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Research Article

Esophageal Contraction Amplitude After Wet and Dry Swallows in Patients with Mild Esophageal Involvement by Chagas Disease

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Abstract

Background: Chagas disease affects the heart, esophagus, and colon. In the esophagus, the changes are similar to those of idiopathic achalasia: non-peristaltic contractions in the body of the esophagus and non-relaxation of the lower sphincter. The loss of the myenteric plexus caused by the disease affects the amplitude of contractions.

Objective: This investigation aimed to assess the amplitude of esophageal contractions in patients with Chagas disease with no or little abnormal radiological results.

Material and Methods: The study assessed 99 patients with Chagas disease (61 with normal radiological esophageal results and 38 with slow transit without dilation) and 40 controls with continuous perfusion manometry. The contraction amplitude in the proximal, middle, and distal esophageal parts was assessed with 10 swallows of 5 mL of water alternated with 10 dry swallows.

Results: The amplitudes were higher with water swallowing than dry swallowing and were lower in Chagas disease patients than controls. Patients with dysphagia did not differ from those without dysphagia, and patients with heart disease did not differ from those without heart disease.

Conclusion: The contraction amplitude is significantly reduced in esophagopathy caused by Chagas disease, even in those with little involvement; dry swallowing causes similar amplitude in the proximal and middle parts of the esophagus of controls and Chagas disease patients; dry swallowing does not cause contractions with different amplitude in proximal, middle, and distal parts in patients with slow transit; the occurrence of dysphagia and heart disease did not influence the amplitude of the contraction.

Keywords: Chagas Disease; Achalasia; Swallowing Disorders; Esophagus; Myenteric Plexus

Introduction

Contractions in the proximal part of the esophagus (where there is mostly striated muscle) are predominantly controlled by the central nervous system, whereas in the middle and distal parts (where the musculature is smooth), they are controlled by the enteric nervous system [1,2].

The striated muscle of the esophagus is directly innervated by vagal lower motor neurons. This part of the esophagus also has a myenteric plexus with cholinergic and nitrergic neurons, which may be important in controlling the excitatory and inhibitory modulation of the striated muscle. However, the central nervous system is more important in controlling the initiation of peristalsis [1].

Esophageal smooth muscle control is complex, exercised by motor neurons of the dorsal motor nucleus of the vagus with synapses on postganglionic neurons of the myenteric plexus (Auerbach). Smooth muscles have more ganglia in the myenteric plexus than striated muscles [3,4].

Esophageal peristalsis is determined by the action of excitatory cholinergic innervation, inhibitory nitrergic innervation, and post-inhibitory excitatory rebound [1]. Central and peripheral control of contractions is essential for transporting the swallowed bolus from the pharynx to the stomach. When this control is compromised, they become uncoordinated (non-peristaltic), with lower amplitude (hypocontractile), or with higher amplitude (hypercontractile) [1], which can cause dysphagia, chest pain, and esophageal food stasis.

Chagas disease, caused by infection with the parasite *Trypanosoma cruzi*, destroys the myenteric plexus of the digestive system, with more severe consequences in the esophagus and colon [3-5]. The heart is also affected [5], suffering the most serious complications of the disease.

Immunological, genetic, and other factors that determine the destruction of neurons [5] and consequent manifestations do not have the same intensity in all patients. Therefore, some do not have any manifestation of esophagopathy, others have moderate esophagopathy, and still others have intense esophagopathy, characterized by megaesophagus. These different Chagas disease manifestations are associated with the intensity of myenteric plexus loss, as demonstrated by the neuron count at different levels of the esophagus [3,4].

Cholinergic neuron loss affects the contraction capacity of the esophagus and may explain the decrease in contraction amplitude, especially in the distal part, observed in the disease [6]. The esophageal response regarding characteristics of the bolus depends on the sensitivity in the distal esophagus [7], which may also be compromised [8].

Although Chagas disease affects several organs, its clinical consequences manifest mainly in the heart, esophagus, and colon [9,10]. The changes in esophageal motility are very similar to those of idiopathic achalasia, non-peristaltic contractions, and non-relaxation of the lower esophageal sphincter [11]. Moreover, cardiac involvement possibly influences esophageal contractions, considering the pathogenesis of Chagas heart disease [9].

