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Original article

Clinical Variations Between Different Forms of Achalasia

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Abstract

Background: Esophageal achalasia is a motility disorder characterized by a lack of esophageal peristalsis and failure of the lower esophageal sphincter (LES) to relax. Patients typically present dysphagia for both solids and liquids, regurgitation, retrosternal chest pain, cough, aspiration, weight loss and heartburn, which affect their quality of life. ***Objective:*** To determine whether the High-resolution manometry (HRM) achalasia subtypes could be differentiated based on symptoms or radiographic findings. ***Methods:*** A cross-sectional study design was used, and data collected from 60 patients between 18 and 65 years and a diagnosis of achalasia using HRM over a period of ten years. The symptom assessment was done in a clinical interview using three international questionnaires for esophageal symptoms. ***Results:*** The mean symptom duration for the 3 groups was 25.03 ± 24.88 months, type I 25 ± 22.76 months and type II 24.98 ± 27.32 months, type III had a median of 27 (18-36) months. The mean esophageal diameter of patients with achalasia was 4.87 ± 1.48 cm. Type I had the greatest dilation (5.37 ± 1.7 cm) when compared to type II (4.46 ± 1.03 cm) and to type III 2.75 (2-3.5) cm. The mean esophageal length of all achalasia patients was different among the groups; type I 24.19 ± 2.96 cm and type II 22.96 ± 2.23 cm, type III had a median of 20.63 (20.13-18.13) cm. ***Conclusions:*** Despite the difference in degree of dilation between the subtypes, symptom duration does not appear to be correlated to the pattern of the achalasia.

Keywords: ***achalasia, manometry, esophagus, weight loss, eckardt score***

Introduction

Esophageal achalasia is a motility disorder characterized by a lack of esophageal peristalsis and failure of the lower esophageal sphincter (LES) to relax [1]. Patients typically present dysphagia for both solids and liquids, regurgitation of esophageal contents, retrosternal chest pain, cough, aspiration, weight loss and heartburn [2]. These symptoms and manifestations affect the quality of life, this is why in the last 25 years interest in understanding the pathophysiology has increased significantly [3]. Achalasia is a relatively rare disease. The incidence of achalasia varies between studies, but many incidence rates reported range between 0.5-1.2 per 100000/year [4].

The multifactorial etiology of this condition is not entirely known, but evidence suggests that the inflammatory degeneration that occurs in the regulatory neurons of the myenteric plexus has an autoimmune component as suggested by the presence of circulating anti-nuclear antibodies (present in 56-68% of patients) and the increased prevalence of circulating IgG antibodies against cytoplasm and nucleus of neuronal cells form myenteric plexus in most patients with achalasia (54.3-100%) [5]. The forceful nature of the rhythmic contractile activity observed in patients in the early stage is likely in part caused by reduction in nitrergic nerves, which leaves the myogenic and neural excitation unopposed by the normally significant inhibition by nitric oxide. It has been hypothesized that the infectious agent represents the trigger of an immune reaction in the myenteric plexus, this immune response eventually overcomes the infectious insult, but only in genetically predisposed individuals it may create susceptibility to this disease and damage the ganglion cells. Several studies have suggested that a chronic latent or active viral or bacterial infections are associated with achalasia. HSV-1, JC virus, bornavirus, VZV, measles, and HPV are among the possible etiologic factors [2,6]. Immunohistochemical studies have demonstrated that selective loss of the nitrergic LES nerve fibers occurs in achalasia, thus resulting in unopposed contractile stimuli [7-9].

Currently, high-resolution manometry (HRM) is considered the gold standard for diagnosing esophageal motility disorders [10]. The use of the Chicago classification has led to the subclassification of achalasia into three clinically relevant subclasses based on the pattern of contractility in the esophageal body: in type I, is defined by absent esophageal body smooth muscle contractility with no compartmentalization of intrabolus pressure [11]; type II is characterized by panesophageal pressurizations [10,11] of intrabolus pressure in at least 20% of sequences [12]; whereas in type III, at least 20% of swallows reveal rapidly propagating or spastic simultaneous contractions [11] with shortened distal latency. Treatment outcome depends on this new subclassification, and therefore the subtype can be used to predict treatment response.

It is a chronic condition without cure [12]. The objective of management is directed toward relieving the esophageal outflow obstruction by lowering the LES tone or disrupting the LES, which thereby leads to an improvement in esophageal emptying and a lessening of the patients' symptoms [13]. Laparoscopic Heller myotomy (LHM) plus partial fundoplication are among the preferred treatment options for achalasia, with the main objective of

eliminating the physiologic barrier at the esophagogastric junction (EGJ) [12,14].

