Diseases of the Esophagus (2009) **22**, 264–273
DOI: 10.1111/j.1442-2050.2008.00914.x

DISEASES OF THE ESOPHAGUS

Original article

Evaluation of the response to treatment in patients with idiopathic achalasia by the timed barium esophagogram: results from a randomized clinical trial

M. Andersson,[1] L. Lundell,[2] S. Kostic,[3] M. Ruth,[4] H. Lönroth,[5] A. Kjellin,[2] M. Hellström[1]

[1]*Department of Radiology, Sahlgrenska University Hospital, Göteborg,* [2]*Department of Surgery, Karolinska University Hospital, Huddinge, Stockholm,* [3]*Department of General Surgery, Borås Central Hospital, and Departments of* [4]*Otorhinolaryngology and* [5]*Surgery, Sahlgrenska University Hospital, Göteborg, Sweden*

SUMMARY. **To choose which treatment would be most effective for the individual patient with newly diagnosed achalasia is difficult for the tending physician. A diagnostic tool that would allow prediction of the symptomatic and functional response after treatment for achalasia is therefore needed. The timed barium esophagogram (TBE) is a method that allows objective assessment of esophageal emptying, but the value of TBE in the clinical management of achalasia remains to be clarified. The aim of this study was first, to assess the ability of TBE to predict symptoms and treatment failure during post-treatment follow-up. Second, to determine whether esophageal emptying as assessed by TBE differs after treatment with pneumatic dilatation or laparoscopic myotomy. Fifty-one patients with newly diagnosed achalasia were prospectively randomized to pneumatic dilatation ($n = 26$) or laparoscopic myotomy ($n = 25$). Evaluation with TBE was performed before ($n = 46$) and after treatment ($n = 43$). The median interval between treatment and post-treatment TBE was 6 months, and the median follow-up time after the post-treatment TBE was 18 months. Following therapeutic intervention, TBE parameters did not differ significantly between treatment groups. However, significant correlations were found between the height of the barium column at 1 min and the symptom scores at the end of follow up for 'dysphagia for liquids' ($P < 0.05$, rho = 0.47), 'chest pain' ($P < 0.05$, rho = 0.42), and the 'Watson dysphagia score' ($P < 0.05$, rho = 0.46). Patients with less than 50% improvement in this TBE-parameter (height at 1 min) post-treatment had a 40% risk of treatment failure during follow-up. In summary, pneumatic balloon dilatation and laparoscopic myotomy similarly affected esophageal function as assessed by TBE-emptying. Lack of improvement in barium-column height post-treatment was associated with an increased risk of treatment failure which should motivate close surveillance in order to detect symptomatic recurrence at an early stage.**

KEY WORDS: **achalasia, balloon dilatation, barium esophagogram, dysphagia, laparoscopic surgery.**

INTRODUCTION

Achalasia is a chronic esophageal motility disorder; the etiology of which is unknown.[1] Degenerative loss of inhibitory ganglionic neurons results in absence of peristalsis in the esophageal body and failure of the lower esophageal sphincter (LES) to relax on swallowing.[2] The primary goal of therapy in achalasia is palliation of symptoms (primarily dysphagia) by reducing the functional obstruction at the level of the LES. The most effective treatments for achalasia are pneumatic dilatation and surgical myotomy. However, controversy remains regarding the optimal therapeutic strategy in patients with newly diagnosed idiopathic achalasia.[3] Randomized comparative studies are scarce, and most reports on the outcomes of treatment describe the effectiveness of only one treatment method. In recent years, laparoscopic surgical myotomy has replaced the open procedure as it leads to comparable results in terms of efficacy while decreasing postoperative morbidity and recovery time.[4] We recently reported

Address correspondence to: Dr Mats Andersson, MD, Department of Radiology, Sahlgrenska University Hospital, SE-41345, Göteborg, Sweden. Email: mats.n.andersson@vgregion.se

M. Andersson and L. Lundell have contributed equally to the conception and the design of the study. S. Kostic, H. Lönroth, and A. Kjellin have contributed with acquisition of data. M. Ruth and M. Hellström have contributed with analysis and interpretation of data. All authors have drafted the article and approved the final version to be published. M. Andersson is responsible for the integrity of the work as a whole.

the short-term results of the first randomized controlled clinical trial comparing pneumatic dilatation with laparoscopic myotomy in newly diagnosed achalasia, suggesting a superiority of the latter therapeutic approach.[5]

A divergence between symptomatic response and objective improvement after treatment has been reported by several investigators.[2,6,7] Studies that have used objective methods, such as manometry, scintigraphy, or radiology, have documented the limitations of using symptomatic improvement as the only endpoint in assessing treatment response.[8–10] The timed barium esophagogram (TBE) has been launched as a standardized technique for evaluating esophageal-emptying in patients with achalasia. TBE includes the ingestion of 250 mL of barium contrast material with radiographs taken after 1 min, 2 min, and 5 min.[11] Vaezi *et al.* found that patients with poor emptying on TBE had a high frequency of recurrent symptoms and repeat treatments within 1 year even if they reported complete symptom relief after pneumatic dilatation.[12]

The aim of our study was therefore to validate the clinical utility of TBE within the framework of a randomized study, comparing laparoscopic myotomy with partial posterior fundoplication and pneumatic dilatation, in patients with newly diagnosed achalasia. The primary objective is to elucidate whether TBE parameters predicted the subsequent symptomatic response to respective therapy, including therapeutic failure.

