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Evaluation of clinical characteristics and lower esophageal sphincter pressure on high resolution manometry in achalasia patients after treatment

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Abstract:

Objective: to describe the clinical characteristics and lower esophageal sphincter (LES) pressures on high-resolution manometry (HRM) in patients with achalasia pre- and post-treatment. Methods: a case series study was conducted in achalasia patients. Clinical symptoms, Eckardt score, upper gastrointestinal endoscopy, esophageal barium swallow, and HRM results were collected on baseline and Eckardt score and HRM results on follow-up were collected. Results: from June 2018 to December 2019, 14 patients were recruited including 6 males and 8 females with mean age of 34.6±10.5 y. The proportion of achalasia type I, II, and III were 28.6, 64.3, and 7.1%, respectively. The Eckardt score, LES resting pressure (for both baseline period and swallow phase) and 4-s integrated resting pressure (IRP4s) significantly decreased after treatment ($p<0.05$). There was a correlation between pre-treatment LES resting pressure (in swallow phase) and change in chest pain score ($p=0.044$, $r=0.546$) and a correlation between pre-treatment IRP4s and change in Eckardt score ($p=0.041$, $r=0.549$). IRP4s had no significant difference between treatment success and recurrence groups. After treatment, 11 patients had clinical success and 3 patients recurred/failed after a median of 4 mo. The diagnosis on HRM after treatment included 5 achalasia (4 type I and 1 type II), 1 esophagogastric junction outflow obstruction (EGJOO), 1 distal esophageal spasm (DES), 6 absent contractility, and 1 ineffective esophageal motility (IEM). Conclusion: Eckardt score, LES pressure, and IRP4s improved significantly after treatment. Besides the role of classification and treatment option, HRM could be used to predict the treatment outcome in achalasia.

Keywords: **achalasia, high resolution manometry (HRM), lower esophageal sphinte, treatment.**

Classification number: **3.2**

Introduction

Achalasia is a rare disease characterized by the absence of normal esophageal peristalsis and impaired lower esophageal sphincter (LES) relaxation. The incidence is 1.1-2.2 per 100,000 population and the prevalence is 10-15.7 per 100,000 population [1, 2]. Typical symptoms include difficulty swallowing, regurgitation, chest pain, heartburn, and weight loss.

Current guidelines recommend high-resolution manometry (HRM) as the gold standard in diagnosing and classifying achalasia [1, 2]. The Chicago classification version 3.0 (CC3.0) classifies achalasia into three subtypes, I, II and III, based on the manometric pattern of esophageal peristalsis [3]. These subtypes each have a different prognosis in treatment responses with type III having the highest risk of treatment failure and recurrence. Thus, diagnosis and classification are valuable for the management of achalasia [4, 5]. The primary treatment goal is to alleviate symptoms and to improve patient's quality of life [1, 6]. However, it is reported that nearly 50% of patients fail to respond to treatment and about 10% of patients recur [7, 8].

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In such cases, physicians usually need to evaluate clinical symptoms, timed barium (for esophageal emptying), and HRM before deciding which treatment is appropriate [1, 9].

Tran Xuan Hung, et al. (2017) [10] studied the changes in clinical symptoms, endoscopy, and barium study in Vietnamese achalasia patients with pneumatic dilatation (PD). They found that the Eckardt score significantly improved after treatment and there was a correlation between and treatment outcomes. The authors, however, did not use esophageal manometry to confirm the diagnosis and classify the subgroups. Therefore, in this study, we aimed to evaluate changes in HRM parameters as well as clinical symptoms in treated achalasia patients.

Methods

Subjects

We conducted a retrospective study on patients who were diagnosed with achalasia on HRM (using CC3.0), treated for achalasia, and performed HRM again after treatment between June 2018 and December 2019 at the Institute of Gastroenterology and Hepatology. Data were collected from archived medical records.

Study design

Study procedures: collected retrospective data included clinical symptoms, Eckardt score, findings on upper gastrointestinal endoscopy and esophageal barium swallow, and HRM results on baseline and Eckardt score and HRM results on follow-up. Patients often visited for follow-up after 1 mo of treatment or when they had symptoms suggesting recurrence.

Treatment outcome was evaluated by the follow-up Eckardt score: treatment success (Eckardt score ≤3) and recurrence/failure (Eckardt score >3) [1].

