after so many decades of real-world practice. This 5-year follow-up study aims to compare the results of endoscope-guided PD and LHM.

Patients and methods

Patients

We reviewed the medical files of the hospital admissions of patients with achalasia between May 1996 and August 2011. The PD patients were enrolled from 1996 and followed up until 2003, and the LHM patients were enrolled from 2006 and followed up until 2011. Twenty-one patients (12 men, 9 women) received LHM in the surgical unit, and 21 (13 men, 8 women) received endoscope-guided PD treatment in our unit. We excluded all patients who had prior treatments such as previous PD, botulinum toxin injection, and Heller operation; patients with esophageal obstructions caused by intrinsic or extrinsic events as determined by x-ray film examination and endoscopy; and patients with episodes of esophageal or gastric tumors, peptic stricture, prior surgical fundoplication, and incomplete chart recording. The mean age was 43.4 ± 17.78 years (range, 17 years to 78 years) in the LHM group and 49.9 ± 20.2 years (range, 18 years to 93 years). All patients had dysphagia of both liquid and solid foods; some had food regurgitation (92.8%), body weight loss (61.9%), chest pains (38.1%), and aspiration pneumonia (4.7%). The diagnosis was confirmed by one or more of the following examinations: endoscopic examinations, barium esophagography, and manometric study. We performed endoscopic ultrasonography or computed tomography to rule out pseudoachalasia. We performed endoscope-guided PD under conscious sedation (after the patients fasted overnight) using a 3-cm-diameter Rigiflex balloon dilator (Microvasive, Watertown, MA, USA). Depending on the tolerance of the patient, the balloon was inflated up to 10–12 pounds per square inch and maintained for 60 seconds, and the step is then repeated for another 15–30 seconds. The patients ingested Gastrografin after the dilation so that we could determine whether esophageal perforation had taken place. LHM was performed by experienced cardiac–vascular surgeons in Kaohsiung Chang Gung Memorial Hospital (KCGMH).

This retrospective chart review study was approved by both the Institutional Review Board and the Ethics Committee of KCGMH, Taiwan (IRB102-2468B). Written informed-consent forms were signed by subjects 18 years and older or by parents or guardians for younger subjects before they underwent endoscopic interventions.

Barium esophagogram

A timed barium esophagogram was performed on the patients before and after PD and LHM at the initial investigation, 6 weeks later, and every 1 year thereafter to objectively assess improvement in esophageal emptying.

Symptom score assessment

Symptom improvement status was determined using the Eckardt symptom score [8] at the initial investigation, 6 weeks later, and every 1 year thereafter. Depending on whether dysphagia, regurgitation, and chest pain occurred occasionally, daily, or several times during the day, a symptom score of 0 to 3 was determined. In addition, a symptom score of 0 to 3 was assigned to the degree of weight loss. Thus, a completely asymptomatic patient would have a symptom score of 0, whereas a severely affected patient could have a symptom score of up to 12. Patients were considered to have reached clinical remission if symptoms had totally disappeared or had improved by at least 2 points and did not exceed a score of 3. Patients who requested further therapy despite having a symptom score of less than 4 were considered to have treatment failure.

Statistical analysis

Statistical analysis was performed using the statistical software SPSS 17.0 (SPSS Inc., Chicago, IL, USA). Numerical data were compared using the Mann–Whitney test. For categorical data, the chi-square or Fisher’s exact test was applied. The responses of both groups to the initial treatment, such as their manometric results, were compared, and their symptom scores were compared using the Mann–Whitney test. In both arms, the cumulative remission rate was analyzed using the Kaplan–Meier method with assessment of symptom scores between grades before and after PD and LHM in every year thereafter, and differences in curves between the two groups were statistically compared by log-rank test. A value of \( p < 0.05 \) was considered statistically significant.
Results

The baseline patient characteristics in the initial treatment are shown in Table 1. Most patients suffered from severe disease with high symptom scores of 6 or more when referred. The mean LES pressure before PD was 40.3 ± 14.3 mmHg (range, 18–78 mmHg) in the LHM group and 34.1 ± 13.3 mmHg (range, 21–60 mmHg) in the PD group. The median (interquartile range, IQR) of the PD group was 60 (30–77) months, and that of the LHM group was 51 (20–71) months.

