

Esophageal transit time in patients with chagasic megaesophagus

Lack of linear correlation between dysphagia and grade of dilatation

Paula Martins, MD, PhD^{a,c}, Cid Sergio Ferreira, MD, PhD^b, José Renan Cunha-Melo, MD, PhD^{a,c,*}, Professor Emeritus of Surgery

Abstract

The aim of this study was to determine the esophageal transit time in control individuals and in chagasic patients with or without megaesophagus.

A total of 148 patients were allocated in 6 groups according to serological diagnostic of Chagas disease and the degree of esophageal dilatation: A, control healthy individuals (n=34, 22.9%); B, indeterminate form (n=23, 15.5%); C, megaesophagus I (n=37, 25.0%); D, megaesophagus II (n=19, 12.8%); E, megaesophagus III (n=21, 14.2%); and F, megaesophagus IV (n=14, 9.5%). After 8-hour fasting, patients were asked to swallow 75 mL of barium sulfate solution. x-Rays were obtained after 8, 30, 60, and 90 seconds, 5, 10, 30, 60, and 90 minutes, 2, 6, 12, 24 hours, and at every 12 hours until no more contrast was seen in the esophagus. This was the transit time.

The transit time varied from 8 seconds to 36 hours (median=90 seconds). A linear correlation was observed between transit time and megaesophagus grade: 8 seconds in groups A and B, 5 minutes in C, 30 minutes in D, 2 hours in E, and 9:15 hours in F. Dysphagia was not reported by 60 of 114 (52.6%) patients with positive serological tests for Chagas disease (37/91—40.7%—of patients with megaesophagus I–IV grades). The esophageal transit time increased with the grade of megaesophagus.

The esophageal transit time has a direct correlation with the grade of megaesophagus; dysphagia complaint correlates with the grade of megaesophagus. However, many patients with megaesophagus do not report dysphagia.

Abbreviations: CFR = complement fixation reaction, EKG = electrocardiogram, FHEMIG = Fundação Hospitalar do Estado de Minas Gerais (Hospital Foundation of Minas Gerais State), GI = Gastrointestinal, IH = indirect hemagglutination, IIF = indirect immunofluorescence, Mega = megaesophagus, Mega I = megaesophagus grade I according to Rezende classification, Mega II = megaesophagus grade II according to Rezende classification, Mega III = megaesophagus grade III according to Rezende classification, Mega IV = megaesophagus grade IV according to Rezende classification, UFMG = Federal University of Minas Gerais, Belo Horizonte, MG- Brazil.

Keywords: barium swallow, chagas disease, dysphagia, esophageal transit time, megaesophagus grade

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^a Department of Surgery, ^b Department of Radiology, School of Medicine, ^c Alfa Institute for Gastroenterology, Hospital das Clínicas, Federal University of Minas Gerais, Belo Horizonte, MG, Brazil.

* Correspondence: José Renan Cunha-Melo, Rua da Groenlandia 212/1001, 30320-060 Belo Horizonte MG, Brazil (e-mail: jrsmelo@medicina.ufmg.br)

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1. Introduction

Chagas disease is an inflammatory, infectious disease caused by the parasite *Trypanosoma cruzi*, which is found in the feces of the triatomine (reduviid) bug.

Chagasic megaesophagus the most common digestive manifestation of Chagas disease in Brazil is a recognized esophageal motility disorder secondary to the destruction of the esophageal Auerbach plexus.^[1–4] Persistent dysphagia, chest pain, and regurgitation are the main symptoms and together with barium swallow and manometric studies constitute the basis for the diagnosis of megaesophagus.^[5–7] The etiology of the disease is confirmed by serological tests, such as hemagglutination, complement fixation reactions, and immunofluorescence for *T. cruzi*.^[1,7]

Radiographic study is the most useful method for the diagnosis of megaesophagus because of its reliability, low cost, and its availability even in small hospitals devoid of sophisticated medical facilities.^[8–11] However, the barium esophagogram is a static method that does not enable any conclusion about the functional capacity of the esophagus in transporting the swallowed bolus to the stomach.