Previous studies have shown that patients with subtype I present with the greatest esophageal dilation compared to the other two subtypes [15]. However, there is controversy regarding esophageal dilation, because other articles mention that type II presents with the greatest dilation, especially in different ethnic groups [16]. Regarding the manometric subtype, it has been established that type I has less retrosternal pain compared to type II and type III, suggesting that retrosternal pain is associated with pan-pressurization rather than with esophageal dilation [17]. It has been described that subtype III has a shorter duration of symptoms compared to subtype I and II [15]. Due to the controversy previously mentioned and a lack of studies in hispanic population, we decided to study the differences in clinical symptoms and radiographic findings related to the achalasia subtypes.

Materials and Methods

This was a cross-sectional study with data collected from 60 patients between 18 and 65 years and a diagnosis of achalasia using HRM from November 2022 to May 2023.Exclusion criteria included Chagas disease, esophageal strictures, gastric or esophageal cancer, peptic strictures, other esophageal motility disorders, and a history of previous esophageal surgical treatment.

The diameter of the esophagus was measured using a upper gastrointestinal series (UGI). The esophageal lengths, defined with an isobaric contour set at 30 mmHg, from the inferior border of the upper sphincter to the superior border of the lower sphincter, were measured using HRM performed with a catheter 4.2 mm in diameter with 36 solid-state circumferential sensors spaced at 1 cm intervals and spanning the whole esophagus. The symptom assessment was done in a clinical interview using three international questionnaires for esophageal symptoms (Eckardt symptom score, eating assessment tool (EAT-10) questionnaire, gastroesophageal reflux disease-health related quality of life (GERD-HRQL) questionnaire) [9]. The UGI and HRM as well as the clinical evaluation were performed prior to any surgical intervention.

High-Resolution Manometry Protocol: A high-resolution esophageal manometry was performed presurgically in every patient. A solid-state HRM probe with 36 circumferential sensors was used (Given Imaging, Yokneam, Israel). With the patient in a sitting position and at 45 degrees, stationary HMR was performed. After a 12-hr. fasting period, the probe was inserted transnasally until it passed the esophagogastric junction and assessed visually on the computer screen. Ten water swallows of 5 mL, separated by 30 seconds were provided. Analyses were performed using Manoview 3.0 (Given Imaging), and patients were classified according to latest Chicago classification into three groups: (1) type I achalasia (without pressurization within the esophageal body), (2) type II (with pan-pressurization), and (3) type III (with spasm). Classification was performed by two gastroenterologists (MAV, E-CA) experts in high-resolution esophageal manometry.18 The surgeon was blinded to the high-resolution manometry analysis.

Esophageal diameter: A barium swallow was used to measure the esophageal diameter. Patients were instructed to drink up to 250 mL of low-density barium sulfate suspension within 30 to 45 seconds. Spot films of the esophagus were taken at 1, 2 and 5 min after the start of the barium ingestion. The distance between the fluoroscope carriage and the patient was kept constant during all three spot films. The width was measured perpendicular to the approximated long axis at the widest point in the esophagus [9].

Esophageal length: ManoView Analysis Software 3.0 was used to measure the esophageal lengths with isobaric contour set at 30 mmHg in all cases. Using the smart mouse, we measured the distance between the inferior border of the upper esophageal sphincter (UES) and the superior border of the LES. We averaged three resting measurements from the inferior border of the upper esophageal sphincter to the superior border of the LES prior to the swallows to obtain a baseline length (BL) and ten measurements after each swallow to obtain a post swallow length (PSL). An index was obtained dividing the esophageal length in cm) by the height in cm) and multiplied by 100.

Duration of symptoms: Upon admission to the protocol, a focused clinical history was done. While the patients reported the duration of their symptoms, the time that was considered was from the beginning of their achalasia symptoms until the time of the performance of the presurgical barium swallow.

Clinical Symptom Scores: The symptom assessment was done in a clinical interview using three international questionnaires for esophageal symptoms (Eckardt symptom score, eating assessment tool (EAT-10) questionnaire, and gastroesophageal reflux disease-health related quality of life (GERD-HRQL) questionnaire) [4]. The dysphagia score was the dysphagia component of the ECKARDT score.

