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Efficacy of pneumodilation in achalasia after failed Heller myotomy

C. M. G. SALEH, F. A. M. PONDS, M. P. SCHIJVEN, A. J. P. M. SMOUT & A. J. BREDENOORD

Department of Gastroenterology and Hepatology, Academic Medical Center, Amsterdam, The Netherlands

Key Points

- Patients suffering from persistent or recurrent symptoms after Heller myotomy are subsequently treated with pneumodilation. There is little data on the efficacy of pneumodilation as secondary treatment. This study investigates the efficacy of PD as secondary treatment.
- Pneumodilation as secondary treatment is safe and has a success rate of 57%, using 30- and 35-mm balloons.
- These results substantiate pneumodilation as an adequate secondary treatment option for patients with recurrent or persistent symptoms after Heller myotomy.

Abstract

Background *Heller myotomy is an effective treatment for the majority of achalasia patients. However, a small proportion of patients suffer from persistent or recurrent symptoms after surgery and they are usually subsequently treated with pneumodilation (PD). Data on the efficacy of PD as secondary treatment for achalasia are scarce. Therefore, this study aimed to investigate the efficacy of PD as treatment for achalasia patients suffering from persistent or recurrent symptoms after Heller myotomy.* ***Methods*** *Patients with recurrent or persistent symptoms (Eckardt score >3) after Heller myotomy were selected. Patients were treated with PD, using a graded distension protocol with balloon sizes ranging from 30 to 40 mm. After each dilation symptoms were assessed to evaluate whether a subsequent dilation with a larger balloon size was required. Patients with recurrent or persistent symptoms (Eckardt score >3) after treatment with a 40-mm balloon were identified as failures.* ***Key Results*** *Twenty-four patients were included in total; 15 patients with achalasia type I, seven with achalasia type II and two with achalasia type III. Median relapse time was 2.5 years after Heller myotomy (IQR: 9 years and 3 months). Three patients were not suitable for PD; one patient was morbidly obese and not fit for any form of sedation and two had a siphon-shaped esophagus leaving 21 patients to treat. Eight patients were successfully treated with a single 30-mm balloon dilation (median follow-up time: 6.5 years; IQR: 7.5 years). Four patients required dilations with 30- and 35-mm balloons (median follow-up time: 11 years; IQR: 3 years). Nine patients failed on the 35-mm balloon dilation and underwent a subsequent dilation with a 40-mm balloon, and all failed on this balloon as well. Thus, PD was successful in 12 of the 21 treatable patients, resulting in a success rate of 57% for treatable patients or 50% for all patients. Baseline Eckardt scores were also higher in those that failed (median: 8; IQR: 2) than those that were treated successfully (median: 5.5; IQR: 2) treated ($p = 0.009$). Furthermore, baseline barium column height at 5 min was higher in patients with failed (median: 6 cm; IQR: 6 cm) treatment than in patients with successful (median: 2.6 cm; IQR: 4.7 cm) treatment ($p = 0.016$). Baseline lower esophageal sphincter pressure was not different between patients who were treated successfully (median: 11 mmHg; IQR: 5 mmHg) and those that failed on PD (median: 17.5 mmHg; IQR: 10.8 mmHg) treatment ($p > 0.05$). Baseline symptom pattern was also not a predictor of successful*

Address for Correspondence
Albert. J. Bredenoord, MD, PhD, Department of Gastroenterology and Hepatology, Academic Medical Center Amsterdam, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands.
Tel: +31 (0)20 566 91 24; fax: +31 (0)20 566 91 57;
e-mail: a.j.bredenoord@amc.uva.nl
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treatment. No adverse events were recorded during or after PD. ***Conclusions & Inferences*** *Pneumodilation for recurrent symptoms after previous Heller myotomy is safe and has a modest success rate of 57%, using 30- and 35-mm balloons. Patients with recurrent symptoms after PD with 35-mm balloon are likely to also fail after subsequent dilation with a 40-mm balloon.*

Keywords *dysphagia, Eckardt symptom sore, lower esophageal sphincter, manometry, esophagus.*

Abbreviations: LES, Lower esophageal sphincter; PD, Pneumodilation.

