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ORIGINAL ARTICLE

Correlation Between Timed Barium Esophagogram and Esophageal Transit Scintigraphy Results in Achalasia

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Abstract
Background Timed barium esophagogram (TBE) and esophageal transit scintigraphy (ETS) have been adopted as useful ways to evaluate achalasia patients. TBE has merit as a simple, non-invasive, and convenient method.
Aims The study sought to compare the results of these two tests and verify their usefulness in evaluating treatment response. In addition, we assessed whether TBE could effectively replace ETS through correlation analysis.
Methods The medical records of 50 achalasia patients treated between September 2011 and June 2014 were reviewed retrospectively. The height and width of the barium column at 1, 2, and 5 min were measured by TBE. Half-life ($T_{1/2}$, min) and R_{30} (percentage of remaining radioactivity 30 s after radioisotope ingestion) were measured by ETS. Both tests were performed before and after treatment, and the tests were carried out 1 and 2 days after procedures. And we analyzed the correlation between the parameters from the two tests.
Results The parameters of TBE and ETS were improved after treatment ($p < 0.05$). Before treatment, the height and width results at 5 min from TBE positively correlated with the $T_{1/2}$ parameter from ETS (correlation coefficients of 0.59 and 0.75, respectively). After treatment, the correlation coefficients between the 5-min height and width of the barium column by TBE and $T_{1/2}$ by ETS were 0.55 and 0.46, respectively.
Conclusions Both TBE and ETS are useful modalities in assessing esophageal emptying and response to achalasia treatment. TBE and ETS results have a statistically significant correlation both pre- and post-treatment. We suggest that TBE could effectively replace ETS for the assessment of achalasia.

Keywords Achalasia · Manometry · Timed barium esophagogram · Esophageal transit scintigraphy

Introduction

Achalasia is a rare esophageal motility disorder characterized by peristaltic dysfunction and incomplete relaxation of the lower esophageal sphincter (LES) [1, 2]. Curative treatment of achalasia is difficult, and patients are susceptible to relapse, so it is important to assess esophageal motor function after treatment. Clinical symptoms have been regarded as the most important criteria for assessing the effectiveness of treatment. However, symptoms may worsen due to temporary edema from damage to the muscle layer of the esophagus after endoscopic pneumatic dilatation (EPD) following treatment. Furthermore, symptoms may improve temporarily due to the psychological stability engendered simply from undergoing treatment. Patients' subjective judgments might not reflect the actual state of symptoms, the evaluation of which requires more objective assessment [3, 4]. High-resolution esophageal manometry (HRM), timed barium esophagogram (TBE), and/or esophageal transit scintigraphy (ETS) have been used as objective tools for this purpose.

High-resolution esophageal manometry has been widely used for classifying three types of achalasia based on the

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Chicago classification criteria [5], but is limited as a post-treatment assessment method for achalasia patients due to invasiveness and discomfort [6, 7]. TBE is a noninvasive and effective method in both diagnosis and evaluation of the response to achalasia treatment because it can assess esophageal morphology as well as function [3, 8, 9]. The treatment success was objectively evaluated by measuring barium column height at 5 min during TBE for achalasia [8]. ETS measurements are also known to reliably indicate improvements in clinical symptoms and LES pressures and are useful for assessing esophageal emptying [10, 11]. We previously reported that older patient age and a reduced R_{30} (the percentage of retained radioactivity in the esophagus at 30 s) determined by ETS after EPD were associated with better prognosis and suggested that ETS can be used to objectively assess short-term responses to EPD [12].

No studies have previously reported the correlation between TBE and ETS measurements. The aims of our study were (1) to examine the TBE and ETS results, both pre- and post-treatment, according to achalasia subtype; (2) to validate the effectiveness of both TBE and ETS as methods of treatment response evaluation; (3) to analyze the correlation between TBE and ETS results pre- and post-treatment; and (4) to assess whether TBE could replace ETS for evaluating achalasia patients.