Statistical Analysis: Descriptive statistic was performed. Normality Test for distribution was made with Shapiro-Wilk test. If the distribution was normal, T student test (unpaired) or ANOVA (unpaired) were used. If the distribution was not normal, Mann Whitney U test or Kruskal- Wallis were used. A linear regression was done between duration of symptoms (months) and esophageal dilation (cm). All the statistical tests were performed 2-sided, p-values less than 0.05 were considered statistically significant. Statistical analyses were performed using the Prism 6 GraphPad program (GraphPad Software, San Diego, CA, USA). Data are expressed as the mean ± standard deviation (SD). We used median, minimum and maximum to analyse the achalasia type III group due to the small number of patients in that group (n=2).

Results

A total of 60 patients with achalasia were included in the study. 33 patients were females (55%), the mean BMI (kg/m2) was 23.58 (SD ± 4.6), mean height was 1.61 cm (SD ± 0.09), mean esophageal length was 23.58 cm (SD ± 2.75), mean post-swallow length (PSL) was 23.34 (SD ± 2.52), esophageal length/height index was 14.54 cm (SD ± 1.45). The mean age was 39.9 years (SD ± 14.5) and the mean symptom duration was 25.03 months (SD ± 24.8). Mean weight loss was 12.9 kg (SD ± 9.26). The most frequent type of achalasia was type II, n=30 (50%), followed by type I, n=28 (46.66%) and type III, n=2 patients (6.66%). We found that the prevalence of overweight and obesity in the achalasia population was 33% and 9% respectively. (**Table 1**)

The mean weight lost was 13.32 ± 11.47 kg in type I and 21.64 ± 6.81, type 3 had a median of 11 kg (10-12). However, this difference was not significant (p=0.8932). The mean symptom duration for the three groups was 25.03 months (SD ± 24.88), 25 ± 22.76 months in type I and 24.98 ± 27.32 months in type II, type 3 has a median of 27 (18-36) months. There was not a significant difference between the three groups (P = 0.99). The mean esophageal diameter of patients with achalasia was 4.87 cm (SD ± 1.48). Type I had the greatest dilation (5.37 ± 1.70 cm) when compared to type II (4.46 ± 1.03 cm) (p=0.006) and to type III 2.75 (2-3.5) cm (p=0.0189). There was not a significant difference between type II and type III (p=0.0545). The comparison between the three groups showed as a significant difference (p=0.003). (**Figure 1**) The mean esophageal length of all achalasia patients was 23.58 cm (SD ± 2.75) and it was different among the groups; type I 24.19 cm (SD ± 2.96) and type II 22.96 cm (SD ± 2.23) (p= 0.018), type III had a median of 20.63 cm (20.13-18.13) (p=0.0225). (**Figure 2**)

Of the 60 patients, all complained of dysphagia and regurgitation. 59 patients complained pyrosis (98.33%). The mean

GERD score was 23.64 (SD ± 12.51), type I 23.51 (SD ± 11.66) and type II 24.19 (SD ± 13.39), type III had a median of 12.5 (10-15) (p = 0.4331). The mean EAT-10 score was 29.63 (SD ± 9.03), type I 28.94 (SD ± 9.17) and type II 30.30 (SD ± 9.10), type III had a median of 29 (26-32) (p= 0.7485). The mean Eckardt score was 9.03 (SD ± 2.81), type I 8.57 (SD ± 2.28) and type II 9.49 (SD ± 3.23), type III had a median of 8.5 (8-9) (p = 0.2499). (**Figure 3**)