INTRODUCTION

Idiopathic achalasia is a rare primary esophageal motility disorder with an estimated annual incidence rate of 1 per 100 000 persons. Achalasia is characterized by aperistalsis of the esophageal body and dysrelaxation of the lower esophageal sphincter (LES) due to progressive destruction and degeneration of the neurons in the myenteric plexus. Unfortunately, the cause of the neuronal degeneration is still unknown.[1]

Aperistalsis and dysrelaxation of the LOS subsequently lead to retention of food and saliva in the esophagus, resulting in the typical symptoms of achalasia namely dysphagia, chest pain, regurgitation of undigested food and weight loss. The disease is also associated with an increased risk for development of squamous cell carcinoma of the esophagus.[2]

Treatment of idiopathic achalasia is focused on symptom relief, which is achieved by disrupting the non-relaxing LOS. Traditionally, the most frequently used treatment options are endoscopic pneumodilation and laparoscopic Heller myotomy.[3] While pneumodilation is characterized by recurrences and need for retreatments, Heller myotomy is considered a more effective treatment for the long term. However, a small proportion of patients suffer from persistent or recurrent symptoms after surgery as well. A recent large prospective, multicenter randomized trial showed that after 2 years, 10% of patients had significant recurrent symptoms after Heller myotomy.[4] Patients with recurrent symptoms after Heller myotomy are usually treated with pneumodilations. Heller myotomy and pneumodilation procedures seem to be well studied as first treatment,[3] but, until now, there is very little data on the efficacy of pneumodilation as secondary treatment for achalasia.[5,6]

This study therefore aimed to investigate the efficacy of pneumodilation as treatment for achalasia patients suffering from persistent or recurrent symptoms after Heller myotomy.

METHODS

Achalasia patients are treated and followed according to standard protocols in our hospital and data are collected prospectively in a database. This study is a retrospective analysis of that prospective database.

Participants

Adult patients (≥18 years) with recurrent or persistent symptoms of achalasia after Heller myotomy were included. Recurrent or persistent symptoms were defined significant if patients presented with an Eckardt score >3. All patients underwent one or more pneumodilations according to protocol as treatment for the recurrent or persistent symptoms of achalasia.

Diagnostic measurements

Eckardt symptom score The Eckardt score is the sum of the symptom scores for dysphagia, regurgitation, and chest pain (with a score of 0 indicating the absence of symptoms, 1 indicating occasional symptoms, and 3 indicating symptoms at each meal) and weight loss (with 0 indicating no weight loss, 1 indicating weight loss of <5 kg, 2 indicating weight loss of 5–10 kg and 3 indicating weight loss of >10 kg; thus the maximum score on the Eckardt scale, indicating the worst symptoms, is 12.[7]

Esophageal manometry Depending on time of manometry, manometry was either performed with conventional manometry or high-resolution manometry.[8,9] Achalasia subtypes were identified according to the Pandolfino *et al*.[8,10]

Manometries were performed before and after last pneumodilation. Manometries were not performed between dilations.

Timed barium esophagogram For barium esophagogram, patients were required to fast the night before the test. During the test, patients stood upright while ingesting a low-density barium sulfate suspension in 30–45 s. Patients drank up to 250 mL suspension. Esophageal radiographs were taken at baseline and 1, 2, and 5 min after last ingestion of barium. The maximal width of the esophagus was measured and the distance from distal esophagus to the top of the barium column.[11]

Interventions

Pneumodilation Pneumodilation was performed according to our institutional protocol using a graded distension protocol with balloon sizes ranging from 30 to 40 mm. Patients were asked to use only clear fluids starting 24 h before the procedure and nil per mouth starting 8 h before the procedure. Under fluoroscopic guidance, a Rigiflex balloon was positioned at the esophagogastric junction and dilated for 1 min at a pressure of 5 PSI, followed by dilation with 7 PSI for another minute.[3,4] Two weeks after each dilation, symptoms were assessed to evaluate whether a subsequent dilation with a larger balloon size was required (in case Eckardt score >3). Patients with recurrent or persistent symptoms (Eckardt score >3) after treatment with 40-mm balloon were identified as failures. After successful treatment patients were instructed to contact our motility department in case of recurrent symptoms or otherwise annually.

Data analysis An Eckardt score >3 was considered as cut-off value for subsequent treatment with pneumodilation. If patients

suffered from recurrent symptoms with Eckardt score >3 after treatment with a 40-mm balloon, treatment was considered a failure.

Follow-up time was defined as the moment of treatment success till present time. If patients developed recurrent symptoms after a period of treatment success, patients were also identified as failures.

Secondly, we defined successful treatment by esophagography, as a barium column height <2 cm after 5 min and manometry, as an LOS relaxation pressure of <10 mmHg.

