Reflux disease and achalasia: Failure of the gatekeeper
Rohof, W.O.A.

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Chapter 11
Esophageal stasis on a timed barium esophagogram predicts recurrent symptoms in patients with long-standing achalasia
Wout Rohof, Aaltje Lei, Guy Boeckxstaens
ABSTRACT

Objective:
In achalasia, early recognition of the need for retreatment is of crucial importance to reduce morbidity and long-term complications such as esophageal decompensation. In clinical practice, symptoms and parameters of esophageal function including lower esophageal sphincter (LES) pressure and esophageal emptying are used to decide whether additional treatment is required. However, which of these tests performs best remains unclear.

Methods:
A cohort of 41 patients with longstanding achalasia (median 17 yrs), underwent esophageal manometry, timed barium esophagogram and symptom evaluation. Patients were followed up for ten years, and were regarded as a therapeutic failure if Eckardt score was > 3 or when retreatment was needed. Predictors of therapeutic failure were evaluated.

Results:
Of the 41 included patients, 7 patients had an elevated LES pressure (>10mmHg) and 26 had esophageal stasis >5cm on timed barium esophagogram. During follow up, 25 patients had recurrence of symptoms and were considered therapeutic failures. Five of these 25 patients had an elevated LES pressure, whereas 22 had esophageal stasis on barium esophagogram. Hence, the sensitivity to predict the need of retreatment is higher for esophageal stasis (88%) compared to LES pressure (20%). Sixteen patients (39%) were in long-term remission, of which 12 patients (75%) did not have stasis at their initial visit.

Conclusion:
In contrast to LES pressure, esophageal stasis is a good predictor of treatment failure in patients with longstanding achalasia. Based on these findings, we propose to use timed barium esophagogram rather than esophageal manometry as test to decide on retreatment.
INTRODUCTION

Achalasia is a primary esophageal motility disorder characterized by the absence of peristalsis in the distal ⅔ of the esophagus and a defective relaxation of the lower esophageal sphincter (LES). This leads to impaired bolus propulsion and stasis of food in the esophagus and thereby to symptoms of dysphagia, regurgitation of undigested food, retrosternal pain and weight loss.\(^1\)

Treatment is aimed at reducing LES pressure and thereby at improving bolus transport. Although initial treatment success rates are as high as 90% after 2 years, success rates decline in time, leading to retreatment in many patients.\(^2,\)\(^3\) Identification of patients in need of retreatment is challenging and often delayed, as symptoms are underreported or absent due to decompensation of the esophagus or impaired esophageal sensitivity. Moreover, patients get used to symptoms or adapt their diet.\(^4,\)\(^7\) However, timely recognition of functional obstruction and subsequent stasis of food in the esophagus is of major importance for at least 2 reasons: First, continuous obstruction and stasis can result in esophageal decompensation and mega-esophagus or sigmoid-like esophagus associated with higher morbidity and refractory symptoms.\(^8,\)\(^10\) Second, esophageal stasis has been suggested to be a risk factor for the development of dysplasia and neoplasia, especially in patients with longstanding disease.\(^11,\)\(^12\) Therefore, objective quantification of esophageal and LES function during the follow up and management of patients with achalasia, especially with longstanding disease, is of imminent importance to prevent these complications.

Manometry has been repeatedly proposed as a useful test to determine whether patients should be retreated. Indeed, several studies have shown that LES pressure ≥ 10 mmHg is a predictor of treatment failure,\(^5,\)\(^13\) suggesting that patients with LES pressure ≥ 10 mmHg should be considered for additional therapy. However, a significant proportion of patients with persistent symptoms has a low or even absent LES pressure, questioning the validity of this parameter. Alternatively, assessment of esophageal emptying has been proposed to better detect the need for additional treatment in naïve patients within one year after initial therapy with pneumatic dilation.\(^6\) To what extent this test performs better than esophageal manometry to predict the need for retreatment during longer follow up, and might be the test of choice to routinely monitor patients with longstanding disease has not been evaluated. Therefore, we compared esophageal manometry and timed barium esophagogram to predict the need for retreatment during a prolonged period of follow up in a cohort of patients with longstanding achalasia.
METHODS

Patients
Patients diagnosed with idiopathic achalasia were eligible for inclusion. Diagnosis was based on the absence of peristalsis and impaired LES relaxation (nadir pressure ≥10 mmHg during swallow-induced relaxation) at esophageal manometry. Forty-one patients with known achalasia participated in the study. Each subject gave written informed consent to participate in the study. The study was approved by the Medical Ethical Committee of the Academic Medical Center (Amsterdam, the Netherlands).