MATERIAL AND METHODS

Patients

The diagnosis of achalasia was based on (i) a typical history without endoscopic evidence of other specific causes, combined with (ii) manometric findings of aperistalsis in the esophageal body and incomplete swallow-induced relaxation of the LES. None of the patients had been treated with pneumatic dilatation or other specific therapeutic interventions. The enrolment criteria and patient characteristics have previously been described in detail.[5]

Randomization and treatment

A computer-based randomization software was used to assign patients to the treatment groups. Stratification for age, gender, and previous medical treatment was performed.Twenty-six patients were allocated to pneumatic dilatation, and 25 patients to laparoscopic myotomy. The methodology of the treatments performed has been reported in detail previously.[5] Pneumatic dilatation was performed as an outpatient procedure using intravenous sedation or a short intubational anesthesia ($n = 5$). A predefined, graded dilatation protocol was followed, starting with a 30 mm balloon in women and a 35 mm balloon in men (Rigiflex ABD, Boston Scientific, Boston, MA, USA). The clinical response was evaluated after 7–10 days, and in patients with persistent symptoms ($n = 8$), the procedure was repeated with a 35 mm balloon in women and a 40 mm balloon in men. In patients allocated to surgical myotomy, a laparoscopic complete anterior cardiomyotomy was carried out. The myotomy extended well above what was considered to be the upper margin of the LES, and distally, the sling fibers of the gastric portion of the sphincter were divided. To prevent postoperative reflux, a partial posterior fundoplication according to Toupet was added.

TBE

The TBE examinations were performed and interpreted with the examiner blinded to the specific individual clinical findings and allocated treatment groups.[13] The patients were given 250 mL of low-density barium sulfate suspension (45% weight in volume) and instructed to drink the amount of barium they could tolerate without regurgitation or aspiration. Three anteroposterior radiographs of the esophagus were exposed at 1 min, 2 min, and 5 min, respectively, after the start of barium ingestion. Subsequent radiological assessments included measurements of the barium column, both the height (the distance from the distal esophagus to the top of the barium column), and the maximum and mean width of the esophagus. Esophageal emptying was assessed by the height of the barium column at the 1-minute and 5-minute time-points, respectively.[10] The estimated volume of the barium column was also included as a measure of esophageal emptying as it has been shown that this variable correlates with the manometric tone of the LES in patients with idiopathic achalasia.[14] The volume of barium in the esophagus was calculated according to the formula: $(\text{mean radius})^2 \times 3.14 \times \text{height}$ (after correction for magnification by dividing the measurements with a factor of 1.35).

The percentage change of the barium-column height and the retained volume of barium between the pre- and post-treatment TBE examinations was also calculated and utilized as an independent variable in the statistical analysis.

Follow-up

The primary end-point of the comparative trial was the cumulative number of treatment failures during follow-up. The exact definition of a treatment failure has been described previously.[5] In short, persistent or recurring dysphagia symptoms requiring additional treatment or the occurrence of a serious

complication or side-effect constituted a treatment failure. Esophageal emptying was, according to the present protocol, scheduled to be assessed by TBE at 6 months post-treatment. Symptomatic follow-up was scheduled at 1, 3, 6, 12, 24, and 36 months after treatment. At each time-point, a self-assessment questionnaire was mailed to the patients which evaluated symptoms by a previously described scoring system.[15] Symptoms assessed were dysphagia for solids, dysphagia for liquids, heartburn, chest pain, and acid regurgitation. The frequency of each symptom was graded on a scale from 0 to 5 (0 = none, 1 = once per month or less; 2 = once a week, up to three to four times a month; 3 = two to four times a week; 4 = once a day; 5 = several times a day). In addition, the more specific Watson dysphagia score was applied. This score combines information about difficulty in swallowing nine types of liquids and solids (0 = no dysphagia, 45 = severe dysphagia).[16] The symptom scores reported at the last follow-up contact were compared with the results of the post-treatment TBE examination.

Manometry was scheduled at the 12-month time-point. Manometry was carried out according to a predefined standardized protocol using routine technologies which have been described in detail previously.[14] Briefly, the catheter assembly incorporated a 6 cm long sleeve sensor attached to the distal end, straddling the LES. The resting LES pressure was recorded at end expiration and referenced to the intragastric pressure. Swallowing-induced LES relaxation was assessed by the nadir pressure, defined as the minimum pressure level reached following 5 mL water swallows.

Statistics and ethics

Continuous variables were presented as the median and interquartile ranges. Spearman's correlation coefficient (rho) was used to measure bivariate correlations between TBE variables (height and volume of the barium column, and percentage change of these values postoperatively) and symptom scores. Pearson's correlation analysis was used to estimate the relationship between the same TBE variables and manometric findings, and to compare the patients' age and TBE characteristics pre-treatment with the degree of improvement in TBE-emptying post-treatment. Intergroup comparison between patients allocated to surgery or dilatation, respectively, was performed by the use of the non-parametric Mann–Whitney test. Wilcoxon signed rank test was used to compare variables pre-therapy with the same variables obtained post-therapy. Data analysis was performed using SPSS software version 15.0 (SPSS Inc., Chicago, IL, USA). *P*-values ≤ 0.05 were considered statistically significant.

The respective local ethics committee had approved the study protocol, and each patient gave informed consent before enrolment into the study.

RESULTS

All in all, seven treatment failures were recorded within the first year after randomization, six in the group treated with dilatation (23%), and one in the group treated with surgery (4%). The difference in the number of treatment failures between the respective treatment strategies was statistically significant ($P = 0.04$). Of the 51 patients that were included in the randomized trial, 46 patients agreed to undergo a TBE examination before treatment, and 43 agreed to post-treatment TBE (four patients in each treatment group declined post-treatment TBE). Thirty-five of the patients were examined at the Department of Radiology, Sahlgrenska University Hospital, Göteborg, and 11 were examined at the Department of Radiology, Karolinska University Hospital, Huddinge, Sweden. Two post-treatment TBE examinations had to be excluded for technical reasons as the technique used deviated from the prescribed protocol (Fig. 1). In two patients (one in each treatment group), treatment failed early, and they crossed over to the alternate treatment before the post-treatment TBE. Complete pre- and post-treatment TBE data were available in 35 of the 51 patients (69%) originally randomized in the treatment study, and these data were subsequently used for comparison of esophageal emptying by TBE after respective treatment. The demographic, manometric, and TBE characteristics of the patients are detailed in Table 1. These characteristics were well balanced in the two study groups. However, the delay from the pre-operative TBE examination to surgery was significantly longer (median = 75 days) than the delay from the pre-treatment TBE to dilatation (median = 12 days).