Adverse events Adverse events were documented, analyzed, and classified according to Cotton *et al.* All events occurring immediately before or during the procedure, or up to 14 days post procedure were defined as adverse events.[12]

Statistical analysis Data analysis was performed using SPSS version 21 and Prism software version 5 (Graph Pad, La Jolla, CA, USA). Data are presented as medians and interquartile ranges (IQR). Comparisons between successful and failed treatment were assessed using the non-parametric Mann–Whitney *U*-test. Differences were considered statistically significant when $p < 0.05$. In addition, plausible correlations were determined using the Spearman Rank Test.

RESULTS

In total, 24 patients were included of which 11 males and nine females, with median age of 53 years, ranging from 22 to 86 years. The median relapse time after Heller myotomy was 2.5 years (IQR: 9 years and 3 months).

Efficacy of pneumodilation

Unfortunately, only 21 patients were eligible for treatment; three patients were not suitable for pneumodilation; one patient was morbidly obese and had comorbidity and could therefore not safely tolerate sedation, and two had a siphon shaped esophagus. Based on Eckardt symptom score, eight patients were successfully treated with one session with 30-mm balloon dilation, with a median follow-up time of 6.5 years (IQR: 7.5 years). Four patients required two sessions with 30- and 35-mm balloon dilations, with a median follow-up time of 11 years (IQR: 3 years). Nine patients underwent three sessions with balloon dilations up to 40-mm, and all nine failed on the 40-mm balloon as well (Table 1). Thus, pneumodilation was successful in 12 of the 21 patients that were treated, resulting in a success rate of 57% for treatable patients or 50% for all patients, when using symptoms as measure for treatment success.

Eighteen of the 21 patients underwent barium esophagogram to objectify treatment success. Ten of 18 patients were successfully treated according to barium esophagogram, with less than 2 cm stasis after 5 min. Thus, success defined as a barium column of ≤2 cm after 5 min resulted in a success rate of 56% for treatable patients. Further details can be found in Table 1.

Table 1 Outcome of pneumodilation after failed Heller myotomy

	Successful treatment with dilation up to 30 mm	Successful treatment with dilation up to 35 mm	Successful treatment with dilation up to 40 mm	Total successfully treated patients
Outcome parameter				
Eckardt score	8 (38%)	4 (19%)	0 (0%)	12 (57%)
Stasis on barium Oesophagogram	6 (33%)	1 (6%)	3 (17%)	10 (56%)
LOS relaxation pressure	6 (35%)	4 (24%)	2 (12%)	12 (71%)

In 17 patients, manometry was repeated after treatment. In 12 patients, LOS relaxation pressure recorded during manometry was less than 10 mmHg. All patients dilated with a single 30-mm dilation and with 30- and 35-mm balloon dilation schemes had LOS relaxation pressures <10 mmHg (12 patients). Thus, based on LOS relaxation pressure of <10 mmHg, a success rate of 71% was found for treatable patients. Further details can be found in Table 1.

Complications

No complications occurred during or immediately after the pneumodilations.

Predictors of treatment success

Before secondary treatment, achalasia types were identified for all patients: 15 patients presented with achalasia type I (two patients were not treatable), seven with achalasia type II (one patient was not treatable) and two with achalasia type III. A total of 54% patients suffering from achalasia type I, 67% of patients suffering from achalasia type II, and 50% of patients suffering from achalasia type III were successfully treated.

Baseline Eckardt scores (before dilation) were significantly higher in those patients that failed (median: 8; IQR: 2) than those that were successfully (median: 5.5; IQR: 2) treated ($p < 0.05$; Fig. 1 and Table 3). There was a significant correlation between Eckardt scores and treatment outcome ($p = 0.011$).

Baseline symptom pattern did not differ between patients that were successfully treated and patients that failed secondary treatment (Table 2).

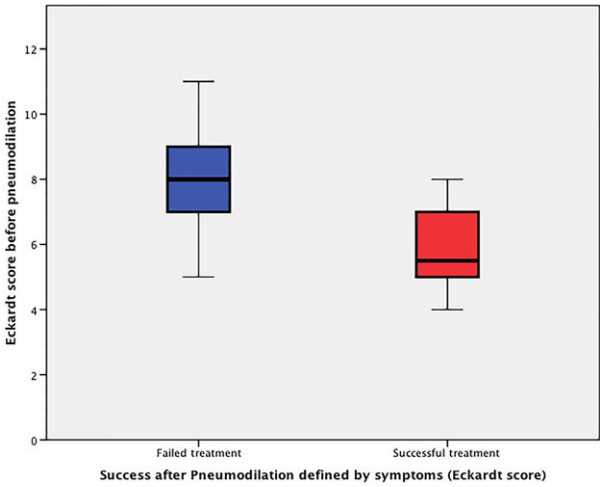

Figure 1 Distribution of Eckardt score in patients with successful and failed treatment.