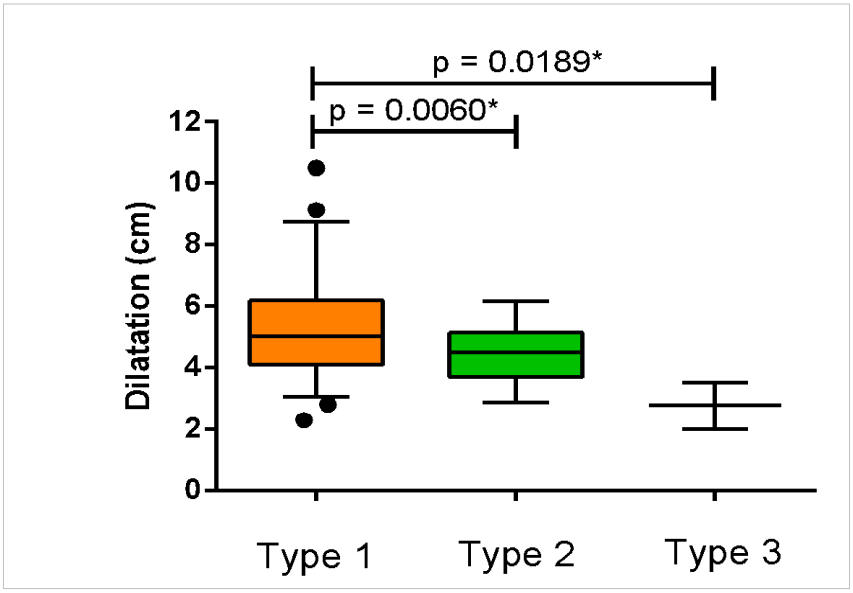

Figure 1: Dilatation in centimeters between the three groups of achalasia.

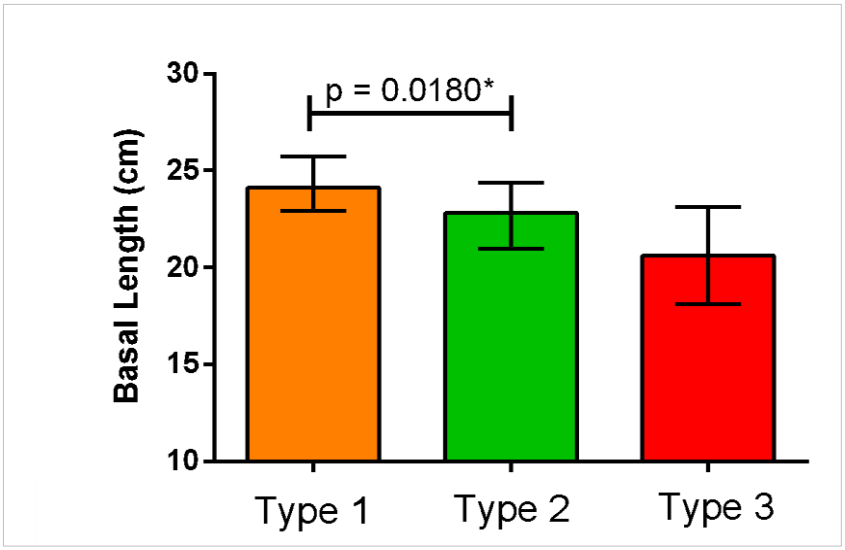

Figure 2: Basal length in centimeters between the three groups of achalasia.

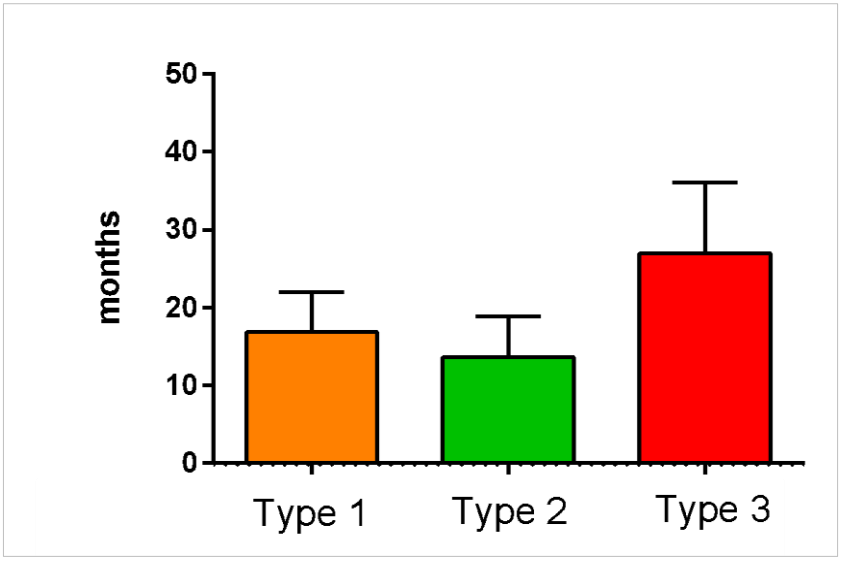

Figure 3: Mean symptom duration between the three groups of achalasia.

Table 1: Clinical and demographical data between different types of achalasia.