All HRM investigations were measured by the Solar GI system (Laborie) with a 22-channel water-perfused catheter.

Statistical analysis: data was entered by EpiData version 3.1 and analysed by SPSS version 23.0. Qualitative variables are presented as number and percentage. Quantitative variables are presented as mean (standard deviation) or median (interquartile range). Differences among independent groups were tested by the paired *t*-test or Wilcoxon signed-rank test.

Results

Patient characteristics

Between June 2018 and December 2019, 14 patients were eligible. The most common subtype was type II (64.3%). Table 1 presents baseline characteristics of the patients in the study.

Table 1. Patient characteristics.

Characteristic	Result*
Age (mean±SD)	34.6±10.5
Gender: female/male	8/6
Clinical symptoms	
Dysphagia	13 (92.9)
Globus	5 (35.7)
Vomiting/nausea	10 (71.4)
Chest pain	6 (42.9)
Heartburn	1 (7.1)
Regurgitation	12 (85.7)
Eckardt score	6.5 (1.3), 3-9
Symptom duration (months)	21 (75), 10-142
Endoscopic findings	
Reflux esophagitis	2 (14.3)
Los Angeles classification: A/B/D	2/0/0
Barrett's esophagus	0 (0)
Achalasia	
Endoscopy diagnosis	12 (85.7)
Barium swallow diagnosis	10 (71.4)
HRM subtypes	
Type I	4 (28.6)
Type II	9 (64.3)
Type III	1 (7.1)

*qualitative variables are presented as number (%); quantitative variables are presented as mean±standard deviation, min - max or median (interquartile range), min - max.

Changes in clinical symptoms and HRM metrics after treatment

The median follow-up duration was 71 days (min-max 22-330). Of all the patients, 9 (64.2%), 3 (21.4%), 1 (8.2%), and 1 (8.2%) were treated with peroral endoscopic myotomy (POEM), pneumatic dilatation, surgery, and pharmacologic therapy, respectively. At follow-up time, 11 patients had an Eckardt score ≤3 and 3 patients had an Eckardt score >3.

The mean Eckardt score decreased from 6.5 (1.3) to 2 (2.3) (p=0.001). All component scores, except chest pain, improved significantly (Table 2).

Baseline and swallow LES resting pressure and IRP4s significantly decreased after treatment (p<0.05). There was no difference in LES length before and after treatment (p=0.053).

Table 2. Changes in Eckardt score and HRM metrics.

Characteristic	Baseline	After treatment	p
Eckardt score	6.5 (1.3), 3-9	2 (2.3), 0-8	**0.001**
Weight loss	1 (1.3), 0-2	0 (0), 0-2	**0.008**
Dysphagia	3 (0.3), 0-3	1 (1), 0-3	**0.006**
Chest pain	1 (1.0), 0-2	0 (1), 0-1	0.083
Regurgitation	2 (2.0), 1-3	0 (1), 0-2	**0.002**
HRM metrics			
Resting LESP, baseline (mmHg)	34.6±10.0	21.3±11.7	**0.005**
Resting LESP, swallow (mmHg)	33.3±7.2	21.0±10.3	**0.003**
IRP4s (mmHg)	26.3±6.2	15.1±9.2	**0.003**
LES length (cm)	3.6±0.8	3.2±0.5	0.053

LESP: lower esophageal sphincter pressure; significant p-values are in bold.

The correlation between changes in pre-treatment HRM metrics and the change in Eckardt score after treatment is listed in Table 3. There was a correlation between the mean LES pressure (swallow phase) and the change in chest pain score (p=0.044, r=0.546) and between IRP4s and the change in Eckardt score (p=0.042, r=0.549).

Table 3. Correlation between pre-treatment HRM metrics and changes Eckardt scores (p values).

Eckardt score	LES (resting baseline)	LES (swallow phase)	IRP4s
Δ weight loss	0.967	0.863	0.803
Δ dysphagia	0.725	0.734	0.184
Δ chest pain	0.152	**0.044**	0.055
Δ regurgitation	0.917	0.976	0.224
Δ total score	0.417	0.295	**0.042**

Δ = before - after; significant p-values are in bold.