Table 2 Distribution of symptoms in patients with successful and failed treatment

	Treatment success	Treatment failure	Total
Dysphagia for solids and liquids	6 (75%)	2 (25%)	8
Dysphagia for solids and liquids and Regurgitation	3 (75%)	1 (25%)	4
Dysphagia for solids and liquids and Retrosternal pain	2 (67%)	1 (33%)	3
Dysphagia for solids and liquids and Weight Loss	0 (0%)	2 (100%)	2
Dysphagia for solids and liquids, Regurgitation and Retrosternal pain	0 (0%)	1 (100%)	1
Dysphagia for solids and liquids, Regurgitation, Retrosternal pain and Weight loss	1 (33%)	2 (67%)	3

Also, pretreatment barium column height (T5) was significantly lower in those patients that responded favorably to treatment (median: 2.6 cm; IQR: 4.7 cm) compared to those that failed (median: 6 cm; IQR: 6 cm; $p < 0.05$; Fig. 2 and Table 3). There was a significant correlation between barium column height and treatment outcome ($p = 0.048$).

Baseline LOS pressure was not different between successfully treated patients (median: 11 mmHg; IQR: 5 mmHg) and those that subsequently failed (median: 17.5 mmHg; IQR: 10.8 mmHg) secondary treatment ($p > 0.05$; Fig. 3 and Table 3). No correlation was found between LOS relaxation pressure and treatment success.

Lastly, 78% of patients that failed on pneumodilation after Heller myotomy, also received pneumodilation before Heller myotomy, while only 42% of patients that were successfully treated by pneumodilation received pneumodilations prior to Heller myotomy.

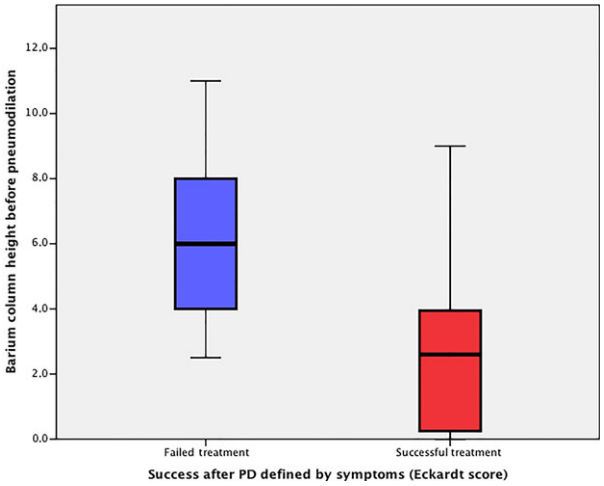

Figure 2 Distribution of Barium Column Height in patients with successful and failed treatment.

Table 3 *p*-value for baseline LOS pressure and baseline Eckardt score

	Treatment success	Treatment failure	P-value
Baseline Eckardt score	Median: 5.5 IQR: 2	Median: 8 IQR: 2	0.009
Baseline barium column height (cm)	Median: 2.6 IQR: 4.7	Median: 6 IQR: 6	0.016
Baseline LOS pressure (mmHg)	Median: 11 IQR: 5	Median: 17.5 IQR: 10.8	0.270

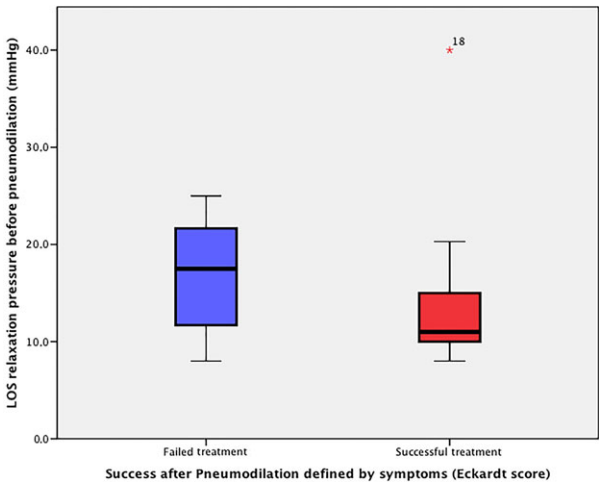

Figure 3 Distribution of LOS pressure in patients with successful and failed treatment.