Pooling the results from both treatment groups, we found a significant improvement in all TBE parameters in response to treatment (Fig. 2). The median height of the barium column at 1 min decreased from 16.5 cm to 7.0 cm ($P < 0.001$), and the volume of retained barium at 1 min decreased from median 81.0 mL to 16.0 mL ($P < 0.001$). There was, however, no significant intergroup difference between the post-treatment TBE parameters (Table 2). Additionally, the improvement in TBE-emptying in the respective treatment groups was not affected by the patients' gender or age. However, in patients treated with pneumatic dilatation, those with a wider esophagus at baseline showed inferior improvement in the height of the barium column in response to therapy ($P < 0.05$, Pearson's $r = -0.53$ at 1 min) (Fig. 3). No such correlation between a wider esophagus and an

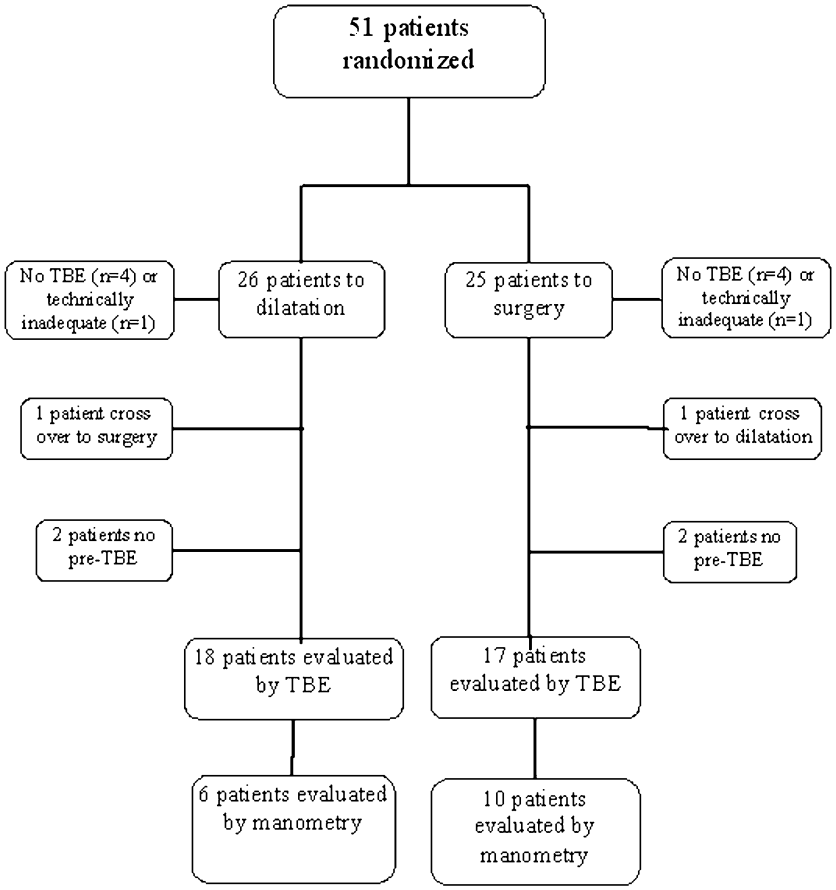

Fig. 1 Study flow diagram of patients with newly diagnosed achalasia randomized to the respective treatment groups and number of patients subsequently evaluated by timed barium esophagogram (TBE) and manometry.

inferior improvement in emptying could be found among patients treated with surgery.

Concerning post-therapy TBE variables and symptom outcomes during postoperative follow-up, complete datasets were obtained from 32 patients, with a median time interval between treatment and the TBE of 6 months (interquartile range 3–16 months) and a median follow-up time after the TBE of 18 months (interquartile range 9–27 months). Five of the 41 technically adequate TBE examinations had to be excluded because of a considerable delay between treatment and the radiological investigation (range 26–48 months). In four patients, complete clinical data were not captured.

We found significant correlations between the height of the barium column at 1 min after barium ingestion and the symptom scores for 'dysphagia for liquids' ($P < 0.05$, rho = 0.47), 'chest pain' ($P < 0.05$, rho = 0.42), and 'Watson score' ($P < 0.05$, rho = 0.46) (Table 3). Moreover, the estimated emptied volume of barium from 1 min to 5 min related to the scores for 'dysphagia for solids' ($P < 0.05$, rho = 0.39),

Table 1 Demographic, manometric, and TBE characteristics (median and interquartile range) of patients with newly diagnosed achalasia subsequently randomized to dilatation or surgery. The difference in the variables between treatment groups was analyzed using the Mann–Whitney test for unpaired, non-parametric data

	Dilatation ($n = 18$)	Surgery ($n = 17$)	P value
Age (years)	40.5 (28.0–60.0)	44.0 (31.5–55.5)	0.86
Gender (M/F)	8/10	11/6	
Resting LES pressure (mm Hg)	21.2 (12.3–36.3) ($n = 16$)	18.6 (12.0–27.1) ($n = 14$)	0.45
Nadir pressure LES (mm Hg)	9.8 (5.1–25.0) ($n = 11$)	6.4 (4.4–7.8) ($n = 11$)	0.06
Time from preoperative TBE to treatment (days)	12.0 (5.0–27.5)	75.0 (25.0–116.0)	0.003
Height of barium column at 1 min pre-treatment TBE (cm)	16.1 (13.5–22.1)	17.4 (11.2–20.7)	0.99
Maximum width of barium column at 1 min pre-treatment TBE (cm)	4.3 (4.0–5.1)	4.7 (3.6–5.9)	0.53
Emptying at 1 min pre-treatment TBE (mL)	139.0 (57.8–172.8)	139.0 (30.5–174.0)	0.93
Time from treatment to post-treatment TBE (months)	6.5 (3.0–17.0)	6.0 (3.0–25.5)	0.77

M, males; F, females; LES, lower esophageal sphincter; TBE, timed barium esophagogram.