This investigation aimed to assess the esophageal contraction amplitude in the proximal, middle, and distal parts after swallowing water (wet swallow) and saliva (dry swallow) in patients with no or little abnormal radiological results of esophageal function. The hypotheses are that in Chagas disease patients with normal esophagus or with slow esophageal transit on radiological examination, without dilation: 1. There is a decreased amplitude of esophageal contraction; 2. The absence of stimulus during swallowing (in this case, liquid bolus) causes little or no variation in the esophageal response in its different segments; 3. The complaint of dysphagia is associated with lower contraction amplitudes; 4. Cardiac changes are associated with lower contraction amplitudes.

Material and Methods

This study assessed 99 consecutive patients with positive serological test results for Chagas disease, treated at the University Hospital of Ribeirão Preto between 2000 and 2005, and 40 healthy volunteers, assessed as a control group. Sixty-one patients with Chagas disease had normal esophageal radiological examination and 38 had slow esophageal transit of barium sulfate, without organ dilation. The esophageal radiograph was obtained in the anteroposterior position, always at the same distance, in upright position, 10 seconds after the patients ingested 100 mL of 100% liquid barium sulfate. The result was considered normal when there was no contrast in the esophagus, and abnormal (stage I) if there was barium sulfate in the esophagus, without increasing its diameter [5].

Esophageal motility was assessed as part of a study on cardiac and esophageal involvement in patients with positive serology test for Chagas disease, diagnosed and evaluated at the University Hospital of the Ribeirão Preto Medical School at the University of São Paulo, Brazil, during the same period. Patients underwent electrocardiography and chest radiography before manometry. The investigation was approved by the University Hospital's Research Ethics Committee.

The inclusion criteria for the Chagas disease group were positive serological test for the disease, living for at least some time where the disease was endemic, and esophageal radiological examination with normal results or with retention of contrast in the distal part of the esophagus, without an increase in diameter. Patients with esophageal dilation, other diseases unrelated to Chagas disease, heart failure, cardiac arrhythmia, and colon dilation (megacolon) were excluded from this investigation. The control group volunteers were asymptomatic, had not lived where the disease was endemic, and had no heart, esophageal, or colon diseases.

Esophageal manometry used an eight-channel probe and continuous water infusion at 0.5 mL per minute in each channel. The probe was located so that a lateral opening was in the lower esophageal sphincter and the openings of the channels that measure the contraction amplitude were located 5 cm (named distal), 10 cm (named middle), and 15 cm (named proximal) from the lower sphincter. The probe was introduced through the nostril, and the measurement channels were located after the volunteer was in the supine position. Each probe channel was connected to external pressure transducers, connected to the PC Polygraph HR (Synectics Medical, Stockholm, Sweden).

After waiting 3 to 5 minutes to stabilize the recording, 10 swallows of 5 ml of water (wet swallow) were performed, alternating with 10 swallows of saliva (dry swallow), with an interval of at least 30 seconds between swallows. The contraction amplitude was measured in mmHg, using intraesophageal pressure as the baseline. The mean of the 10 swallows was considered the amplitude value of each volunteer or patient.

The contraction amplitude was measured for wet and dry swallows, comparing the three groups and, in patients with Chagas disease, the effect of dysphagia complaints, electrocardiogram (ECG)

changes, and cardiac area. They were considered to have dysphagia when they answered "yes" to the question "Do you have any difficulty swallowing liquids and/or solids?". ECG changes compatible with the consequences of Chagas disease have been previously described [12]. A radiologist examined the chest X-ray images to verify whether they had cardiomegaly.

The results were statistically analyzed through the linear regression model with mixed effects (random and fixed effects), adjusted for age and sex [13]. The Tukey test was used for multiple comparisons. The dysphagia, ECG, and cardiomegaly assessment results were analyzed through the regression model. The study used the SAS system for Windows, release 9.4 (SAS Int, Cary, NC 2013). The results are presented as mean, standard deviation, and median. Results with $p \leq 0.05$ were considered significant.

Results

Of the 99 patients with Chagas disease, 61 had normal esophageal radiological examinations - 15 men and 46 women, aged 19 to 70 years (mean: 42.9 ± 12.7 years) - and 38 had abnormal esophageal radiological examinations (slow transit, without increase in esophageal diameter) - 22 men and 16 women, aged 31 to 78 years (mean: 51.5 ± 11.1 years). The control group had 20 men and 20 women, aged 21 to 70 years (mean: 37.5 ± 14.3 years).