Subjects and Methods

This study was a retrospective study utilizing a prospectively collected database. The Institutional Review Board of Gangnam Severance Hospital approved this study.

Patients

The records of 50 patients with achalasia at Gangnam Severance Hospital in Seoul, Korea, treated between September 2011 and June 2014, were analyzed. The diagnosis of achalasia was based on the results of clinical symptoms, endoscopy, TBE, ETS, and/or HRM. Forty-one patients were assessed by HRM. Nine patients were diagnosed by clinical symptoms and TBE findings because they could not tolerate the manometry catheter or it could not be adequately positioned across the esophagogastric junction (EGJ). Forty-seven patients underwent endoscopic procedures, and three treated only with pharmacological treatment. Forty-seven patients received EPD, botulinum toxin injection, or per oral endoscopic myotomy (POEM). Ten patients underwent endoscopic treatment more than twice because of symptomatic recurrence. The demographic, radiographic, and manometric data of patients are presented in Table 1. All patients were assessed before and after treatment according to a standardized protocol (Fig. 1). The patients were followed up with TBE and ETS after treatment, and the questionnaire (including the Eckardt score and dysphagia grade) was updated at every patient visit to the outpatient clinic. Eckardt score was measured before and 7 days after treatment. Treatment success was defined as a resolution of symptoms (Eckardt score of zero) or a decrease of more than two points with a total score of no more than three.

Endoscopic Treatment

Endoscopic pneumatic dilatation was performed using a Rigiflex balloon dilator (Microvasive, Milliford, MA, USA; diameter from 30 to 35 mm). The balloon was inflated twice to 9 psi. For all patients, the first inflation was for 30 s, and the second was for 60 s. Botulinum toxin injection was performed using Botox® (Allergan Inc, Antwerp, Belgium) 100 units diluted in 4 mL saline. Each 0.5 mL Botox® was injected in the 4 quadrants at 1 cm above the EGJ and 5 cm more proximally, using a standard 7-mm sclerotherapy needle. The technical method of POEM, which was originally suggested by Inoue [13], is as follows: Creation of mucosal entry → Making submucosal tunnel → Circular muscle incision → Closure of the entry incision.

High-Resolution Manometry

HRM was performed using a 36-channel manometry system from Sierra Scientific Instruments (Los Angeles, CA, USA). The manometric catheter was gently passed through the nasal canal with the patient in a sitting position after at least a 6-h fast, and patients were evaluated while swallowing ten 5–10 mL volumes of water. Data were digitized and were displayed and analyzed using the ManoView^{AR} Analysis Program from Sierra Scientific Instruments. The diagnosis of achalasia by HRM was made when the integrated relaxation pressure (IRP) was 15 or greater, and failed peristalsis was observed. In type I achalasia, there is 100 % failed peristalsis [14]. In type II achalasia, at least 2 swallows are associated with panesophageal pressurization greater than 30 mmHg. Type III patients have spastic contractions for 20 % or more of the swallows with or without compartmentalized pressurization [5].

Timed Barium Esophagogram

Timed barium esophagogram was performed both before and 1 day after treatment. The TBE was performed with the patient standing, including anteroposterior, left posterior, and anterior oblique projections under fluoroscopy (Shimavision 2000HG; Shimadzu, Kyoto, Japan) after barium ingestion (150 mL barium sulfate was prepared at a concentration of 45 % w/v). The distance (cm) from the

Table 1 Patient demographics, radiographic, and manometric characteristics before treatment

