M.J. Ehsani Ardakani MD[1]
M. Foroutan MD[1]
N. Amani MD[2]
I. Neshandar Asli MD[3]
M. Hosseinnezhad Yazdi MD[4]
A. Yousefi MD[4]
H. Mohaghegh Shalmani MD[4]
M. Baladast MD[4]
M. Naseri MD[5]
M.R. Zali MD FACG[6]

1. Assistant Professor of Gastroenterology and Hepatology, Research Center for Gastroenterology and Liver Disease, Shaheed Beheshti University of Medical Sciences, Tehran, Iran.
2. Assistant Professor, Department of Nuclear Medicine, Shaheed Beheshti University of Medical Sciences, Tehran, Iran.
3. Professor, Department of Nuclear Medicine, Shaheed Beheshti University of Medical Sciences, Tehran, Iran.
4. Research Center for Gastroenterology and Liver Disease, Shaheed Beheshti University of Medical Sciences, Tehran, Iran.
5. Assistant Professor, Department of Radiology, Shaheed Beheshti University of Medical Sciences, Tehran, Iran.
6. Professor of Gastroenterology and Hepatology, Research Center for Gastroenterology and Liver Disease, Shaheed Beheshti University of Medical Sciences, Tehran, Iran.

Corresponding Author:
Mohammad Javad Ehsani Ardakani
Address: Research Center for Gastroenterology and Liver Disease, 7th Floor, Taleghani Hospital, Tabnak St, Evin, Tehran, Iran.
Tel: +98-21-22418871
Fax: +98-21-22402639
E-mail: article@rcgld.org

Received March 16, 2006;
Accepted after revision July 17, 2006.

Summer 2006; 4: 1-6

Esophageal Transit Scintigraphy, Manometry, and Barium Swallow in Assessment of Response to Balloon Dilatation in Achalasia

Background/Objective: Achalasia is a motility disorder of unknown etiology, characterized by absent esophageal peristalsis and loss of lower esophageal sphincter relaxation. Balloon dilatation is the most effective non-surgical treatment for patients with achalasia. Manometry, scintigraphy and radiology are three techniques that provide an objective measure of success after balloon dilatation. The objective of this study was to determine the best predictor of success after balloon dilatation in patients with achalasia.

Patients and Methods: 17 patients with achalasia of cardia who referred to Taleghani Hospital in 2003, were evaluated, both symptomatically and objectively (esophageal manometry, timed barium esophagogram, and scintigraphic emptying index), before and after treating with pneumatic dilatation of esophagus. The degree of patient symptom improvements after treatment was recorded and correlated with improvement in some indices derived by the above-mentioned three methods.

Results: 12 (70.6%) of 17 patients had score improvements of $\geq$80%. All the pre-treatment diagnostic indices were significantly ($P<0.05$) different from those after therapy. There was no significant difference between the two groups in terms of improvement in symptoms according to the indices of barium swallow or scintigraphy. No association between the patient symptom scores and improvement in either the barium height or emptying index was found.

Conclusion: In evaluation of efficacy of pneumatic dilatation of esophagus for treatment of achalasia, we should not only rely on transit or barium study.

Keywords: achalasia, pneumatic dilatation, manometry, barium study, scintigraphy

Introduction

Disorders of the upper digestive tract have a great impact on society in terms of both direct and indirect healthcare costs and social burden.[1] One of these disorders, achalasia, is a motility disorder first described in 1674 by Willis. It has a small incidence in general population.[2] Being of unknown etiology, this disorder is characterized by decreased lower esophageal sphincter (LES) relaxation as proved by manometry, and by esophageal dilation, minimal LES opening with a bird-beak appearance in radiography. The esophagus has a poor emptying that produces complaints of dysphagia, regurgitation, and chest pain.[3]

Non radionuclide based diagnostic techniques include both non-invasive tests (barium series) and invasive procedures (fiberoptic endoscopy, esophageal manometry), some of which are not well tolerated by patients or are not readily available in all centers.

Esophageal manometry continues to be used widely in clinical practices, primarily because of its value.[4] This is a useful method for evaluating the increased LES tone and for determining the residual pressure after the treatment. Barium esophagogram is simple and widely available. In addition to its role in.

diagnosing achalasia, it can be used in the objective evaluation of patients after the therapy.

Radionuclide transit/emptying scintigraphy provides means for characterizing exquisite functional abnormalities with a set of low-cost procedures which are easy to perform and widely available. This method entails a low level of radiation and closely reflects the physiology of the tract under evaluation. Being well tolerated, it requires minimum cooperation by the patients and provides quantitative data for better comparison and monitoring the response to the treatment.