The reliability of roentgenographic studies for the diagnosis of idiopathic achalasia has been questioned because, in spite of the good clinical improvement of symptoms in treated patients, no correlation between the symptoms of dysphagia and esophageal dilatation, as demonstrated by the barium swallow pictures, can be noted.^[12] Tests that measure the gastrointestinal transit have become increasingly available and are now frequently employed by clinicians to evaluate symptoms. Fluoroscopic studies have been proposed to evaluate patients with dysphagia in whom megaesophagus is suspected to establish a functional correlation between the severity of dysphagia, esophageal motor dysfunction, and grade of dilatation.^[13–15]

The esophageal denervation seen in patients with Chagas disease is progressive.^[16,17] It is not rare to see a patient complaining of dysphagia in whom a normal esophageal diameter is found at esophagogram.^[6,8,9,18] This has been explained by a destruction of the nerve plexuses capable of causing physiological impairment before any gross morphological alteration can be detected. Once started the organ dilatation, progresses until a clear esophageal enlargement can easily be seen,^[16,17] what may occur many years after the primary infection.^[2,3]

The use of barium swallow with fluoroscopy is more precise than the ordinary static barium swallow to evaluate the functional activity of the esophagus especially in patients with myenteric neural plexus destruction but with small or no esophageal dilatation.^[9,10,13,14,15,18]

The classification of chagasic megaesophagus according to the severity of organ dilatation, graded from I to IV, was proposed by Rezende in 1959 and 1960.^[8,9,10,19] This classification resembles the one proposed for idiopathic achalasia^[12] and is well known and used all over Brazil. However, it classifies the megaesophagus taking into account only the static picture of a barium swallow study, without functional correlations.

The aim of the present study was to determine the esophageal transit time in control individuals and in patients with the undetermined clinical form of Chagas disease as well as in patients with grades I to IV of chagasic megaesophagus. It is also intended to establish a correlation between the severity of dysphagia complaint and the grade of megaesophagus. The results might have application in clinical practice settings helping medical doctors to make a more appropriate selection for surgical treatment of megaesophagus patients and also as an alert for a more deep investigation in cases with megaesophagus but no dysphagia complaint.

2. Materials and methods

2.1. Patients

Between 1992 and 1996, after informed consent, 148 patients (34 control individuals and 114 with a final diagnosis of Chagas disease) were prospectively studied at the Hospital das Clínicas, Federal University of Minas Gerais (UFMG). The distribution of chagasic patients was as follows: 23 presented the indeterminate form and 91 showed different grades of megaesophagus (37 grade I, 19 grade II, 21 grade III, and 14 grade IV megaesophagus) according to Rezende classification.

All patients from endemic areas of Chagas disease attended at the Hospital das Clínicas/UFMG, Surgical Gastroenterology outpatient clinic complaining or not of difficulty in swallowing solid or liquid meals, even if the symptoms were episodic, were considered for specific tests for Chagas disease: complement fixation reaction (CFR), indirect hemagglutination (IH), and

indirect immunofluorescence (IIF) for *T. cruzi* (20). The patients had the diagnosis for *T. cruzi* infection confirmed if 2 of 3 of the above tests were positive. In cases with dubious or discordant results a fourth test, ELISA, was done. Tests were considered positive if CFR was reactive, a title $\geq 1:40$ at IH and an IIF title $\geq 1:32$ were detected. Patients with the indeterminate form were referred to our unit by Hemominas (FHEMIG), when a suspicion of Chagas disease was raised during routine tests to select blood donor candidates. The final diagnosis for each patient was based on a clinical examination, thorax X-ray, barium swallow with fluoroscopy, electrocardiogram (EKG), and routine blood tests such a hemogram, BUN, creatinine, glucose, electrolytes. The patients were grouped in 6 groups as described below.