Comparison characteristics between treatment success and recurrence/failure group

The post-treatment HRM diagnoses included achalasia type I (4 patients), achalasia type II (1), absent contractility (6), esophagogastric junction outflow obstruction-EGJOO (1), distal esophageal spams-DES (1), and ineffective esophageal motility-IEM (1) (Fig. 1).

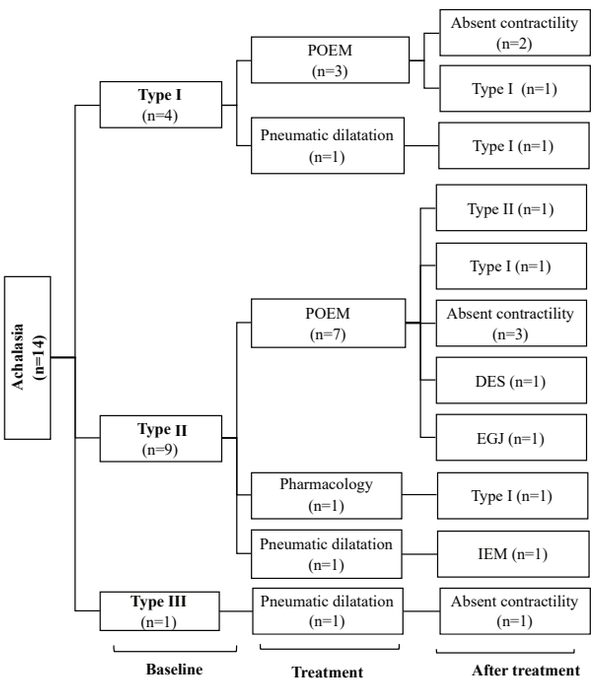

Fig. 1. HRM diagnosis after treatment.

The overall success rate was 78.6%. The success rates of type I, II, and III were 75.0%, 77.98%, and 100% (1 patient), respectively. In the success group, the number of patients receiving POEM, PD and surgery was 7, 3, and 1, respectively. There were 3 patients in the recurrence/failure group, 2 patients were performed POEM and 1 patient received pharmacologic therapy (Table 4). There were no differences in age, gender, symptom duration, Eckardt score, LES pressures (both baseline and swallow), IRP4s, and LES length before treatment between the 2 groups. After treatment, there was no significant difference in post-

Table 4. Characteristics of patients in recurrence/failure group.

Case no.	Age	Gender	Type		Treatment	Erkardt score		Resting LESP baseline (mmHg)		Resting LESP swallow (mmHg)		IRP4s (mmHg)		LES length (cm)	
			Baseline	*After treatment*		*Baseline*	*After treatment*	*Baseline*	*After treatment*	*Baseline*	*After treatment*	*Baseline*	*After treatment*	*Baseline*	*After treatment*
1	54	M	Type II	Type II	POEM	9	8	23.8	23.9	24.2	24.2	19.3	19.2	4.0	3.8
2	20	F	Type I	Absent contractility	POEM	5	4	41.3	21.7	36.6	21.9	23.9	14.2	3.4	3.0
3	34	M	Type II	Type I	Pharmacology	6	5	36.0	29.8	32.4	24.2	26.3	20.6	3.0	3.0

treatment HRM metrics between 2 groups (Table 5).

Table 5. Comparison clinical HRM metrics between treatment success and recurrence/failure group.

Characteristics	Success (n = 11)	Recurrence/failure (n = 3)	p*
HRM metrics			
IRP4s	14.6±9.9	18.0±3.4	0,582
IRP4s ≥15 mmHg	45.5%	66.7%	0.515
Δ resting LESP (baseline) (mmHg)	13.2 (-11.1-40,8)	6.2 (-1-19.6)	0.586
Δ resting LESP (swallow) (mmHg)	16.3 (-5.9-34.3)	8.2 (0-14.7)	0.499
Δ IRP4s (mmHg)	11.9 (-5.2-36.8)	5.7 (0.1-9.7)	0.392
Δ LES length (cm)	0.4 (-0.7-2.3)	0.2 (0-0.4)	0.696

Δ = before - after; LESP: lower esophageal sphincter pressure; data are presented as mean±standard deviation, min - max or median (interquartile range), min - max; significant p-values are in bold.
*Mann-Whitney U test.

Discussion

In this study, we described the changes in clinical symptoms and lower esophageal sphincter pressure on HRM in post-treatment achalasia patients.