In some studies, radionuclide esophageal emptying has been typically used in the objective assessment of response to treatment in achalasia.[5] This procedure evaluates esophageal emptying after ingestion of a standard amount of a radiolabeled liquid or solid (^{99m}TC) meal after a short period of fasting.

The test provides a quantitative estimate of the efficacy of emptying in different regions of the esophagus and is well tolerated by patients because it requires no intubation. However, the test is less sensitive and specific than manometry for establishing the diagnosis of specific esophageal motility disorders. Because of its capacity in providing information on bolus transit through the esophagus, scintigraphy can complete the manometric results.[6]

There is relatively scarse information on standardization, both in the scintigraphic technique, per se and in image processing.

The most effective therapeutic modality for achalasia is pneumatic dilatation (PD) plus surgical myotomy.

Determination of success after treatment of achalasia is an important aspect of treating this disease. For both therapeutic modalities, mentioned above, however, the published articles on the effectiveness of the treatment are mainly based on patients' reports. Therefore, means to determine the objective evaluation of esophageal function after the treatment are of paramount importance. During the past years, there have been numerous studies conducted on this issue.

Manometry is a reliable procedure in the diagnosis and post-treatment evaluation of achalasia. Nonetheless, it is a relatively invasive procedure and several patients cannot tolerate it. So, non-invasive procedure, such as barium swallow and scintigraphy, might be useful in assessment of patients with achalasia who underwent balloon dilatation. The objective of this study was to determine the efficacy of barium swallow and scintigraphy compared to manometry the goold-standard test in evaluation of post-PD response in patients with achalasia.

Patients and Methods

This study was conducted on 17 patients with achalasia of cardia visited in 2003 in Taleghani Hospital, a referral center of gastroenterology in Tehran, Iran. The diagnostic criteria for achalasia included incomplete LES relaxation, aperistalsis in manometry, symptoms of dysphagia, regurgitation and chest pain. Endoscopic evaluation was performed for all patients to rule out secondary achalasia. The exclusion criteria included secondary achalasia, if the patient could be a candidate for injection of botulinum toxin or undergoing surgical myotomy, and those with the diagnosis of pseudo-achalasia. All patients had indication of PD.

After taking informed written consent, all patients completed a standardized pretreatment evaluation consisting of clinical symptom assessment, esophageal manometry, timed barium esophagogram, and scintigraphic emptying index. Patients were evaluated one month after PD to determine how much the symptoms were improved and underwent an additional manometry, barium esophagogram and scintigraphy. The degree of improvements in patient symptoms after the treatment was recorded and correlated with the amount of improvement in either of the three indices mentioned above.

Subjective and objective assessments

All patients were interviewed before and one month after the balloon dilatation. The total symptom scores consisting of dysphagia to solid and liquids, active and passive regurgitation and chest pain, were recorded. The frequency of each symptom was graded on a scale ranging from 0 to 3 (0: none; 1: sometimes; 2: daily; 3: each meal). The maximum total score was 15 points for each patient. Total symptom improvement was assessed by comparing the pre- and post-PD symptom scores. The patients were

then categorized into two groups with ≤80% and >80% symptoms improvement.[7]

Esophageal manometry

Esophageal manometry was performed before and one month after the therapy in all patients by an expert gastroenterologist. This procedure was performed by 4-cannula water perfusion system (Medtronic Co, Polygraph HR, USA). We used a polyvinyl catheter 4.5 mm in diameter, the pressure sensors of which were positioned 5 cm apart. Under local anesthesia, the catheter was passed through the nostrils down to esophagus. Intraluminal pressures were recorded on a polygraph by graph for windows version 2.04 function testing software. The LES pressure was studied by stational pull-through technique. Relaxation of LES was carried out by asking the patient to drink a sip of water. The esophageal body waves were studied by wet swallow, i.e., to drink 3–5 mL of 25 ˚C water every 20 seconds. The distance between the LES and sensors was 5 cm. Incomplete or loss of relaxation of LES and simultaneous contraction confirmed the diagnosis of achalasia. A LES resting pressure of <10 mm Hg and a residual pressure of <6 mm Hg was considered as response to treatment.