Study design
At inclusion (between 2000-2002), symptoms were evaluated and patients underwent esophageal manometry and timed barium esophagogram. Patients were followed up yearly during an outpatient clinic visit or by telephone by their treating physician. In 2011 new symptom scores were obtained by telephone and patient record files were evaluated for recurrent treatment and complications related to achalasia.

Symptom evaluation
Symptoms were scored using the Eckardt score, which is the sum of the scores for dysphagia, regurgitation and chest pain on a scale from 0 to 3 (0 = absent, 1 = occasional, 2 = daily, 3 = each meal) and weight loss (0 = no weight loss, 1 = < 5 kg, 2 = 5-10 kg, 3 = > 10 kg). The total score ranges from 0 to 12 points. Clinical remission was defined as an Eckardt score of ≤ 3. With an Eckardt score of ≥3 retreatment was proposed.

Esophageal manometry
Esophageal manometry was performed using a 10 lumen assembly that incorporated a sleeve sensor at its distal end to monitor LES pressure (Dentsleeve Int, Mississauga, ON, Canada). Side holes monitored pressure in the stomach (1 cm below the distal margin of the sleeve) and at 2, 5, 8, 11, 14, 17 and 20 cm above the LES. A side hole in the pharynx monitored swallows. The side holes and sleeve were perfused at 0.6 ml/min with degassed distilled water by a pneumohydraulic capillary perfusion pump (Dentsleeve Int, Mississauga, ON, Canada). Pressures were sensed by external transducers connected to a polygraph (Synectics Medical, Sweden). LES pressure was determined as the visual mean over a 1 minute period, at end-expiration and referred to the end-expiration intragastric pressure.

Timed barium esophagogram
Esophageal emptying was assessed with the patient in an upright, slightly left posterior oblique position. The patient ingested a low density barium sulphate suspension. Patients were instructed
to drink the amount of barium they could tolerate without regurgitation or aspiration (100-250 ml). Radiographs were taken at 1, 2 and 5 min after barium intake as described by de Oliveira et al. (14) The distance in centimetres from the distal oesophagus (identified by the bird’s beak appearance of the esophagogastric junction) to the top of a distinct barium column (barium height) was measured. The barium height at five minutes was used to determine completeness of emptying. In the study by Vaezi et al, emptying was considered incomplete when the height of stasis after 5 minutes was over 50% of the pre-treatment height of stasis. As we did not perform pre-treatment measurements in our cohort, emptying was considered incomplete if more than 5 cm of stasis was present after 5 minutes, which is comparable to 30-50% of the pre-treatment level of stasis in earlier studies. The maximum width of the barium column after ingestion was measured as the esophageal width.

**Statistical analysis**

At first visit, patients with an Eckardt score ≤ 3 were regarded as in remission. In 2011, patients were considered in long-term remission if no additional treatment was performed and Eckardt score was still ≤ 3. Continuous variables are presented as mean ± SEM and tested using a Student’s t-test. Categorical data are tested using a Pearson’s chi-square, and correlation determined using Pearson’s correlation test. Log-rank tests on Kaplan-Meier estimates were used to determine if patients with LES pressure ≥10 mmHg and patients with esophageal stasis ≥ 5 cm had a higher risk of becoming a treatment failure. Patients were censored if they deceased. Cox proportional hazard models were used to estimate hazard ratios for treatment failure. All reported p-values were 2 tailed, and a value of 0.05 was regarded as statistically significant.