The median improved symptom score of the LHM group was 4 (range, 3–5) at Week 6, 4 (4–5) at Year 1, 5 (4–6) at Year 2, 5 (4–6) at Year 3, 6 (5–7) at Year 4, and 5 (5–7) at Year 5. The same score of the PD group was 5 (4–6) at Week 6, 5 (5–6) at Year 1, 5 (2–7) at Year 2, 5 (3–7) at Year 3, 4 (2–7) at Year 4, and 4 (2–7) at Year 5. No significant difference was found between these two study groups at Week 6, Year 1, or Year 2. However, the PD group obtained lower median improved scores than the LHM group at Year 3 (p = 0.045), Year 4 (p < 0.001), and Year 5 (p = 0.029).

The median body weight (BW) change in the LHM group was 1.2 kg (range, 1–1.8) at Week 6, 2.1 kg (1.4–2.5) at Year 1, 1.4 kg (1.1–2.6) at Year 2, 3 kg (2.6–3) at Year 3, 3.3 kg (3.2–5) at Year 4, and 3.6 kg (3.4–4.4) at Year 5. The same change in the PD group was 1.5 kg (0.8–2) at Week 6, 2.2 kg (1.4–2.6) at Year 1, 2.4 kg (1.3–3.7) at Year 2, 2.8 kg (1.6–3.8) at Year 3, 3.5 kg (2.1–4.3) at Year 4, and 3.9 kg (2.5–4.1) at Year 5. No significant difference in BW change was observed in these two groups.

The responses to the initial treatments in both groups according to symptom score are shown in Figure 1. Both groups were followed up at regular intervals for a median of 4.62 years. For PD, the cumulative remission rates were 81% (1 year), 76.2% (2 years), 66.7% (3 years), 61.9% (4 years), and 47.6% (5 years). For LHM, the same rates were 90.5% every year for the 1st to 5th years. The LHM patients had significantly better remission rates than the PD patients (p = 0.033, by log-rank test). The LHM group had a longer hospital stay than the PD group [median (IQR) = 8 (6.5–10) days vs. 3 (2–3) days, p < 0.001] and more reflux complications (52.4% vs. 19.0%, p = 0.024). Nine patients were available for follow up at the 5th year in the PD group and six patients in the LHM group.

Relapse occurred in 11 patients in the PD group during the follow-up period. Four experienced only chest pain and/or very mild dysphagia and needed no further treatment. Seven suffered from recurrent symptoms of dysphagia that affected their quality of life. Two received a second PD, which was successful. Four patients chose surgery, and one refused further treatment. Cox’s proportional hazard model was used to analyze the risk factors associated with treatment failure (relapse), and the result showed that age, symptom score, sex, post-treatment complications, and hospitalization period were not relevant to clinical remission. However, the treatment choice for achalasia was a possible risk factor of treatment failure (PD vs. LHM, hazard ratio: 4.36, p = 0.057) (Table 2).

Four patients (21.9%) had complications after the initial PD. Two had a minor bleeding event, but they recovered after medical treatment. These patients had stable vital signs and hemoglobin levels still within normal limits. Both patients and two others suffered from mild symptomatic reflux esophagitis. All four of them achieved remission with proton-pump inhibitor (PPI) therapy once daily for 4–8 weeks. In the LHM group, as high as 54% had reflux events, compared with the 19% of the PD group (p = 0.024). No perforation occurred in either group. All of these patients survived.

Discussion

Our results showed that the cumulative remission rates were better in the LHM patients, especially at Year 5...
(90.5%), when they dropped to 47.6% in the PD patients. However, the LHM group suffered from more reflux complications than the PD group.

Controversy surrounds the choice of LHM as the primary treatment for achalasia or as second-line treatment following failure of nonsurgical intervention after so many decades in real-world practice. Some surgeons heuristically believe that LHM is more technically difficult following PD, but others claim that PD does not hinder future myotomy [9]. While the debate on which technique is superior continues, the first randomized controlled trial comparing LHM and PD, conducted by the European Achalasia Trial group, suggested that after 2 years of follow up, LHM, compared with PD, is not associated with superior rates of therapeutic success [7]. Those who favor PD believe that PD and LHM are equally efficient. However, the follow-up duration of that study was not long enough for a conclusion to declare equality between the two.

In the current study, the balloon used for dilation was only 30 mm. Graded balloon dilation starting with a 3 cm Rigiflex balloon as the initial dilator and progressing to 3.5 and 4 cm balloons in the absence of a response to the previous balloon seems to be the safest approach for successful PD [10]. A review of 21 studies using Rigiflex balloons demonstrated that the initial success rate depends on balloon size, with larger balloons showing better outcomes. Success rates of 74%, 80%, and 90% were achieved when 30 mm, 35 mm, and 40 mm balloons, respectively, were used [11].