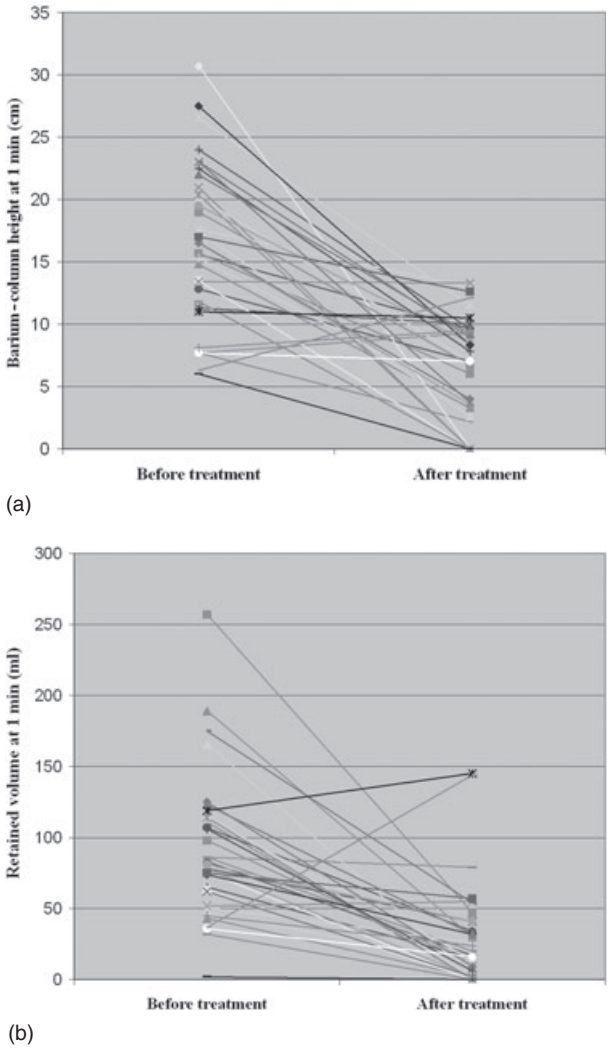

Fig. 2 Change in barium-column height (a) and retained volume of barium (b) at 1 min from pre- to postoperative timed barium esophagogram examinations (patients treated with surgery and dilatation pooled). The median height of the barium column at 1 min decreased from 16.5 cm to 7.0 cm, and the volume of retained barium at 1 min decreased from median of 81.0 mL to 16.0 mL. The difference between the values obtained before and after treatment was statistically significant ($P < 0.001$).

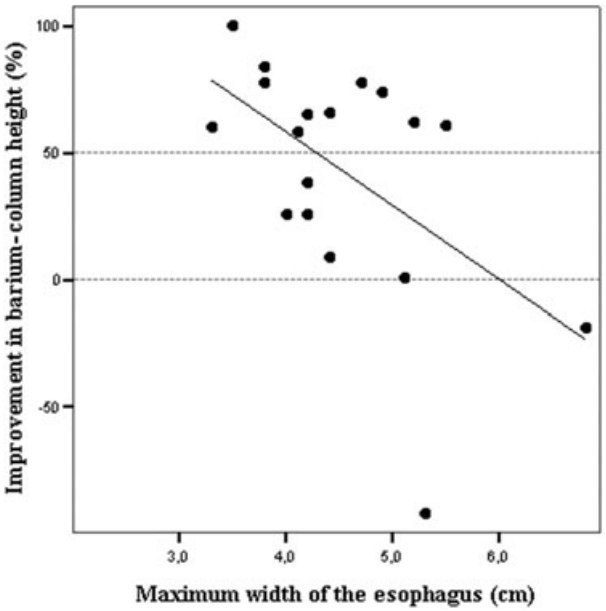

Fig. 3 Scatterplot showing inverse relationship between the maximum width of the esophageal body measured at baseline and the degree of improvement in the height of the barium column at 1 min at timed barium esophagogram performed median 6 months after pneumatic dilatation ($n = 18$). The regression line is shown. The correlation was statistically significant ($P < 0.05$, Pearson's $r = -0.53$).

'dysphagia for liquids' ($P < 0.05$, rho = 0.40), 'chest pain' ($P < 0.05$, rho = 0.41), and 'Watson score' ($P < 0.05$, rho = 0.40).

In four of the seven patients with treatment failures, the failure occurred early post-treatment and additional treatment was performed without prior examination with TBE. Thus, post-treatment TBE data were available in three of the patients with treatment failures within the first year. An additional patient failed treatment 32 months after the primary dilatation and subsequently had a laparoscopic myotomy (Fig. 4). All four of these patients displayed poor improvement of esophageal emptying as recorded at the post-treatment TBE (mean increase of 14% in barium-column height at 1 min, range 26% decrease to 92% increase) (Fig. 5). We could estimate

Table 2 Post-treatment timed barium esophagogram characteristics (median and interquartile range) of patients with newly diagnosed achalasia treated with dilatation and surgery, respectively. The difference in the variables between the treatment groups was analyzed using the Mann–Whitney test for unpaired, non-parametric data