**RESULTS**

**Patients**

The cohort of patients consisted of 26 (63%) males and 15 (37%) females with a mean age of 54 years at the time of the initial visit (range 32-86 years). All patients were included between February 2000 and December 2002. At that time, all patients had been diagnosed with and treated for achalasia. Ten patients (24%) were diagnosed and treated 5-10 years, 10 patients (24%) between 10-15 years and 21 patients (51 %) > 15 years before the first study visit. The median time after diagnosis was 17 years (range 5-63 years). Thirty-nine patients were initially treated by graded pneumatic dilations and 2 patients by Heller myotomy. In 2011, 34 of the 41 patients (83%) were available for follow up, the 7 remaining patients had died; 2 from a complication of achalasia: one patient died of esophageal squamous cell carcinoma and one of aspiration pneumonia. The flowchart of the study is shown in Figure 1.
LES pressure and esophageal emptying at initial presentation

At the start of the study, 26 (63%) patients were in clinical remission, and 15 patients were treatment failures with Eckardt scores ranging from 4 to 8. Patients in remission and treatment failures had a comparably low mean LES pressure. (Table 1.) Seven patients had an elevated LES pressure (≥10 mmHg), of which 3 patients were in clinical remission and 4 were therapeutic failures. Thus, only 4 of the 15 therapeutic failures at initial presentation had an elevated LES pressure. (Figure 2.) Patients with an elevated LES pressure (n=7) reported similar symptom scores as patients with a LES pressure <10 mmHg (3.9 ± 0.70 vs. 2.9 ± 0.34 respectively (p=0.23)). Furthermore, there was no correlation between LES pressure and symptoms (r=0.05 p=0.76), or between LES pressure and the height of the barium column (r=0.17 p=0.29).

In contrast, patients initially in remission had significantly less stasis of barium 2 and 5 minutes after ingestion compared to treatment failures (Table 1.). Additionally, 13 out of 15 treatment failures had >5cm esophageal stasis after 5 minutes. However, esophageal stasis was also observed in 13 of 26 patients with a symptom score < 4. Symptom scores were comparable for patients with and without stasis (3.4 ± 0.36 vs 2.4 ± 0.53 respectively, p=0.10). There was only a slight correlation with symptom scores and the height of barium after five minutes (r=0.43 p<0.01).
### Table 1 | Patient characteristics at initial presentation

<table>
<thead>
<tr>
<th>Initial presentation</th>
<th>In remission (n=26)</th>
<th>Therapeutic failure (n=15)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (yrs)</strong></td>
<td>53 ± 3.2</td>
<td>55 ± 3.5</td>
<td>0.84</td>
</tr>
<tr>
<td><strong>Time after diagnosis (yrs)</strong></td>
<td>17 ± 2.3</td>
<td>18 ± 2.2</td>
<td>0.78</td>
</tr>
<tr>
<td>- 0-10 yrs</td>
<td>8</td>
<td>2</td>
<td>0.45</td>
</tr>
<tr>
<td>- 10-15 yrs</td>
<td>6</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>- &gt; 15 yrs</td>
<td>12</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td><strong>Eckardt score</strong></td>
<td>1.9 ± 0.2</td>
<td>5.1 ± 0.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Esophageal manometry:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- LES pressure (mmHg)</td>
<td>6.2 ± 1.4</td>
<td>8.6 ± 1.8</td>
<td>0.29</td>
</tr>
<tr>
<td><strong>Timed Barium Esophagram:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Barium height at 1 min (cm)</td>
<td>11 ± 0.9</td>
<td>14 ± 1.9</td>
<td>0.11</td>
</tr>
<tr>
<td>- Barium height at 2 min (cm)</td>
<td>8.8 ± 0.9</td>
<td>13 ± 1.9</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>- Barium height at 5 min (cm)</td>
<td>5.5 ± 1.0</td>
<td>11 ± 2.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>- Max. barium width (cm)</td>
<td>3.7 ± 0.3</td>
<td>4.7 ± 0.6</td>
<td>0.09</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Initial presentation, divided for the need for retreatment during follow up</th>
<th>In long term remission (n=16)</th>
<th>Recurrence (n=10)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eckardt score</strong></td>
<td>1.9 ± 0.2</td>
<td>1.9 ± 0.4</td>
<td>0.96</td>
</tr>
<tr>
<td><strong>Esophageal manometry:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- LES pressure (mmHg)</td>
<td>6.7 ± 2.1</td>
<td>5.4 ± 1.3</td>
<td>0.29</td>
</tr>
<tr>
<td><strong>Timed Barium Esophagram:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Barium height at 1 min (cm)</td>
<td>9.9 ± 1.3</td>
<td>14 ± 0.9</td>
<td>0.05</td>
</tr>
<tr>
<td>- Barium height at 2 min (cm)</td>
<td>6.6 ± 1.1</td>
<td>12 ± 0.7</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>- Barium height at 5 min (cm)</td>
<td>3.4 ± 1.1</td>
<td>8.9 ± 1.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>- Max. barium width (cm)</td>
<td>3.6 ± 0.3</td>
<td>4.0 ± 0.4</td>
<td>0.44</td>
</tr>
</tbody>
</table>