In all three groups, the contraction amplitude was greater with water swallowing than with dry swallowing (Table 1, $p < 0.01$). The amplitude was higher in the distal part of the esophagus, decreasing towards the middle and proximal parts (Table 1). When evaluating dry swallowing, this increase from the proximal to the distal part was not observed in patients with Chagas disease and abnormal radiological examination ($p > 0.05$).

In patients with Chagas disease with normal (Table 2) and abnormal (Table 3) radiology, no difference was observed in the mean amplitude between patients with or without dysphagia, with or without ECG changes, and with or without cardiomegaly.

Discussion

The disease described by Brazilian physician Carlos Ribeiro Justiniano das Chagas in 1909 has been affecting the health of Latin American residents for many years, particularly Brazilians [14]. His excellent description of the various aspects of the disease earned Carlos Chagas two Nobel Prize indication, in 1913 and 1921 [15]. However, more than a century of knowledge about the disease has not prevented its presence in regions of Brazil [16], other Latin American countries [17], Europe [18] and North America [19].

	Proximal	Middle	Distal
Wet			
Controls	67.7 (25.5)	92.1 (43.0)	110.2 (43.3)
CDN	53.1 (32.6)	61.5 (32.6)	74.9 (50.9)*
CDA	32.1 (18.3)	40.5 (28.6)	48.6 (37.2)
Dry			
Controls	52.6 (28.1)	59.4 (36.5)	79.9 (36.9)
CDN	39.6 (22.7)	38.7 (21.0)*	48.5 (36.1)*
CDA	26.4 (15.2)	27.3 (14.6)	29.6 (14.8)

Table 1: Amplitude of esophageal contractions, in mmHg, after wet and dry swallows in controls (n = 40) and Chagas disease patients with normal (CDN, n = 61) and abnormal (CDA, n = 38) esophageal radiologic examination, measured 15 cm (proximal), 10 cm (middle), and 5 cm (distal) from the lower esophageal sphincter. Mean (Standard Deviation).

$p < 0.01$ wet vs dry $p < 0.05$ controls vs CDN and CDA $^*p < 0.05$ vs CDA

	Proximal	Middle	Distal
Dysphagia			
No (n = 48)	54.2 (32.9)	63.6 (33.5)	77.2 (54.0)
Yes (n = 13)	49.1 (32.8)	56.0 (29.7)	66.4 (37.9)
ECG			
Normal (n = 15)	49.6 (24.5)	65.9 (28.1)	67.6 (36.3)
Abnormal (n = 46)	54.2 (35.1)	60.1 (34.1)	77.2 (55.0)
Cardiomegaly			
No (n = 47)	55.2 (35.7)	63.5 (34.5)	77.3 (53.4)
Yes (n = 14)	45.9 (18.1)	54.8 (25.1)	66.8 (42.5)

Table 2: Influence of dysphagia, electrographic (ECG) changes, and cardiomegaly on the amplitude of esophageal contractions, in mmHg, after wet swallows in patients with Chagas disease and normal esophageal radiologic examination, measured 15 cm (proximal), 10 cm (middle), and 5 cm (distal) from the lower esophageal sphincter. Mean (Standard Deviation).

$p > 0.05$ No vs Yes $p > 0.05$ Normal vs Abnormal

The destruction of the esophageal myenteric plexus due to infection with the protozoan *Trypanosoma cruzi* is not the same in all patients; therefore, they have different consequences for the heart, esophagus, and colon. This variation has a geographic component, with different frequencies of manifestations depending on

	Proximal	Middle	Distal
Dysphagia			
No (n = 11)	36.7 (22.0)	48.8 (32.0)	64.4 (51.3)
Yes (n = 27)	30.2 (16.6)	37.1 (27.0)	42.2 (28.5)
ECG			
Normal (n = 7)	35.5 (24.1)	39.4 (24.3)	47.6 (15.0)
Abnormal (n = 31)	31.3 (17.1)	40.8 (29.8)	48.9 (40.8)
Cardiomegaly			
No (n = 25)	29.3 (16.3)	39.9 (28.5)	45.1 (29.3)
Yes (n = 13)	37.5 (21.2)	41.6 (30.0)	55.5 (49.8)

Table 3: Influence of dysphagia, electrographic (ECG) changes, and cardiomegaly on the amplitude of esophageal contractions, in mmHg, after wet swallows in patients with Chagas disease and abnormal esophageal radiologic examination, measured 15 cm (proximal), 10 cm (middle), and 5 cm (distal) from the lower esophageal sphincter. Mean (Standard Deviation).