At baseline, type II achalasia was the most common subtype (64.3%), which is in line with previous studies where type II accounted for about two-thirds of achalasia patients [5, 6]. Type II patients often have more favourable outcomes and type III patients have the worst prognosis and are at a higher risk of recurrence (up to 30%) [5]. Therefore, HRM is required to confirm the diagnosis of achalasia and subtypes before selecting treatment modality [1, 2].

POEM was the most common treatment choice in our study. It is a safe treatment with a low rate of serious adverse events, comparable efficacy to surgery, and has a lower rate of recurrence than pneumatic dilatation (PD) after a 2-year follow-up [1, 11]. A preliminary Vietnamese study evaluating the response to POEM found a significant improvement in the Eckardt score at 7 months of follow-up [12]. Therefore, POEM is more frequently indicated for achalasia patients, especially for type III achalasia [1]. Two of nine patients in our study failed to respond to POEM. In such cases, Heller myotomy is preferable because it is more effective than PD [1, 8].

The total Eckardt score and its weight loss, dysphagia, and regurgitation scores, improved significantly after treatment. Rohof, et al. (2013) [13] found no difference in weight loss score before and after achalasia treatment by pneumatic dilatation or surgery. Both the weight loss and chest pain components in the Eckardt score have been shown to be less reliable, which means they might not reflect treatment response very well [14]. There are several explanations for this. Weight loss is a less common symptom, and the Eckardt score cannot determine whether weight changes result directly from patient's improvement after intervention or from other causes. Chest pain, despite a more common symptom, is caused by obstruction or spasm. Treatment only resolves obstruction and improves esophageal motility but not esophageal spasm, which may result in persistent chest pain after treatment.

In this study, we found that HRM metrics including LES pressures and IRP4s, significantly decreased after treatment. However, 5 patients remained having IRP4s >19 mmHg (cut-off value for water perfused catheter).

Persistent or recurrent achalasia significantly affects quality of life. The most common symptoms in these patients are dysphagia and regurgitation. Dysphagia can suggest post-treatment conditions such as incomplete myotomy, fibrosis, gastroesophageal reflux disease (GERD), absent contractility or functional dysphagia [1]. GERD occurs frequently after treatment (10-31% post PD, 5-35% post-Heller surgery and up to 60% post POEM) but is often effectively managed by proton pump inhibitor (PPI) therapy [1]. Patients with recurrent symptoms should be reassessed for another optimal therapy.

LES pressure and IRP4s in the success group were lower than in the recurrence/failure group, but the difference was not significant. In some previous studies [9], HRM was used to evaluate short-term response to treatment for 3 mo and IRP4s below the cut-off value were used as a factor to define the technical treatment success. Although some patients in our study responded well to treatment, others had persistent achalasia or developed other motility disorders (for example, absent contractility or DES). This suggests follow-up assessment after treatment cannot be based solely on clinical evaluation but requires HRM to examine LES relaxation and other conditions that patients might develop.

Pre-treatment resting LES pressure (in swallow phase) was correlated with the change in the chest pain score and pre-treatment IRP4s was correlated with the change in the total Eckardt score. This suggests that higher LES pressures and IRP4s could predict better improvement after treatment. Similarly, Mehta, et al. (2005) [15] showed that the successful group had higher LES pressure than the nonresponse group. Some studies on Heller myotomy also found that high preoperative LES pressure is an independent factor of a good treatment. However, the difference in LES pressure between a responder and nonresponder after achalasia treatment is inconsistent among distinct studies [16]. In a Tang, et al.' study (2015) [17], the changes in the total Eckardt score and weight loss were positively correlated with baseline IRP, and IRP changes after POEM were positively correlated with the Eckardt score changes.

These results suggest that a prognostic model to predict treatment outcomes of achalasia can be developed based on clinical symptoms and HRM metrics.

Small sample size is our major limitation. Future large cohort studies with longer follow-up times are needed to provide a comprehensive picture for achalasia patients treated with different modalities and whether a prognostic model can be developed from HRM metrics as well as clinical parameters.

Conclusions

The Eckardt score and IRP4s significantly decreased in achalasia patients after treatment. HRM is important in the diagnosis and classification of achalasia and can help select appropriate treatment and predict outcome.

COMPETING INTERESTS

The authors declare that there is no conflict of interest regarding the publication of this article.

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