Recurrence rate during follow up

Of the 26 patients in remission, 16 patients (61%) remained in clinical remission until the end of the study. (Figure 1.) Retreatment was performed in the other 20 patients; 10 patients were initially in remission and 10 were initial treatment failures. Five initial treatment failures (33%) were not additionally treated: 2 patients refused additional treatment, and 3 patients died shortly after study participation. These patients were regarded as treatment failure. Of the 20 patients requiring retreatment, 17 patients received PD, 2 patients underwent LHM and in 1 patient an esophagectomy was performed because of refractory symptoms. During the follow up period, 30 pneumatic dilations were performed in the 17 patients after a median of 3.0 years (range 2-8), 5 with a balloon size of 30 mm, 24 with a size of 35 mm and 1 with a size of 40 mm. Twenty-one
of 34 (62%) patients had sufficient symptom control (=Eckardt score ≤3) in 2011, regardless of additional treatment or initial treatment failure, but only 16 of 41 patients (39%) were in long-term remission. (Figure 1.)

**Esophageal stasis and recurrence rate**

At the initial visit, 15 patients had normal esophageal emptying (<5 cm) whereas 26 patients presented with stasis. Importantly, 12 of 15 patients (80%) without stasis (<5 cm) at initial presentation remained in remission, even up to 10 years after the timed barium esophagogram, compared to only 5 of 26 patients (19%) with esophageal stasis (p<0.01, log-rank). (Figure 3.) Of the 26 patients with initial esophageal stasis, 14 patients were initially in remission (symptom score ≤3). However, 9 of these patients (64%) had recurrent symptoms requiring additional treatment, after a median of 4 years (range 1-8 years). In contrast, 11 of 12 patients who were initially in remission and had no esophageal stasis did not need additional treatment. This was significantly higher than in patients with esophageal stasis (p=0.01, log-rank). (Figure 3.)

**Lower esophageal sphincter pressure and recurrence rate**

Additionally, we evaluated LES pressure as a marker to predict recurrence during follow up. Seven patients had an elevated LES pressure (≥10 mmHg), whereas 34 patients had a LES pressure <10 mmHg. Five of 7 (71%) patients with an elevated LES pressure needed additional treatment, which is comparable to 20 of 34 (59%) patients with LES pressure <10 mmHg (p=0.40, log-rank). (Figure 3.) Of the 7 patients with an elevated LES pressure, 3 patients were initially in remission. During follow up, 1 of these patients needed retreatment (33%), which was comparable to 9 of the 23 (39%) patients with LES pressure <10 mmHg (p=0.72 log-rank). (Figure 3.)