	Dilatation ($n = 18$)	Surgery ($n = 17$)	P value
Height of barium column 1 min (cm)	8.4 (3.9–10.2)	6.7 (0.0–9.0)	0.08
Improvement in height pre-, post-treatment (%)	60.5 (21.8–75.0)	70.0 (50.5–100.0)	0.14
Maximum width of barium column at 1 min (cm)	2.6 (2.2–3.9)	2.8 (2.1–4.2)	0.70
Improvement in maximum width pre-, post-treatment (%)	62.5 (50.5–77.5)	60.0 (52.5–100.0)	0.82
Volume of barium column 1 min (mL)	14.5 (2.0–54.3)	24.0 (0.0–37.5)	0.77
Improvement in retained volume of barium at 1 min pre-, post-treatment (%)	78.5 (48.5–95.5)	77.0 (48.0–100.0)	0.68
Height of barium column 5 min (cm)	2.3 (0.0–8.2)	2.6 (0.0–8.6)	0.80
Improvement in height at 5 min pre-, post-treatment (%)	66.5 (29.4–100.0)	72.0 (48.0–100.0)	1.00
Volume of barium column 5 min (mL)	1.5 (0.0–28.8)	12.0 (0.0–27.0)	0.60
Improvement in retained volume of barium at 5 min pre-, post-treatment (%)	94.5 (28.3–100.0)	46.0 (–9.0–100.0)	0.40

Table 3 Results of two-tailed Spearman correlation analysis between post-treatment TBE variables and symptom scores at the end of follow up (median 18 months from the TBE examination)

	Dysphagia for solids	Dysphagia for liquids	Heartburn	Chest pain	Acid regurgitations	Watson score
Height of barium column at 1 min (cm)	N.S. rho = 0.36	$P < 0.05$ rho = 0.47	N.S. rho = –0.04	$P < 0.05$ rho = 0.42	N.S. rho = 0.08	$P < 0.05$ rho = 0.46
Volume of barium column at 1 min (mL)	N.S. rho = 0.36	N.S. rho = 0.31	N.S. rho = –0.08	N.S. rho = 0.13	N.S. rho = 0.00	N.S. rho = 0.26
Height of barium column at 5 min (cm)	N.S. rho = 0.30	N.S. rho = 0.17	N.S. rho = –0.14	N.S. rho = 0.07	N.S. rho = –0.18	N.S. rho = 0.15
Volume of barium column at 5 min (mL)	N.S. rho = 0.33	N.S. rho = 0.22	N.S. rho = –0.08	N.S. rho = 0.00	N.S. rho = –0.07	N.S. rho = 0.09
Emptied volume of barium from 1 to 5 min (mL)	$P < 0.05$ rho = 0.39	$P < 0.05$ rho = 0.40	N.S. rho = 0.03	$P < 0.05$ rho = 0.41	N.S. rho = 0.13	$P < 0.05$ rho = 0.40

N.S., non-significant; TBE, timed barium esophagogram.

that if less than 50% improvement in the barium-column height was recorded at 1 min, then this was associated with a positive predictive value of 40% in the prediction of treatment failure during follow-up (mean = 29 months). In addition, if more than 50% improvement in this parameter was noted, then such an observation exerted a negative predictive value of 100% for treatment failure (Fig. 6).

The Watson dysphagia score in patients examined with TBE decreased from median of 28.5 (22.1–42.0) pre-treatment to median of 18 (4.3–30.0) post-treatment with no significant difference between the treatment groups. The median Watson score did not differ significantly between patients with complete emptying ($n = 13$) and patients with signs of barium retention at 5 min ($n = 16$) (Watson score 10.5 *vs.* 21.8). One of the patients with complete emptying showed treatment failure during follow-up.

Only 17 patients agreed to undergo manometry during follow-up. Thus, it was not meaningful to statistically compare the results of manometry between the treatment groups. In patients treated with surgery and examined with TBE ($n = 10$), the median resting LES pressure was 5.2 (2.5–13.4) mm Hg post-treatment, and the median relaxing LES nadir pressure was 1.5 (0.7–4.1) mm Hg. In patients treated with pneumatic dilatation and also examined with TBE ($n = 6$), the corresponding values were 3.7 (2.0–6.5) mm Hg and 2.9 (0.6–5.5) mm Hg, respectively. In all patients treated, the resting LES pressure decreased from median 20.8 (14.4–27.0) mm Hg pre-treatment to median 5.0 (2.4–7.5) mm Hg post-treatment ($P < 0.01$). The median LES nadir pressure decreased from 6.4 (4.8–10.5) mm Hg to 1.9 (0.7–4.1) mm Hg ($P < 0.05$). No significant correlations were found between the post-treatment manometric recordings and TBE parameters.

DISCUSSION

The principal aim of all current therapies in achalasia is to relieve the functional obstruction in the distal esophagus while minimizing side-effects, such as post-therapy gastroesophageal reflux. The evaluation of treatment success has been based usually on symptom improvement, but comparisons across studies are complicated by the lack of standardized criteria for treatment success. TBE is a method that allows objective assessment of esophageal emptying after treatment.[10,11] We used TBE in a randomized, prospective treatment study comparing laparoscopic myotomy combined with a partial posterior fundoplication and pneumatic dilatation, thus avoiding selection bias in the treatment groups. By using TBE in this setting, we were unable to document obvious differences in esophageal emptying between the two treatments. In a retrospective study of previously