Pneumatic dilatation

All PDs were performed using a Rigiflex balloon dilator in the supine position. Dilation was performed with a 3.0-cm balloon (Microvasive, Boston Scientific Corp, Rigiflex ABD, USA). Patients fasted for at least six hours. All patients were sedated with 2.5 mg intravenous midazolam. After upper gastrointestinal endoscopy by an expert gastroenterologist using a video-endoscope (Pentax EG-2091, Japan) the Rigiflex dilator was passed over a guide-wire. The balloon was inflated to seven PSI for 60 seconds. Gastrographin swallow was performed after the procedure to identify perforation of esophagus, if any.

Barium esophagogram

A timed barium esophagogram was performed before and one month after the therapy (Gigantos Siregraph B, Siemens Co, Germany). Ten out of 17 patients accepted to undergo a second timed barium esophagogram.

All patients were asked to fast overnight before the procedure. With the patient in an upright, slightly left-posterior oblique position, radiograms of esophagus were taken (Gigantos Siregraph B, Siemens Co, Germany) one, two, and five minutes after the last swallow of 150 mL of low density barium (45% w/v) over 30–45 seconds. The distance in centimeters, from the distal esophagus, identified by the bird's beak appearance of the esophagogastric junction, to the top of a distinct barium column (*i.e.*, the "barium height") was then measured. We used the barium height on five minutes films to determine the degree of complete emptying. This was based on our observations that in all healthy individuals, esophagus becomes empty of barium after five minutes of its ingestion.

Esophageal transit scintigraphy

A radionuclide esophageal emptying process was performed before PD and one month after it. The results were assessed without any vision of the history, symptoms or results of other clinical diagnostic tests.

All patients were asked to fast 4–6 hours before the procedure and were trained with water on how to swallow the radioactive meal like a bolus. While standing, the patients were asked to keep the radioactive meal in their mouths; after the start of acquisition and taking 10 frames, they were asked to swallow the meal as a bolus and then, in 20-second intervals, to have dry swallows. We used ADAC system (Genius 5.1, Phillips Co, USA) with a gamma camera and a low energy general-purpose collimator.

The total time of film recorded was one-minute 120 frames every 0.5 second.

The meal contained 0.5-1 mCi of TC-perthechnetate in 20 mL water.

We derived the emptying rate (ER), as the scintigraphic index, by the following equation:

$$ER = \frac{P - V_{10}}{P - B}$$

Where P represents the peak radioactivity, V10 the activity 10 seconds after the peak, and B is the background radiation-mean count of the first five seconds.

Statistical analysis

The extent of improvement after the treatment was calculated as the percentage of reduction of symptoms as expressed by patients. The patients were divided into two groups; group 1 with <80% (failure),

and group 2 with ≥80% improvements (success).[7]

According to the level of improvement in esophageal barium emptying and LES pressure, the patients were classified into two groups; group 1 with <50% improvement (failure), and group 2 with ≥50% improvement (success).[8] Based on the scintigraphic emptying index, the patients were also classified into two groups; group 1 with <2-fold improvement as compared to the pre-treatment index (failure), and group 2 with ≥2-fold improvement (success).[9] Groups 1 and 2 patients, were compared for demographic and indices measured by the three diagnostic tests.χ^2 and Fisher's exact test were used, when appropriate, for comparing the categorical variables.

Results

Demography

Table 1 presents the demographic characteristics, clinical symptom scores, barium height and the emptying index after two seconds of the 17 patients with achalasia who underwent PD. All patients presented with dysphagia, mostly (75%) to solid foods, as the initiating symptom. Most (94%) of them had a gradual improvement. The most frequent symptoms, besides dysphagia, included regurgitation (70%), heartburn (55%) and chest pain (45%). The mean ± SD age of 17 patients was 42.3±15.9 years. Half of the patients aged <44 years. The mean ± SD duration of dysphagia was 82.5±168.6 (range: 1–720) months. One patient complained of slightly progressive dysphagia since 20 years ago.

The mean ± SD clinical symptom score was decreased from 8.24±1.95, before the treatment to 1.9±2.6, after the treatment ($p < 0.001$).

The relationship between symptoms and paraclinical Indices

All the diagnostic indices before the treatment were significantly ($P<0.05$) different from those after the therapy.

No correlation was found between patients' symptom scores and the extent of improvement in neither the barium height nor the emptying index. Twelve (71%) of 17 patients had improvement of ≥80% in their symptom scores (Table 2).

Thirty-eight percent of patients had ≥50% improvement in the barium height after the treatment. From 12 patients with ≥80% improvement in their symptom scores, six had also ≥50% improvement in their barium height. As a result, 50% of patients had discordance between the improvements in their symptoms and barium height.