	Control	Type I ($n = 15$)	Type II ($n = 17$)	Type III ($n = 9$)	Unclassified ($n = 9$)	p value
Age (years)		43.8 ± 16.5	45.1 ± 18.4	60.8 ± 10.9	34.0 ± 11.6	0.016
Sex (M:F)		4:11	10:8	4:4	2:7	0.181
LES pressure (mmHg)		19.1 ± 8.8	28.3 ± 13.5	34.4 ± 16.9		0.037
Eckardt score		4.6 ± 1.9	5.0 ± 1.7	3.3 ± 1.3	5.3 ± 2.6	0.139
Timed barium esophagogram						
LES width (mm) max		6.7 ± 2.1	6.9 ± 1.6	6.7 ± 2.6	5.0 ± 2.2	0.229
Barium height (cm)						
1 min	0	15.0 ± 6.8	15.6 ± 8.6	4.7 ± 9.0	22.4 ± 6.4	0.009
2 min		11.9 ± 7.8	15.1 ± 7.9	3.0 ± 5.3	18.4 ± 5.8	0.004
5 min		11.0 ± 7.9	12.3 ± 7.2	1.3 ± 3.4	17.1 ± 5.8	0.002
Barium width (cm)						
1 min	0	4.7 ± 1.7	3.9 ± 1.8	1.3 ± 2.2	5.3 ± 1.9	0.034
2 min		43 ± 1.7	3.7 ± 1.9	1.0 ± 1.7	5.1 ± 2.0	0.009
5 min		3.9 ± 2.0	3.5 ± 2.0	0.4 ± 1.1	5.3 ± 2.0	0.002
Esophageal transit scintigraphy						
T1/2 (min)	<5	14.8 ± 15.6	13.4 ± 17.2	4.0 ± 2.0	135.7 ± 209	0.036
R_{30} (%)	11.6 ± 1.7	37.4 ± 17.7	38.1 ± 22.4	21.9 ± 19.1	62.5 ± 20.2	0.024

distal esophagus to the top of a distinct barium column (barium height) and the maximal esophageal width (barium width) at 1, 2, and 5 min after barium ingestion as well as the maximum LES width were measured. Changes in the height and width of retained barium measured in the post-treatment TBE (differences between barium column values from before and after treatment) were also calculated as an independent variable in the statistical analysis. All measurements were reviewed by two gastrointestinal radiologists to achieve consensus and were performed on picture-archiving and communication system (PACS) images.

Esophageal Transit Scintigraphy

Esophageal transit scintigraphy was performed before and 2 days after treatment. The ETS images were acquired using a gamma camera in an anterior scan in the sitting position (Genesys Vertex; Adac Lab., Milpitas, CA, USA). The point of interest was determined by radioactive markers at the sternal notch and the xiphoid process for acquiring static images. The patients swallowed 0.4 cm^3 of 111-MBq free Tc99 m pertechnetate suspended in 35 ml of normal saline at 0 s (s). A time–radioactivity curve was generated from results that were acquired from 0 to 5 min with static images at 15 and 30 s. The residual fraction of retained radioactivity was determined at 15, 30, and 180 s. R_{30} was the percentage of remaining radioactivity at 30 s after swallowing the radioisotope ingestion compared to 0 s. Half-life ($T_{1/2}$, min) was defined as the time required for radioactivity to reach the half-maximal value in the esophagus. If radioactivity did not reach $T_{1/2}$ within 5 min, a linear fit was applied to the emptying curve to estimate $T_{1/2}$.

Statistical Analysis

Frequencies and means ± standard deviations were used as descriptive statistics. Comparisons of manometry, TBE, and ETS data and demographic data arranged by achalasia subtype were carried out using the Kruskal–Wallis test. Paired data were analyzed by use of Wilcoxon signed-rank test. Spearman's correlation (ρ) was used due to non-normally distributed data. Results were considered statistically significant when p values were less than 0.05. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) v20.0 for Windows (SPSS, Chicago, IL, USA).