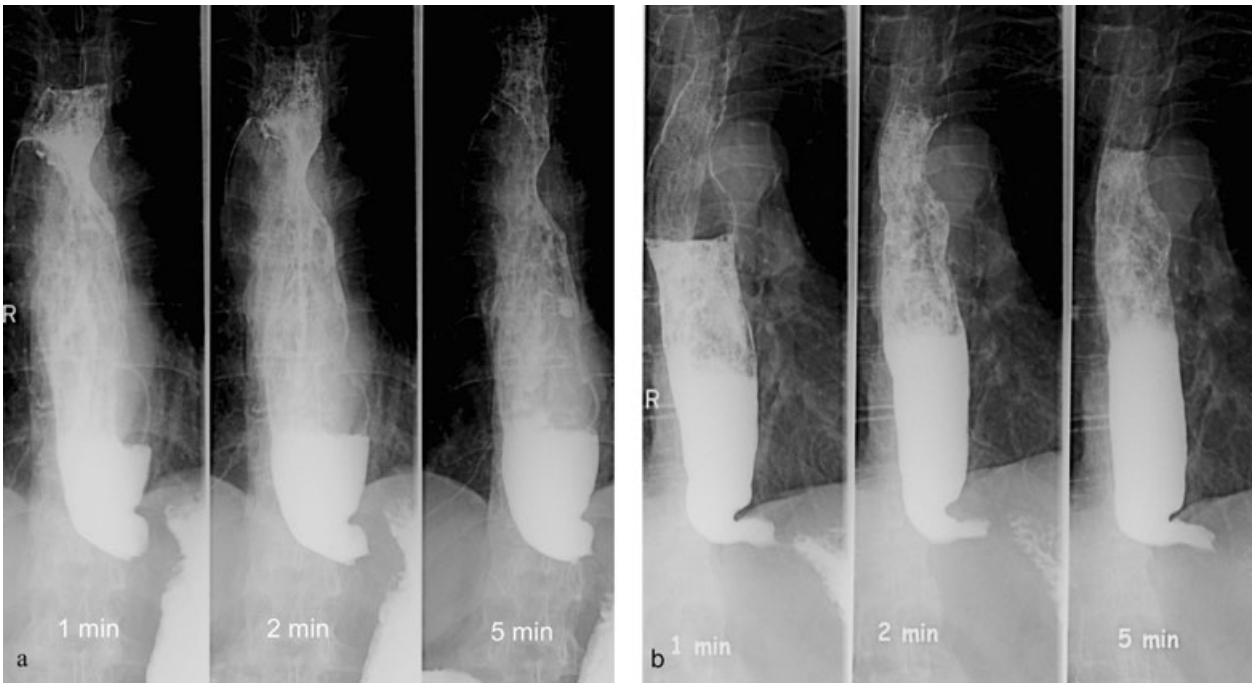

Fig. 4 Pre- and post-therapy timed barium esophagogram (TBE) examinations in a 63-year-old male patient with idiopathic achalasia. The post-therapy TBE (b) performed 7 months after pneumatic dilatation shows deterioration of esophageal emptying compared with the situation on the pre-therapy examination (a). The barium column at 1 min showed an increase in height of 92% on the post-therapy examination. The patient was symptomatic and was offered additional treatment, but he hesitated and a laparoscopic myotomy was not performed until 25 months later.

untreated patients with achalasia, Vela *et al.*[17] likewise found no difference in TBE emptying between patients treated with Heller myotomy ($n = 72$) or pneumatic dilatation ($n = 111$).

Although limited data have been published regarding achalasia-associated symptoms after treatment, careful questioning has disclosed that the prevalence of symptoms after treatment for achalasia is substantial.[18] When analyzing our own TBE variables, we found intermediate rates of esophageal emptying (neither absent nor complete emptying) in the majority of patients, irrespective of the treatment given. This finding corresponds well with the symptomatic outcome as most patients reported some degree of dysphagia, although considerable improvements, compared with the baseline recordings, were noted. For instance, the 'Watson dysphagia score' decreased from a median of 28.5 (interquartile range 22.1–42.0) before therapy to 18 (interquartile range 4.3–30.0) after, with no significant difference between the treatment groups. Moreover, we observed that the degree of esophageal emptying ('barium-column height at 1 min') was associated with the reported symptom score for 'dysphagia for liquids' and the 'Watson score' obtained after median of 18 months follow-up. The substantial scattering of both the objective- (TBE) and the subjective outcome variables illustrates the difficulties associated with the definition of a cut-off value that can discriminate between a successful and unsuccessful response to treatment in a meaningful way. However, when using a stricter end-point, that is, the need for additional treatment as a result of persistent or recurring dysphagia ('treatment failure'), we found that TBE variables had a predictive value. Patients who after therapy showed a less than 50% improvement in the barium-column height at 1 min had a 40% risk of

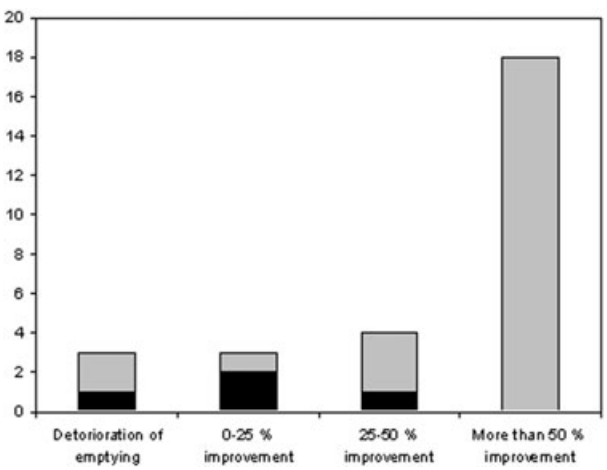

Fig. 5 Bar chart showing the frequency of treatment failures in groups of patients with different degrees of change in the barium-column height at the 1 min time-point from the pre- to the post-therapy timed barium esophagogram examination. The height of the bars indicates the number of patients in each group, the black portions indicate patients with subsequent treatment failures, and the gray portions indicate the number of patients without treatment failure at the end of follow-up.