DISCUSSION

Pneumodilation is an effective primary treatment for achalasia, particularly in the short term.[4] The efficacy of pneumodilations as primary treatment has been thoroughly investigated, however, there is still little evidence on the efficacy of pneumodilations as

secondary treatment after failed Heller myotomy. In this study, we show that the efficacy of pneumodilations after failed Heller myotomy is modest with a success rate of only 57%.

Fifty-seven percent of success rate was achieved when patients underwent one to two sessions with 30- and 35-mm balloon dilations; after a single session with 30-mm balloon dilation the success rate was only 33%, but this increased after dilation with a 35-mm balloon for those that did not respond initially in the absence of adverse events.

However, the patients that failed after 35-mm balloon also failed after 40-mm balloon dilation. The latter implies that pneumodilation with a 40-mm balloon does not add much in this particular patient group. Fortunately, it did not seem to cause much harm either and no perforations or bleedings occurred. It thus seems advisable to at least consider endoscopical or surgical myotomy in a patient that fails after 35 mm balloon dilation instead of directly performing a 40 mm dilation. Indeed, recent short-term follow-up data show that POEM is indeed feasible and effective in these patients.[13,14]

The efficacy of pneumodilation after failed Heller myotomy is only modest; however, it should be borne in mind that the patients in this study are a selection of non-responders to previous treatments. It also needs to be stressed that these conclusions are based on rather low numbers and further study should determine whether 40-mm balloon dilation is indeed never useful in these patients.

In addition to symptomatic outcome, stasis on barium esophagogram and manometry parameters were used as treatment outcome as well. When observing barium column height as outcome measure, we observed a 56% success rate, similar to the success rate based on symptomatic outcome. A success rate of 71% was achieved when looking at LOS relaxation pressure. Still, several patients with normal LOS pressures still experienced symptoms, resulting in a lower success rate based on symptoms.

Furthermore, we observed that the patients that did not respond to pneumodilation also had significantly higher Eckardt scores before treatment. Baseline barium column height also was a poor marker for treatment success to pneumodilation. Baseline LOS pressure and symptom patterns did not differ between patients that responded or failed on pneumodilations. These parameters can therefore not serve as predictors of successful treatment.

As mentioned, the literature on the efficacy of pneumodilation after failed Heller myotomy is very limited. A study conducted by Guardino *et al.* showed similar results with a success rate of 50%, in a group of 10 patients.[5] However, in their study, success was defined in two ways: symptomatic success was defined as a reduction in the occurrence of dysphagia and regurgitation to 2–4 times per week and physiologic success was defined as a reduction of ≥80% in the height of the barium column 5 min after a bolus. A study by Cusumano *et al.* showed a 76% success rate for pneumodilation after failed Heller myotomy, in a group of 27 patients. In contrast to our study, success was not only based on a symptom questionnaire and barium esophagogram but also on endoscopy. Cusumano *et al.* classified there results as excellent, good, moderate, and poor. Excellent results were defined as no symptoms, decreased dilation of the esophagus, good emptying and the presence of a gastric air pocket during esophagography. Also, endoscopy should present no stenosis, esophagitis or food stasis. Poor results were defined as daily symptoms and worsened results of esophagography and endoscopy, than before pneumodilation.[6]

Limitations of our study include a relatively small sample size and its retrospective nature. However, achalasia is a rare disease and only a small proportion of patients fail after Heller myotomy. Also, each time an achalasia patient visits our outpatient clinic the symptoms are noted routinely using the Eckardt symptom score and there is a strict protocol for pneumodilations limiting the impact of the retrospective design.

In conclusion, pneumodilation for recurrent symptoms after previous Heller myotomy is safe and has a modest success rate of 57%, using 30- and 35-mm balloons. Patients with recurrent symptoms after pneumodilation with 35-mm balloon are likely to also fail after subsequent dilation with a 40-mm balloon.

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DISCLOSURE

No competing interest declared.

AUTHOR CONTRIBUTION

CMGS study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, statistical analysis, and approval of final submitted draft; AJB and AJPMS study concept and design, interpretation of data, critical revision of the manuscript for important intellectual content, study supervision, and approval of final submitted draft.

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