Considering the emptying index, 85% of patients had an improvement of ≥2-fold of their pre-PD indices while 15.4% had an improvement <2-fold.

Twenty-eight percent of patients with improvement of ≥80% in their symptom score after the treatment, had an improvement of ≥2-fold in their emptying index after the treatment; 72% had <2-fold improvement.

The correlation between the barium height, the emptying index and the LES pressure was also not significant.

Discussion

There was no significant difference between mean age of patients in two groups of symptom score improvement (≥ 80) and no improvement (< 80). These are not compatible with previous findings that

Table 1. Demographic data, clinical symptom score, "barium height" and "emptying index after 2 seconds" in patients, before and after pneumatic dilation

	Pre-Treatment Mean (SD)	Post-Treatment Mean (SD)	P-value
Sex	5/12 (M/F)		
Age (Years)	42.3 (15.9)		
Clinical Symptom Score	8.2 (2.0)	1.8 (2.6)	0.001
LES Resting Pressure	44.1 (10.6)	22.8 (11.0)	<0.005
LES Residual Pressure	17.2 (9.7)	5.5 (6.0)	0.006
Barium Height (2nd Minute)	21.0 (6.9)	19.0 (5.3)	0.05
Emptying Index after 2 Seconds	23.2 (19.2)	66.6 (30.0)	<0.005

LES: Lower Esophageal Sphincter

showed an age-dependent response to pneumatic dilatation that young patients had a poor response to the therapy.[10-12]

The most frequent symptoms in our patients were dysphagia (100%), regurgitation (70%), heartburn (55%) and chest pain (45%), which are in keeping with the previous studies except for a higher frequency of heartburn than chest pain.[5]

Sevety-five percent of patients presented with dysphagia for solid foods as their initiating symptom, which is compatible with the rate of 70%–97% reported earlier.[3]

We yielded 71% short-term good response after PD. It is in parallel with the rate of 50%–85% described by most of the authors.[3]

As we have evaluated the factors which do not appear to have a substantial influence on the response to PD, including gender of patients, duration of esophageal symptoms before the treatment, the pretreatment LES pressure, and barium indices before treatment are similar to the most recent studies. [5] In addition, we could not find that the emptying index, after 2 seconds of radionuclide study before PD, to have effect on response to treatment.

Noting the assessment of symptoms according to paraclinic indices, a few studies have used post-therapy manometric data to identify predictors of treatment success.[13,14] In a study on 29 achalasia patients, there was a significant correlation between the extent of improvement in symptom scores and the change in the LES pressure.[13] Wehrmann et al. have also found that a post-therapy LES pressure of <10 mm Hg is the single most valuable factor predicting the clinical response.[15] Our study, however, like the studies conducted by Kadakia and Wong, Kim et al. and Vaezi, did not show any significant correlations between these two indices.[5,13,14] Perhaps, a reason for this finding is that we had only one patient with LES pressure <10 mm Hg after the first session of PD.

Furthermore, no significant correlation between the barium height or improvement in scintigraphic emptying index and improvement in symptom scores was found.

All the diagnostic indices measured before the treatment were significantly ($P<0.05$) different from those after the therapy. This suggests that scintigraphy, as well as the other two tests, can be used for assessment of the patients with achalasia treated by PD. In a study on 22 patients with achalasia in 2002, Stan et al. found that esophageal scintigraphy was a useful technique in evaluation of response of patients to pneumatic dilation.

A recent study reported that subjective and objective parameters of improvement are discordant in around 30% of patients post-PD.[8] Nevertheless, in our study, 50% of patients with good to excellent improvement in their symptom scores had discordant results considering their level of improvement in their barium emptying index; 72% of them had discordant results regarding their emptying index of radionuclide study. Taking into consideration, these results and those of a study done in 2002 by Vaezi et al. reflect that a portion of failures in long-term follow-up after PD occurs because in a subset of patients the extent of improvements in symptoms discords with that in barium emptying.[16] Finally, these studies conclude that the results of timed barium esophagogram are better predictors for long-term success after PD than assessment of symptoms. As a consequence, we also recommend long-term follow-up of the dis-

Table 2. Age, clinical symptom score, "barium height" and "emptying index after 2 seconds" in two groups stratified by the extent of improvements in symptom scores