Fig. 6 Example of timed barium esophagogram (TBE) in a 56-year-old female patient with successful outcome after laparoscopic myotomy for achalasia. The pre-therapy TBE examination (a) demonstrates poor esophageal emptying. The height of the barium column at the 1 min time-point was 22.5 cm. The post-therapy TBE (b) shows complete emptying of the esophagus and a decrease of its diameter. The patient remained in remission during follow up and reported a Watson score of 0 (no dysphagia) 33 months after the post-therapy TBE.

experiencing treatment failure. None of the patients with more than 50% improvement developed a treatment failure. Using corresponding criteria for lack of improvement (at 5 min), Vaezi *et al.* found that, on the one hand, treatment failure within 1 year of a dilatation could be predicted in nine out of 10 patients. On the other hand, only two of 22 patients with successful (>50%) improvement in barium-column height failed therapy within 1 year.[12] The choice of the 5-min time-point in that study was based on the observation that most healthy individuals have emptied their esophagus by 1 min, and all by 5 min. Complete emptying at 5 min at TBE has been used thus as a criterion for an adequate treatment result in achalasia.[2,19] We were unable to confirm the absolute reliability of that criterion in our study as one of 13 patients with normalized emptying at 5 min failed treatment during follow-up.

Another finding, which may have an impact on the subsequent course, was our observation that patients with a wide esophagus prior to treatment with pneumatic dilatation tended to show less improvement in barium-column height after treatment. A wide esophagus pre-treatment has been shown to increase the risk of failure after pneumatic dilatation,[2,12,20] and our finding may support the notion that laparoscopic myotomy should be the primary treatment for achalasia patients with such a radiological status of the esophagus.[21]

Calculating the difference in barium retention between 1 and 5 min at TBE has been proposed as a measure of esophageal emptying.[11] In this context it was somewhat unexpected to find that emptying calculated in this way correlated positively with the dysphagia scores (i.e. the larger the emptying the more dysphagia symptoms). However, this association is likely explained by the strong correlation between this measure and the height of the barium column at 1 min ($P < 0.001$, $r = 0.80$). A plausible explanation is that a larger initial barium column will result in greater subsequent emptying because of the increased hydrostatic pressure exerted on the LES compared with a smaller column.

Several studies have investigated the use of manometry in the early post-therapy period to identify those with an unfavorable long-term clinical response. A decrease in resting LES pressure to less than a certain cut-off level[8,22–24] or a decrease in sphincter tone of more than 50%[6,25] have been suggested to be followed by a beneficial long-term outcome. The picture is, however, far from consistent as others have found manometry to exert no

predictive value.[7,26] An apparent disadvantage with manometry is the discomfort for the patient, and only a minority of our patients was willing to undergo a second manometry investigation. As a consequence, results from this test could not be used in the evaluation of esophageal function after respective treatments. A significant decrease in both the basal pressure and the swallowing-induced relaxing pressure of the LES was observed after therapy, but it was not meaningful to statistically compare manometric results between treatment groups because of the insufficient quantity of data.

TBE is a simple, reproducible, and easily performed radiological method to assess esophageal emptying.[11,13] TBE is better tolerated than repeat esophageal manometry as shown in our study and by others.[27] Only 17 of the patients scheduled for post-treatment manometry agreed to be examined compared with the 43 patients that completed post-treatment TBE. It can easily be performed in small hospitals, where manometry may not be available. Suboptimal treatment and follow-up of patients with achalasia may lead to persistent poor esophageal emptying, to progressive dilatation, and ultimately, to end-stage megaesophagus, requiring esophagectomy.[4,11,28] It is therefore reasonable that the finding of poor improvement in esophageal emptying at a post-treatment TBE examination should motivate further surveillance. If symptoms increase, or are severe, during follow-up, TBE also seems to be of value to obtain objective parameters. If esophageal emptying is further impaired, then the decision to embark on re- or cross-over therapy can be facilitated. A surveillance protocol consisting of TBE and clinical evaluation at yearly intervals after treatment for achalasia has been proposed.[4]

Our study had several limitations. First, the relatively small number of patients means that the study lacks in power to detect minor differences in TBE-emptying after treatment with surgery or dilatation. However, as achalasia is a rare disease, it is difficult to identify large populations of subjects with achalasia. Second, TBE was scheduled 6 months post-therapy in our study. For the purpose of detection of treatment failures, it would have been more appropriate to perform TBE about 1 month post-therapy as relapses occur with a higher frequency in the first few months after treatment.[22] However, a study using TBE 1 and 6 months after pneumatic dilatation has demonstrated a gradual decrease of the width of the esophagus over time, resulting in a smaller diameter at 6 months compared with the diameter at 1 month.[29] For the evaluation of the association between esophageal emptying and the long-term symptomatic outcome, as well as for the comparison of the effect of the treatments on emptying, the choice of the 6 months time-point may be justified. Third, we performed multiple correlations between the TBE and outcome variables, increasing the risk for a type 1 error. Multiple correlations are characteristic of an exploratory study and emphasize the need for a confirmatory study. Lastly, 69% of the patients randomized to surgery or pneumatic dilatation could be evaluated with TBE both pre- and post-treatment. Although this rate of participation is good, it is possible that the sample studied does not represent all the patients included in the study. However, the demographic and disease-specific characteristics of the two study groups were well balanced. A difference between groups in the delay between the pre-treatment TBE and treatment (significantly longer in the surgery group) can be explained by the better availability of dilatation compared with surgery. As achalasia is a disease that progresses very slowly, this difference seems to be without clinical significance.

In conclusion, we were, in this randomized study, unable to detect any difference in esophageal emptying between patients treated with either a laparoscopic myotomy or pneumatic dilatation. TBE variables, as assessed at 6 months after therapy, related to symptom scores at a median of 18 months later. Measurements obtained at the 1 min time-point were the most valuable. Less than 50% improvement in these variables after therapy had a positive predictive value of 40% for development of treatment failure during follow-up. Examination with TBE before and after treatment for achalasia may therefore be of value for the early detection of suboptimal disease control and risk of treatment failure.