**Predictive values of esophageal stasis and LES pressure**

Subsequently, we determined sensitivity, specificity and predictive values of esophageal stasis and LES pressure to detect patients requiring retreatment. The sensitivity and specificity of esophageal stasis ≥ 5 cm to predict treatment failure, either immediately or during follow up, were 88% and 75%. Positive and negative predictive values are 85% and 80% respectively. These findings indicate that esophageal stasis ≥5 cm is a good predictor of the need for retreatment, with a fair specificity. LES pressure ≥ 10 mm Hg has a sensitivity and specificity of 20% and 88% respectively to predict the need for retreatment, whereas positive and negative predictive values are 71% and 41%. Thus, if elevated, LES pressure is a fairly specific predictor for treatment failure, however it identifies less than half of the patients that will require retreatment during follow up. Finally, using a proportional hazard Cox regression model, esophageal stasis ≥ 5 cm was identified as a risk factor for recurrent disease in patients in remission with a hazard ratio of 8.0 (95%CI 1.5-20). In contrast, initial symptom scores and a LES pressure of ≥10 mmHg were no risk factors for the need of retreatment. (Table 2)
Esophageal stasis predicts recurrent symptoms | Chapter 11

Figure 2 | Individual height of stasis on a timed barium esophagogram and lower esophageal sphincter pressures for initial treatment failures (n=15), patients with recurrent disease (n=10), and patients in long-term remission (n=16). Patients in long-term remission have significantly less stasis compared to initial treatment failures and to patients with recurrence. The LESP is comparable in all groups. (*=P<0.01 Student’s t-test)

Figure 3 | Kaplan-Meier curves for LES pressure and esophageal stasis are shown. Figure 3A and 3B demonstrate the need for retreatment divided for LES pressure (A) and stasis (B) in all patients, thus irrespective of symptoms at the time of assessment. Patients with esophageal stasis (≥5cm) significantly more often need retreatment (p<0.01, log-rank), whereas patients with a high LES pressure (≥10 mmHg) do not (p=0.40, log-rank). Figure 3C and 3D show comparable curves for the subgroups of patients who where initially in remission (Eckardt ≤3). Patients with a low LES pressure (3C) have a comparable long-term outcome compared to patients with an elevated LES pressure (p=0.72, log-rank). Patients with esophageal stasis of less than 5 cm (3D) are significantly more often in long term remission (p=0.01, log-rank).
### DISCUSSION

This study shows that stasis on a timed barium esophagogram but not basal LES pressure is an important predictor of recurrent symptoms and the need for retreatment in patients with longstanding achalasia. Therefore, when significant stasis on a timed barium esophagogram is observed, even in the presence of a LES pressure < 10 mmHg, additional therapy may be warranted.

Currently, the most commonly used treatment modalities for achalasia are laparoscopic Heller myotomy (LHM) and PD. Both treatments have high short-term success rates of 80-100%, gradually decreasing in patients with longstanding disease (≥10 yr) to 40-60%. The cohort presented in the current study is unique with a mean follow up of 26 years after diagnosis. Of the 41 patients, 62% had adequate symptom control (= Eckardt score ≤3). However, to reach this rate of symptom control, 49% of patients needed retreatment during the 10 year follow up period. Most long follow up studies demonstrate similar retreatment rates, of up to 87% of patients after a follow up of 12 years after initial PD. Notably, not only after PD but also after LHM symptom control decreases to around 60% with a longer follow up period, as recently demonstrated by several studies. Early recognition of incomplete therapeutic response or the need for retreatment is of crucial importance to reduce morbidity and long-term complications such as esophageal decompensation. Furthermore, inadequately treated patients have a higher risk to develop dysplasia and eventually esophageal squamous carcinoma. Importantly, additional treatment both after initial PD or LHM has satisfactory results with success rates of 60-80% and improvement of esophageal emptying. Therefore regular follow up visits to determine the need for retreatment are indicated.

To determine if retreatment is indeed indicated, symptoms are currently most commonly used in clinical practice. Symptom scores including the Eckardt score use typical symptoms such as dysphagia, regurgitation and chest pain. However, since symptoms are not always reported or even