Variables	Type I n=28 (Mean)	Type II n=30 (Mean)	Type III n=2 (Median)	p Value
Female (%)	13 (46.4)	19 (63.3)	1	0.8272
Mean age (years)	40.9 ± 15.31	38.53 ± 13.68	52.9 (41-64)	0.3318
BMI (kg/m2)	23.98 ± 4.40	23.07 ± 4.90	26.7 (25.3-28.1)	0.3887
Overweight (%)	18 (35.2)	13 (24.5)	2 (100)	0.0507
Obesity (%)	5 (9.8)	4 (7.5)	0	0.7367
Mean score dysphagia ±SD	2.6 ± 0.5	2.8 ± 0.44	3	0.1469
Mean score regurgitation ±SD	1.11 ± 0.32	1.03 ± 0.19	1	0.2861
Mean score pyrosis (± SD)	1.9 ± 0.49	1.30 ± 0.46	2	0.0984
Weight loss (kg)	13.32 ± 11.47	12.64 ± 6.8	11 (10-12)	0.8932
Mean symptom duration (months)	25 ± 22.7	24.98 ± 27.3	27 (18-36)	0.9937
Basal length (cm)	24.19 ± 2.96	22.96 ± 2.23	20.63 (20.1-18.1)	0.0225
Index BL/Ht	14.53 ± 1.59	14.32 ± 1.02	12.63 (11.56-13.7)	0.025
Esophageal dilation (cm)	5.37 ± 1.70	4.46 ± 1.03	2.75 (2-3.5)	0.003
Mean chest pain (± SD)	1.66 ± 1.069	1.56 ± 1.88	1 (0-2)	0.6963
Mean dysphagia (± SD)	2.61 ± 0.573	2.80 ± 0.448	3	0.1469
GERD Score	23.5 ± 12.5	24.19 ± 13.3	12.5 (10-15)	0.4331
EAT score	28.94 ± 9.1	30.3 ± 9.10	29 (26-32)	0.7485
Eckardt score	8.57 ± 2.28	9.49 ± 3.23	8.5 (8-9)	0.2499

Discussion

The representative symptoms of the disease did not present significant differences between the groups; however, the average dysphagia was presented during each meal and chest pain was occasional in all groups. Previous studies have described that chest pain was significantly less common in type I patients than in types II or III, suggesting that the genesis of the pain is more related to esophageal pressurization rather than to esophageal dilatation [17]. Although the clinical differentiation between subtypes is difficult when there is limited symptom variation.

We also found that patients with achalasia type I had the greatest esophageal dilation, type II were intermediate in dilatation, and type III showed the least dilation. This is consistent with previous studies that described that pattern I is the most advanced dilation of the three patterns of achalasia, followed by type II and lastly by type III [16-20]. There is disagreement with other studies which mention that the maximum esophageal diameter in type II was significantly higher than that of type III this contrary to other studies that found type I significantly wider than type III [21,22].

According to the degree of dilation, achalasia patterns seem to progress from III to II to I, although this progression does not correlate with symptom duration. This contradicts earlier studies that mention that patients with achalasia type III had a shorter duration of symptoms compared to type I and II [23-25].

Conclusions

Patients with achalasia type I had the greatest esophageal dilation, type II were intermediate in dilatation, and type III showed the least dilation. Chest pain appears to be more connected to esophageal pressurization than esophageal dilatation. Despite the difference in degree of dilation between the subtypes, symptom duration does not appear to be correlated to the pattern of the achalasia.

Ethics approval and consent to participate

This work was performed according to the principles expressed in the Declaration of Helsinki. The study was approved by the Ethical Committee from the Regional Hospital of High Specialty of Bajío, and a written informed consent was obtained from all patients.

Conflicts of Interest

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

Authors' contributions

All authors made substantial contributions to the conception or design of the work and reached agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Alfonso Sánchez-Terán: acquisition, analysis, and interpretation of data for the work; Drafting the work and revising it critically for important intellectual content; Final approval of the version to be published. Catalina Naranjo-Pardo: analysis and interpretation of data for the work; Revising it critically for important intellectual content; Final approval of the version to be published. Omar Varela-Barraza: analysis of data for the work; Revising it critically for important intellectual content; Final approval of the version to be published. Tatiana Prado-Salcedo: acquisition, analysis, and interpretation of data for the work; Drafting the work and revising it critically for important intellectual content; Final approval of the version to be published. Michelle Macías-Grajeda: acquisition, analysis, and interpretation of data for the work; Drafting the work and revising it critically for important intellectual content; Final approval of the version to be published.

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