References

1 Park W, Vaezi M F. Etiology and pathogenesis of achalasia: the current understanding. Am J Gastroenterol 2005; 100: 1404–14.
2 Birgisson S, Richter J E. Achalasia: what's new in diagnosis and treatment? Dig Dis 1997; 15 (Suppl 1): 1–27.
3 Lopushinsky S, Urbach D. Pneumatic dilatation and surgical myotomy for achalasia. JAMA 2006; 296: 2227–33.
4 Pohl D, Tutuian R. Achalasia: an overview of diagnosis and treatment. J Gastrointestin Liver Dis 2007; 16: 297–303.
5 Kostic S, Kjellin A, Ruth M *et al.* Pneumatic dilatation or laparoscopic cardiomyotomy in the management of newly diagnosed idiopathic achalasia. Results of a randomized controlled trial. World J Surg 2007; 31: 470–8.
6 Gelfand M, Kozarek R. An experience with polyethylene balloons for pneumatic dilation in achalasia. Am J Gastroenterol 1989; 84: 924–7.
7 Kim C, Cameron A, Hsu L *et al.* Achalasia: prospective evaluation of relationship between lower esophageal sphincter pressure, esophageal transit, and esophageal diameter and symptoms in response to pneumatic dilation. Mayo Clin Proc 1993; 68: 1067–73.
8 Eckardt V F, Aignherr C, Bernhard G. Predictors of outcome in patients with achalasia treated by pneumatic dilation. Gastroenterology 1992; 103: 1732–8.
9 Robertsson C S, Hardy J G, Atkinson M. Quantitative assessment of the response to therapy in achalasia of the cardia. Gut 1989; 30: 768–73.
10 Vaezi M, Baker M, Richter J. Assessment of esophageal emptying post-pneumatic dilation: use of the timed barium esophagogram. Am J Gastroenterol 1999; 94: 1802–7.

11 de Oliveira J, Birgisson S, Doinoff C *et al.* Timed barium swallow: a simple technique for evaluating esophageal emptying in patients with achalasia. AJR Am J Roentgenol 1997; 169: 473–9.
12 Vaezi M, Baker M, Achkar E, Richter J. Timed barium esophagogram: better predictor of long term success after pneumatic dilation in achalasia than symptom assessment. Gut 2002; 50: 765–70.
13 Kostic S, Andersson M, Hellstrom M, Lonroth H, Lundell L. Timed barium esophagogram in the assessment of patients with achalasia: reproducibility and observer variation. Dis Esophagus 2005; 18: 96–103.
14 Andersson M, Kostic S, Ruth M *et al.* Characteristics of timed barium esophagogram in newly diagnosed idiopathic achalasia: clinical and manometric correlates. Acta Radiol 2007; 48: 2–9.
15 Kostic S, Rice T, Baker M *et al.* Timed barium esophagogram: a simple physiologic assessment for achalasia. J Thorac Cardiovasc Surg 2000; 120: 935–43.
16 Watson D, Pike G, Baigrie R. Prospective double blind randomized trial of laparoscopic Nissen fundoplication with division and without division of short gastric vessels. Ann Surg 1997; 22: 642–52.
17 Vela M, Richter J, Wachsberger D, Connor J, Rice T. Complexities of managing achalasia at a tertiary referral center: use of pneumatic dilatation, Heller myotomy, and botulinum toxin injection. Am J Gastroenterol 2004; 99: 1029–36.
18 Frankuisen R, Herwaarden Mv, Heijkoop R *et al.* Persisting symptoms and decreased health-related quality-of-life in a cross-sectional study of treated achalasia patients. Aliment Pharmacol Ther 2007; 26: 899–904.
19 Cohen N. An endpoint for pneumatic dilation of achalasia. Gastrointest Endosc 1975; 22: 29.
20 Vela M F, Richter J E, Khandwala F *et al.* The long-term efficacy of pneumatic dilatation and Heller myotomy for the treatment of achalasia. Clin Gastroenterol Hepatol 2006; 4: 580–7.
21 Sweet M, Nipomnick I, Gasper W *et al.* The outcome of laparoscopic Heller myotomy for achalasia is not influenced by the degree of esophageal dilatation. J Gastrointest Surg 2008; 12: 159–65.
22 Ponce J, Garrigues V, Pertejo V, Sala T, Berenguer J. Individual prediction of response to pneumatic dilation in patients with achalasia. Dig Dis Sci 1996; 41: 2135–41.
23 Alonso P, Gonzales-Conde B, Macenille R, Pita S, Vazquez-Iglesias J. Achalasia: the usefulness of manometry for evaluation of treatment. Dig Dis Sci 1999; 44: 536–41.
24 Wehrmann T, Jacobi V, Jung M, Lembcke B, Caspary W. Pneumatic dilation in achalasia with a low-compliance balloon: result of a 5-year prospective evaluation. Gastrointest Endosc 1995; 42: 31–6.
25 Ghoshal U, Kumar S, Saraswat V, Aggarwal R, Misra A, Chouhuri G. Long-term follow-up after pneumatic dilation for achalasia cardia: factors associated with treatment failure and recurrence. Am J Gastroenterol 2004; 99: 2304–10.
26 Gockel I, Junginger T, Eckardt V. Effects of pneumatic dilation and myotomy on esophageal function and morphology in patients with achalasia. Am Surg 2005; 71: 128–31.
27 Vaezi M. Quantitative methods to determine efficacy of treatment in achalasia. Gastrointest Endosc Clin N Am 2001; 11: 409–24.
28 Csendes P, Csendes A, Cortez C, Burgos A. Evolutive radiological changes of the esophagus in patients with achalasia who did not receive treatment. Surg Today 2007; 37: 183–6.
29 Vaezi M, Richter J, Wilcox C *et al.* Botulinum toxin versus pneumatic dilatation in the treatment of achalasia: a randomized trial. Gut 1999; 44: 231–9.