Results

Timed Barium Esophagogram and Esophageal Transit Scintigraphy Findings According to Subtype

Before treatment, the barium column heights were 15.0, 15.6, and 4.7 cm, and the barium column widths were 4.7, 3.9, and 1.3 cm at 1 min during the TBE for type I, type II, and type III patients, respectively. The $T_{1/2}$ values were 14.8, 13.4, and 4.0 min, and the R_{30} values were 37.4, 38.1, and 21.9 % as determined by ETS for type I, type II, and

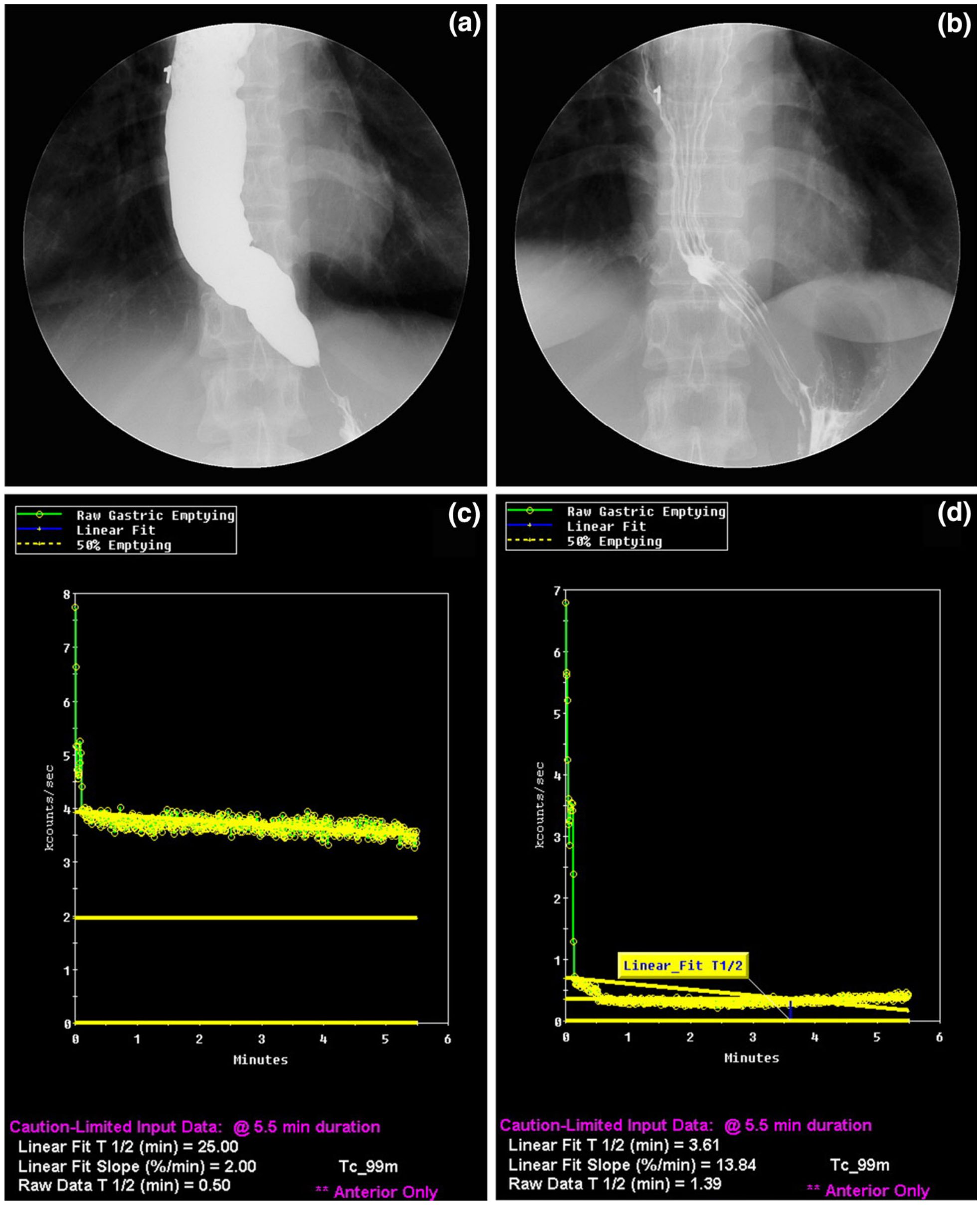

Fig. 1 Achalasia patient with 56-year-old woman. **a** On initial esophagogram, a bird-beak appearance of the esophagogastric junction was noted, with esophageal dilatation. **b** On initial transit scan, marked stasis of radioisotope in the esophagus was seen, with delayed esophageal emptying on the time–activity curve of the dynamic scan. **c** On follow-up esophagogram after balloon dilatation, the esophagogastric junction was dilated, with good passage of barium contrast and decreased esophageal lumen. **d** On follow-up transit scan after balloon dilatation, esophageal emptying was improved dramatically