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**Table 2 | Adjusted hazard ratios for recurrence are given for patients with longstanding achalasia who where initially in remission.**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Adjusted hazard ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial symptom score</td>
<td>0.81 (0.3 - 2.1)</td>
<td>0.42</td>
</tr>
<tr>
<td>Barium height</td>
<td>8.0 (1.5 – 21)</td>
<td>0.01</td>
</tr>
<tr>
<td>≥5 cm vs &lt;5 cm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LES pressure</td>
<td>1.7 (0.4 – 7.3)</td>
<td>0.40</td>
</tr>
<tr>
<td>&lt;10 mmHg vs ≥10 mmHg</td>
<td></td>
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</tr>
</tbody>
</table>
absent due to decompensation of the esophagus or impaired esophageal sensitivity, identification of patients in need of retreatment may be difficult and is often delayed. In our study, 13 of 26 (50%) patients initially in “remission” had over 5 cm of stasis on their timed barium esophagogram, of which 9 eventually needed retreatment due to recurrent symptoms. Additionally, symptoms only weakly correlate with esophageal stasis (correlation coefficient is 0.43), and do not correlate with LES pressure. This underlines that symptoms and objective parameters of esophageal function often do not match, as repeatedly demonstrated before, emphasizing that symptoms are not reliable to determine therapeutic strategy in patients with achalasia.6,21,22

An alternative for symptoms as predictor for retreatment may be basal LES pressure.13,23 Several studies indeed demonstrated that patients with a basal pressure above 10 mmHg are at risk to develop recurrent symptoms.4,5 Hence, the decision to repeat PD is often based on the presence of an increased basal LES pressure (>10 mm Hg). Also in our study, the specificity of this criterion to predict the need for retreatment was acceptable, i.e. 71%. Based on these findings, graded pneumatic dilation is often repeated aiming at reducing basal LES pressure to less than 10mmHg. However, we here show that a low LES pressure is not necessarily indicative of clinical success. In most of our patients (83%), basal LES pressure was <10 mmHg, even in case of high symptom scores or persistent stasis. Of these, 59% required retreatment during follow up. Hence, in our series, basal LES pressure > 10 mmHg only identifies 20% of patients that will require retreatment, resulting in sensitivity of 20% to detect treatment failures. Other studies with large numbers of patients also failed to identify LES pressure a predictor of therapeutic failure, both after LHM or PD.2,8,24 One possible explanation could be that esophageal emptying and clearance (and most likely symptoms) depend on other factors than LES pressure. Indeed, 19 of 26 patients with a low LES pressure had esophageal stasis while we found no correlation between LES pressure and the height of stasis. The ability of the esophagogastric junction to open, largely determined by its distensibility, may be a more important determinant of flow across this region.25-27 Indeed, we recently demonstrated that impaired distensibility of the esophagogastric junction rather than low LES pressure was associated with poor esophageal emptying and treatment failure.27

Based on these findings, assessment of esophageal emptying could be a more integrated and clinically more useful parameter. Indeed, our data of the current study demonstrate that patients with stasis of ≥ 5cm have an 8-fold increased risk for retreatment compared to patients with < 5cm stasis, irrespective of initial symptoms or LES pressure. Our data support a study of Vaezi et al, in which 90% of patients with persistent stasis but without symptoms failed therapy within one year after initial treatment.4 Of our patients with persistent stasis but without symptoms, 69% needed retreatment during the follow up period, although only 10% within the first year. In contrast, in patients without esophageal stasis failure rates are only 20% after an additional follow up of 10
years. This confirms the study of Vaezi et al. reporting a failure rate in patients without stasis of 23% after 6 years of follow up. The current study shows that esophageal stasis on a timed barium swallow has a sensitivity of 88% and a specificity of 75% to detect patients in need for retreatment. In addition, the timed barium is a simple and widely available test with very limited radiation exposure (0.08 mSv). Therefore, assessment of esophageal stasis is a safe and easy to perform test that is not only helpful directly after treatment as demonstrated by multiple studies, but also during long-term follow up, up to at least 26 years as demonstrated by this study.

In conclusion, stasis on a timed barium esophagogram is an important functional predictor of treatment failure in patients with longstanding achalasia, in contrast to LES pressure. Although several studies have advised to perform regular follow up, current guidelines do not advice on functional testing in the follow up of achalasia. Based on our data, however, we argue that regular follow up visits may be indicated, not only to inform about symptoms, but also to perform a timed barium esophagogram in order to assess esophageal emptying. Clearly, prospective trials are required to confirm the benefit of (serial) functional testing and early additional treatment for the prevention of sigmoid-like esophagus and the development of dysplasia.
REFERENCE LIST