Complications and the long-term effectiveness of the procedure are the main concerns in the decision making for treatment choice. In this study, more complications occurred in the surgical group than in the PD group, but only because as high as 54% of the LHM group had reflux events, compared with 19% of the PD group (p = 0.024). This has been the main drawback of LHM as abnormal acid exposure after surgery could be long lasting despite partial fundoplication. Fortunately, all reflux events in both groups could be controlled by PPIs. Generally, the prevalence of reflux symptoms is low, so only a minority of patients need long-term PPIs [12–14]. However, although reflux can usually be overcome by such inhibitors, the risk of its long-term complications (albeit rarely occurring), such as stricture, Barrett’s esophagus, and adenocarcinoma, should be taken into account. In contrast, reflux symptoms in post-PD patients are usually mild and transient. They can easily be controlled by a short course of PPI treatment. The most severe complication of PD is perforation, which occurs in approximately 1–2% of patients. Such perforation is usually minor but can be dangerous if ignored [15,16]. No perforation was found in the current study. Furthermore, achalasia patients are at risk of esophageal cancer, although the reported incidence rates of carcinoma in these patients are relatively low [17]. Brücher et al. [18] found that in patients with long-standing achalasia, the risk for developing esophageal cancer is about 140 times that of the general population. In the current study, no esophageal cancer was reported during the follow-up period.

In terms of 5-year effectiveness, LHM was superior (90.5% remission rate at Year 5 vs. 47.6% in the PD group). Thus far, LHM is still generally considered to be superior to PD in treating achalasia and is regarded the first choice of treatment for the condition. LHM is usually suggested for young patients (<40–45 years), male patients, patients with pulmonary symptoms, and patients with failed response to one or two initial dilations [1,19,20].

The novel endoscopic esophagomyotomy for achalasia, POEM, can accomplish longer myotomy. This is a remarkable advancement because it was difficult for surgeons to extend the length of myotomy to the thoracic esophagus, especially with advanced disease or severe fibrosis. Studies on this technique have obtained good short-term results without serious complications, but long-term follow-up results are necessary [21–25]. Moreover, POEM can be a challenging and demanding technique even for experienced endoscopists. It can be hazardous in case of complicated purulent mediastinitis. Validations with long-term effectiveness and safety reports could be another breakthrough in the treatment of esophageal achalasia. Long-term follow up with POEM to test long-term effectiveness and the cautious monitoring of safety issues are important.

Our study has potential limitations. This is a single-center report, and the small sample size, nonrandom sampling, and different study periods could have resulted in selection bias. Caution must be taken in extrapolating the results. Besides, this is a retrospective chart review study with observations based on hospitalized patients with a diagnosis of achalasia. Prospective multicenter data with a larger sample size would be more convincing.

Second, the PD patients had no symptom scores less than 5d which is a limitation because their pretreatment scores were higher. Finally, the follow-up rate decreased after the 4th year.

### Table 2

Univariate and multivariate analyses of risk factors associated with treatment failure.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Comparisons</th>
<th>Univariate</th>
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<th></th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>HR (95% CI)</td>
<td>p</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>Treatment</td>
<td>PD vs. LHM</td>
<td>4.36 (0.96–19.80)</td>
<td>0.057</td>
<td>4.36 (0.96–19.80)</td>
</tr>
<tr>
<td>Sex</td>
<td>F vs. M</td>
<td>1.02 (0.33–3.15)</td>
<td>0.968</td>
<td>—</td>
</tr>
<tr>
<td>Age (y)</td>
<td>&lt;40 vs. &gt;40</td>
<td>2.35 (0.77–7.13)</td>
<td>0.131</td>
<td>—</td>
</tr>
<tr>
<td>Symptom score</td>
<td>8–9 vs. 4–7</td>
<td>1.61 (0.54–4.79)</td>
<td>0.395</td>
<td>—</td>
</tr>
<tr>
<td>LES pressure (mmHg)</td>
<td>&lt;30 vs. ≥30</td>
<td>2.33 (0.71–7.65)</td>
<td>0.162</td>
<td>—</td>
</tr>
<tr>
<td>Complications</td>
<td>yes vs. no</td>
<td>0.97 (0.30–3.15)</td>
<td>0.957</td>
<td>—</td>
</tr>
<tr>
<td>Hospital stay (d)</td>
<td>per 1 d increase</td>
<td>0.80 (0.62–1.04)</td>
<td>0.100</td>
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</tbody>
</table>

CI = confidence interval; HR = hazard ratio; LES = lower esophageal sphincter; LHM = laparoscopic Heller myotomy; PD = pneumatic dilation.
In conclusion, this study shows that the 5-year cumulative effectiveness of LHM is better than that of PD despite LHM’s association with more reflux events (52.4%).

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References