type III patients, respectively. The results of TBE and ETS from type I or II patients indicated significantly delayed esophageal emptying compared to type III achalasia patients before treatment ($p < 0.05$).

Treatment Response

Eckardt score was improved after treatment (from 4.6 ± 2.0 to 1.0 ± 1.5, $p < 0.05$). The differences between pre- and post-treatment parameters regardless of the achalasia subtype showed a significant improvement by both TBE and ETS (Table 2). The mean height of the barium column at 5 min decreased from 11.1 cm to 3.4 cm, and the mean width of the barium column at 5 min decreased from 3.5 cm to 1.3 cm ($p < 0.05$). There is also a significant improvement of TBE and ETS parameters in the successful treatment group (Table 3).

Correlation Analysis

Before treatment, we found a positive correlation between the height and width of the barium column at 1, 2, and 5 min and the $T_{1/2}$ in ETS (Fig. 2) and a positive correlation between the width of the barium column and the R_{30} in ETS. However, there was no significant correlation between the height of the barium column at 1, 2, or 5 min and the R_{30} in ETS (Table 4). After treatment, we also found a statistically significant positive correlation between changes in both

Table 2 Changes of parameters in timed barium esophagogram and esophageal transit scintigraphy

		p value
△ Eckardt score	−3.6 ± 2.2	<0.001
Timed barium esophagogram		
△LES width, max (mm)	3.8 ± 2.8	<0.001
△Barium height (cm)		
1 min	−8.5 ± 11.2	<0.001
2 min	−7.6 ± 10.1	<0.001
5 min	−7.8 ± 8.3	<0.001
△Barium width (cm)		
1 min	−1.8 ± 2.6	<0.001
2 min	−2.0 ± 2.3	<0.001
5 min	−2.1 ± 2.2	<0.001
Esophageal transit scintigraphy		
$T_{1/2}$ (min)	−6.8 ± 15.4	0.001
R_{30} (%)	−24.5 ± 27.8	<0.001

Table 3 Changes of parameters in timed barium esophagogram and esophageal transit scintigraphy in treatment success group

	Treatment success[a]	*p* value
Timed barium esophagogram		
△LES width	4.0 ± 3.1	<0.001
△Barium height (cm)		
1 min	−7.5 ± 11.6	<0.001
2 min	−6.9 ± 9.8	0.002
5 min	−7.7 ± 8.2	<0.001
△Barium width (cm)		
1 min	−1.5 ± 2.4	0.002
2 min	−1.6 ± 1.9	<0.001
5 min	−1.7 ± 1.9	<0.001
Esophageal transit scintigraphy		
△$T_{1/2}$ (min)	−12.1 ± 33.1	0.004
△R_{30} (%)	−21.0 ± 20.6	0.002

[a] Treatment success: a decrease to zero or a decrease of less than 3-points of Eckardt score

height and width of the barium column at 1, 2, and 5 min and changes in $T_{1/2}$ in ETS (Fig. 3). The correlation coefficients for parameters from the two tests are listed in Table 4. The two outliers of scatterplots were cases in which the half-life values in ETS were excessively high (excessively delayed results: 189 and 500 min) (Figs. 2, 3).