	<80% Improvement Mean (SD)	≥80% Improvement Mean (SD)	P-value
Age (years)	52.5 (15.1)	38.8 (15.2)	0.1
LES Resting Pressure (before treatment)	41.4 (3.4)	45.6 (13.5)	0.5
LES Resting Pressure (follow-up)	20.7 (13.7)	24.1 (9.7)	0.6
Barium Height(before treatment)	20.1 (8.2)	22.7 (6.2)	0.5
Barium Height(follow-up)	18.8 (4.8)	19.0 (6.0)	0.8
Emptying Index(before treatment)	37.5 (29.1)	16.7 (9.2)	0.07
Emptying Index(follow-up)	61.2(42.1)	68.5(26.77)	0.6

LES: Lower Esophageal Sphincter

cordant groups in our study, for determining the extent of improvements in both barium emptying and scintigraphic index.

Additionally, since there was no correlation between the emptying index and LES pressure, assessment of the reliability of the radionuclide study to evaluate the treatment result, in a study on a larger sample size, seems to be necessary. In this study, there was no correlation between the barium study and manometric indices. However, our results demonstrated that we should not rely only on the transit study or barium study for the assessment of the efficacy of PD.

Acknowledgements

We are grateful to Sara Poursaadati for assistance in manometry, Dr. Jodeiri, Dr. Hashemi, Dr. Agah and the staff of the Department of Nuclear Medicine, Taleghani Hospital, especially, Dr. Malek for performing esophageal transit scintigraphy.

References

1. Mariani G, Boni G, Barreca M, Bellini M, Fattori B, Radionuclide gastroesophageal motor studies. J Nucl Med 2004 n; 45(6): 1004-1028.
2. Stan M, Balan G, Rusu M, Ciortescu I, Popa F. Sequential esophageal scintigraphy contribution on cardia achalasia diagnosis. Rev Med Chir Soc Med Nat Iasi 2002; 107(2): 303-306.
3. Michael F, Vaezi MF, Richter JE. Diagnosis and management of achalasia. Am J Gastroenterol 1999; 94 (12): 3406-3412.
4. Chawda SJ, Watura R, Adams H, Smith PM. A comparison of barium swallow and erect esophageal transit scintigraphy following balloon dilation for achalasia. Dis Esophagus 1998; 11(3): 181-188.
5. Vaezi MF.Quantitative methods to determine efficacy of treatment in achalasia. Gastrointest Endosc Clin N Am 2001; 11(2):409-424.
6. Spechler SJ. AGA technical Review on treatment of patients with dysphagia caused by benign disorders of the distal esophagus. Gastroenterol 1999; 117(1): 233-254.
7. Yaghoobi M, Mikaeli J, Montazeri G, Nouri N, Sohrabi MR, Malekzadeh R. Correlation between clinical severity score and the lower esophageal sphincter relaxation pressure in idiopathic achalasia. Am J Gastroenterol 2003; 98(2): 278-283.
8. Vaezi MF, Baker ME, Richter JE. Assessment of esophageal emptying post-pneumatic dilation: use of the timed-barium esophagram. Am J Gastroenterol 1999; 94: 1802-1807.
9. Stan M, Balan G, Rusu M, Ciortescu I, Popa F. The scintigraphic assessment of the patients suffering from cardia achalasia treated by pneumatic dilatation. Rev Med Chir Soc Med Nat Iasi 2002; 107(2): 286-289.
10. 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: 2135-2141.
11. Wong RKH, Maydonovitch C. Utility of parameters measured during pneumatic dilation as predictors of successful dilation. Am J Gastroenterol 1996; 91: 1126-1129.
12. Khan A, Shah WH, Alam A, Butt AK, Shafqat F, Castell DO. Pneumatic balloon in achalasia: a prospective comparison of balloon distention time. Am J Gastroenterol 1998; 93: 1064-1067.
13. Kadakia SC, Wong RKH. Graded pneumatic dilation using Rigiflex achalasia dilators in patients with primary esophageal achalasia. Am J Gastroenterol 1993; 88: 34-38.
14. Kim CH, Cameron AJ, HSU JJ, Talley NJ, Trastek VF, Pairolero 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: 1067-1073.
15. Wehrmann T, Jacabi V, Jung M, Lembcke B, Caspary WF. Pneumatic dilatian in achalasia with low-campliance balloon results of a 5-year praspective evaluation.Gastrointest Endosc 1995; 42.31-36.
16. Vaezi MF, Baker ME, Achkar E, Richter JE. Timed barium oesophagram: better predictor of long-term success after pneumatic dilation in achalasia than Symptom assessment. Gut 2002; 50: 765-770.