$p > 0.05$ No vs Yes $p > 0.05$ Normal vs Abnormal.

the country. The disease may not cause any clinical or radiological consequences to the esophagus, which ranges from normal to severe function and anatomy impairment (megaesophagus or dolichomegaesophagus, stage IV in the radiological classification) [5]. These stages are related to the intensity of the myenteric plexus impairment [3,4].

The patients included in this investigation had less significant involvement of the myenteric plexus [3,4], though enough to change the amplitude of esophageal contraction with both water and dry swallowing. There was also no significant difference in amplitude between patients with normal radiology and stage-I patients after wet swallows - except for the distal part of the esophagus, where there was difference between those with normal and abnormal radiology, lower amplitude in patients with abnormal radiology.

Patients with Chagas disease generally have smaller contractions than controls, considering the area under the amplitude and duration curve [20]. This investigation found a difference in amplitude between water and dry swallows, with a significant difference in the distal part of the esophagus between those with and without radiological involvement, suggesting that patients with radiologic esophageal alteration have a more important impairment of the cholinergic innervation of the distal esophagus.

The difference between the three esophageal segments may be related to their different number of neurons - it increases from the proximal to the middle part and from the middle to the distal part [3,4]. The contraction in the distal part has a greater amplitude than in the other segments when swallowing water. In healthy people, the difference between the proximal and middle esophagus disappears with dry swallowing, while the significant increase in the distal part remains. In chagasic patients, the difference between the proximal, middle, and distal esophagus disappears after dry swallows, demonstrating a similar response in each segment.

Patients with dysphagia did not have a lower contraction amplitude than those without dysphagia. The distal mean amplitude in patients without dysphagia tend to be higher in those with abnormal radiologic examination because some patients have high amplitude values, which may indicate that the destruction of inhibitory innervation was more intense than the destruction of excitatory innervation. Another possibility is that the occurrence of dysphagia is due to other factors, such as coordination between the different parts of the esophagus. Non peristaltic contractions and failures are observed in the disease and may be associated with dysphagia, but they are more intense changes than those observed in this investigation. A component of sensitivity and perception may be present, as well as the transit time alteration of the swallowed bolus.

There was no difference in the contraction amplitude between those with signs of heart disease (verified by changes in the ECG and the presence of cardiomegaly) and those without them. Some results indicate the association between left ventricular systolic dysfunction and esophageal function [21] and demonstrate parasympathetic heart dysfunction in the digestive form of the disease [22].

This study has limitations. High-resolution manometry is a more modern method and provides more information about esophageal contractions than continuous perfusion [23], but it was not available when these patients were studied. Assessment of esophageal transit associated with contractions would be of great importance in understanding the effect of decreased amplitude on transit and the occurrence of dysphagia. The participants' mean age in the three groups was different, which could influence the results. However, the age of most participants does not indicate their condition would be influenced by aging.

Conclusion

In esophagopathy caused by Chagas disease, even in its less intense forms: 1. The amplitude of the contraction is compromised, with a significant reduction; 2. The absence of stimulus (absence of a liquid bolus during swallowing) causes a lack of differences in the proximal and middle parts of the esophagus; 3. In patients with Chagas disease and esophageal slow transit, dry swallowing does not cause contractions with different amplitude in the distal part, in comparison with the proximal and middle parts; 4. Dysphagia was not associated with a lower contraction amplitude; 5. Heart disease was not associated with a lower contraction amplitude.

Conflicts of Interest

The author Roberto O Dantas declares no potential conflicts of interest.

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Ethical Approval

The investigation was approved by the Human Research Committee of the University Hospital of Ribeirão Preto, Ribeirão Preto Medical School USP.

Author Contribution

Roberto O Dantas participated in the design of the study, data acquisition and interpretation, manuscript writing, and approval of the final version for submission.

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