Discussion

The evaluation of responses to achalasia treatment has generally been based on symptom improvement. Clinical symptoms including dysphagia, regurgitation, retrosternal pain, and weight loss are used to calculate the Eckardt score to assess disease severity [15]. However, symptom scores lack standardized criteria for treatment response [4]. Earlier reports indicated that achalasia patients with chronic symptoms could mistake minimal improvements for dramatic change in esophageal emptying, highlighting the need for more objective assessment [16, 17]. Esophageal manometry, TBE, and/or ETS are thus performed as objective tests.

A LES pressure below 10 mmHg determined by manometry is the most effective predictor of long-term achalasia treatment success [18]. Manometry is known as the most accurate method of achalasia diagnosis and evaluation, and it enables both quantitative and qualitative assessments of esophageal motility function [19–21]. Recently published paper also suggested the impedance bolus height on HRM has a correlation with manometric variables when compared to barium column height on TBE [2]. However, repetitive manometric tests have a disadvantage for long-term follow-up due to invasiveness and difficulty inserting the catheter, especially in a sigmoid esophagus. Thus, there would be limitations on using this method for evaluating treatment efficacy during follow-up.

Previous studies have reported that TBE and ETS are modalities useful for evaluating treatment responses [4, 8, 11]. These tests, due to their convenience relative to manometry, enable the detection of disease recurrence at an early stage. Our previous studies have reported the effectiveness of each test but are insufficient to assess the correlation between results from the two tests [22, 23].

Our study is the first study to assess the correlation between TBE and ETS results and shows that the test results have a statistically significant correlation before and after treatment of achalasia. The TBE and ETS parameters were showed significant improvements following treatment. In the post-treatment group, a positive correlation was observed between changes in the height and width of the barium column and changes in the half-life in ETS. Interestingly, in addition, our results showed that esophageal emptying was not delayed in type III patients compared to type I and II patients. We reported previously that patients with vigorous achalasia had narrower esophageal lumen and shorter transit times than those of classic achalasia group [24]. The relationship between TBE findings and subtypes defined by HRM has not been clearly elucidated [3, 20, 25, 26]. Another paper also reported that the esophageal width of type I and II achalasia patients was larger than that of type III achalasia, which was consistent with our studies, and the report showed a significant correlation between the barium column height and clinical symptom scores after EPD [25].

Timed barium esophagogram is an easily performed test to evaluate treatment effects due to this correlation between

Table 4 Results of two-tailed Spearman's correlation analysis between timed barium esophagogram and esophageal transit scintigraphy (pre- and post-treatment)

TBE	ETS							
	Half-life		R_{30}		Half-life[a]		R_{30}^{a}	
	ρ	p value	ρ	p value	ρ^{b}	p value	ρ^{b}	p value
LES width	−0.44	0.001	−0.38	0.029	0.1	0.516	0.39	0.042
Barium height at 1 min	0.45	0.001	0.33	0.068	0.44	0.002	0.47	0.015
Barium height at 2 min	0.48	<0.001	0.27	0.142	0.47	0.001	0.33	0.104
Barium height at 5 min	0.59	<0.001	0.33	0.069	0.55	<0.001	0.35	0.082
Barium width at 1 min	0.62	<0.001	0.55	0.001	0.24	0.11	0.33	0.096
Barium width at 2 min	0.67	<0.001	0.51	0.003	0.32	0.031	0.28	0.161
Barium width at 5 min	0.75	<0.001	0.54	0.001	0.46	0.002	0.42	0.033

[a] Change in the result of a test before and after the treatment

[b] The correlation coefficients for post-treatment were analyzed based on the changes in the results of TBE and ETS before and after the treatment

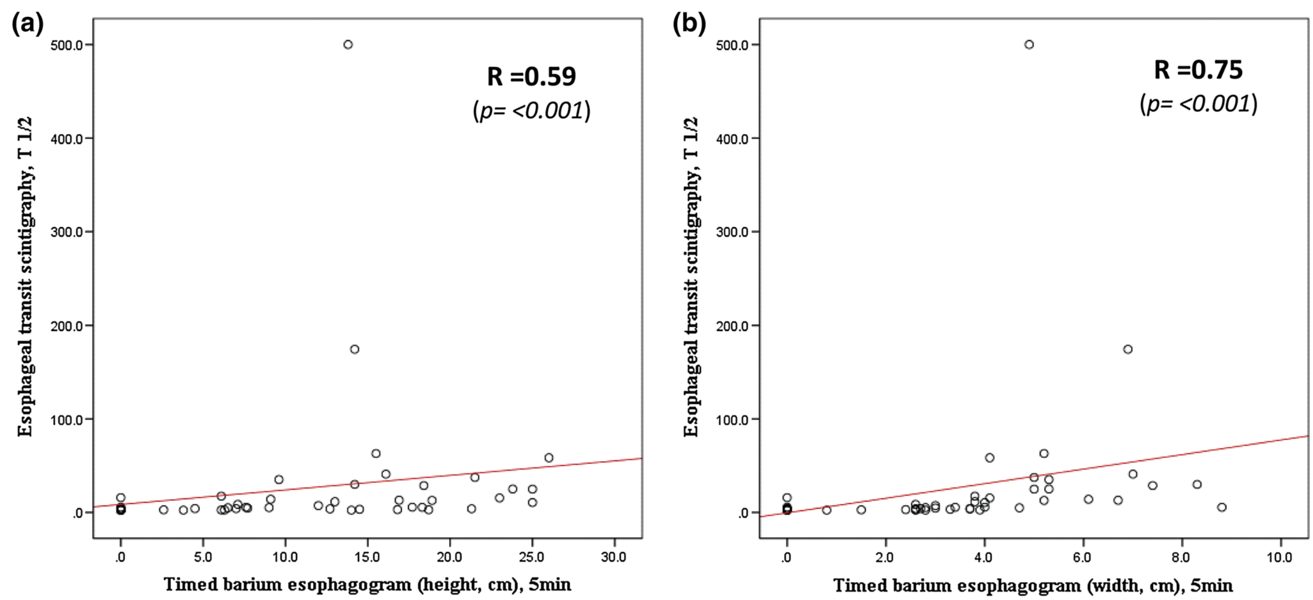

Fig. 2 Scatterplot showing the positive relationship between the barium column height (**a**) and width (**b**) at 5 min in the timed barium esophagogram and $T_{1/2}$ in esophageal transit scintigraphy before treatment. The *regression line* is shown. The correlation was statistically significant [$p < 0.05$, Spearman's $r = 0.59$ (**a**), 0.75 (**b**)]

the improvement of symptoms and esophageal barium emptying after treatment [8, 9, 26–28]. A reduction in the height of the barium column at 1 min of more than 50 % is a favorable predictor of treatment success associated with symptomatic improvement [9]. TBE helps to easily confirm anatomical structure of the esophagus and characteristics of achalasia (e.g., Bird's beak sign) and assess motor function of the esophagus based on time-series images [3, 8]. ETS results are also known to correlate with patient symptoms and LES pressure and can provide quantitative analysis as a physiological method. As such, ETS is an effective test that can highly accurately predict responses of achalasia patients to treatment [29, 30]. A prior study from our institution reported that older patient age (age $\geq$ 40) and a post-EPD reduction in R_{30} ($\geq$20 % decrease in R_{30}) were independently associated with good prognosis and suggested that this might provide valuable clinical data for achalasia patients [12].

It was confirmed that both TBE and ETS were effective for diagnosis and follow-up assessment of achalasia patients. However, ETS also has disadvantages; it cannot verify detailed anatomical structures, such as the esophageal mucosal lesion or the diameters of the esophagus or the EGJ. Moreover, ETS has not been widely used in many clinics, neither its testing method nor the analyses of the resulting data have been standardized yet, and ETS is a

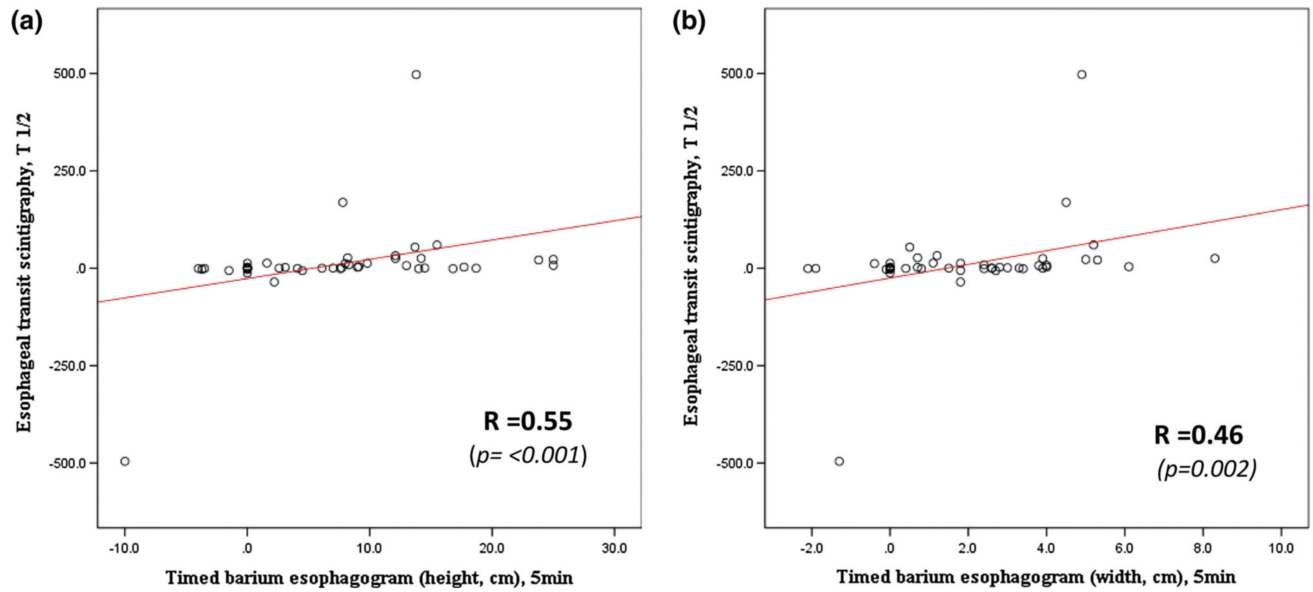

Fig. 3 Scatterplot showing the positive relationship between the barium column height (**a**) and width (**b**) at 5 min in the timed barium esophagogram and $T_{1/2}$ in esophageal transit scintigraphy after treatment. The *regression line* is shown. The correlation was statistically significant [$p < 0.05$, Spearman's $r = 0.55$ (**a**), 0.46 (**b**)]

relatively expensive tool compared to other methods. While conventional esophagography could detect structural abnormality well, it is limited in the functional diagnosis of achalasia. TBE has the advantage of measuring changes in barium column height across time to assess esophageal emptying [8]. Therefore, TBE might be the best alternative modality for the follow-up of achalasia patients after treatment.

Our study has limitations. First, type of treatment and timing of assessment have an impact in results. Our analyses were limited to patients that had various types of endoscopic treatments, and radiologic studies were carried out 1 and 2 days after treatment. The other treatments such as Heller myotomy or evaluation after few months post-treatment may lead to unlike the present results. Second, the sample size was relatively small, because achalasia is a rare disorder, which makes it difficult to enroll a large population of patients. Third, this study was a retrospective study in a single tertiary care hospital. However, all patients were treated using our routine protocol, and data have been collected prospectively.

In conclusion, TBE and ETS are useful modalities in assessing esophageal emptying and responses to treatment. Considering its advantages (simple, noninvasive, and convenient), TBE may be considered the most appropriate tool to replace ETS to evaluate achalasia patient responses to treatment as well as to verify anatomical structure.

Conflict of interest None.

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