By the time the study was done the clinical approach for those patients included EKG, serology for Chagas disease and, in some cases, barium swallow in the presence of vague dyspepsia complaints. The Radiology Department protocol for barium esophagogram in our institution included at least 2 exposures, the second being 30 seconds after contrast ingestion. When the appearance of the esophagus at the x-ray film was referred as normal by the radiologist report the patient was asked to sign an informed consent to be included in the control group of the study. In this way patients without dysphagia, serological tests negative for Chagas disease barium swallow showing an esophageal diameter $< 3.0\text{cm}^9$ constituted the control group. Patients with Chagas disease confirmation were allocated in their respective group according to the severity of their megaesophagus, as follows: indeterminate form of Chagas disease—patients without dysphagia, constipation or heart symptoms, with at least 2 serological tests positive for Chagas disease, and both barium swallow and EKG normal.^[1,3,20–22] The grades of chagasic megaesophagus were determined according to Rezende classification^[9,20]: grade I—patients complaining or not of dysphagia, serological immune tests positive for Chagas disease, and megaesophagus grade I at roentgenography.

Chagasic megaesophagus grade II—same as grade I plus megaesophagus grade II. Chagasic megaesophagus patient grade III—same as for grade I plus megaesophagus grade III. Chagasic megaesophagus grade IV—same as grade I plus megaesophagus grade IV. Patients with positive serological test and presenting the isolated cardiac form of Chagas disease were excluded from the study.

2.2. Radiological transit time

Barium esophagogram was done according the standard radiological technique of the Radiology Department.^[9,11,18,19] After 8-hour fasting, while standing, the patient was asked to swallow 75 mL of a low-density barium sulfate suspension (Celobar, Beecham). This moment was marked as time zero and the esophageal contrast progression was followed by fluoroscopy. The voltage was set at 100 to 110 kv (Siemens Erlangen, Germany) and upright radiographs in a slightly left posterior oblique position were taken. The first x-ray was taken 8 seconds after the order to swallow was placed. Subsequent x-rays were taken at 30, 60, and 90 seconds, 15, 30, 60, 90 minutes, and 2, 6, 12, and 24 hours after the swallowing. Additional x-rays were taken at every 12 hours if necessary. The x-ray documentation was interrupted when no barium column was noted in the esophageal lumen. The transit time was considered as the time in which no barium column could be detected at the x-ray.

The x-ray films were processed and analyzed by a radiologist sided by a 3rd-year resident in Radiology and by a Surgeon. Cases

in which the classification was difficult to establish were further analyzed by a third radiologist. If no consensus was achieved the patient was excluded from the study. The esophagus was considered normal or abnormal and classified into one of the megaesophagus grades when at least 2 out of the 3 radiological reports were coincident. All patients with a definite diagnosis for megaesophagus were further submitted to endoscopy to rule out diseases that mimic megaesophagus and to evaluate esophageal mucosa before therapeutic manipulations.

Pregnant women, diabetic patients, alcohol or drug users, and patients with muscular, neurologic, endocrine, or neoplastic diseases were excluded from the study. Patients in whom the immune tests for Chagas disease were inconclusive, or those in whom the radiological tests were interrupted before the complete emptying of the esophagus as well as chagasic patients with the pure cardiac clinical presentation were also excluded.

Data collected in the 1990's decade were recently recovered from our database and were analyzed using χ^2 parametric test or Kruskal-Wallis nonparametric test when applied. For the analyses of esophageal transit time, the median was considered significant for a *P* value <.05.

The study was conducted in observance to the Ethical Committee for Research in Human Beings guidelines of the UFMG including informed consent with comments about radiation exposure and its risks signed by all patients involved (Approval by the Ethical Committee of the Federal University of Minas Gerais under number ETIC 213/02).

3. Results

The distribution of patients according to the megaesophagus grade, sex, and age is depicted in Table 1.

No dysphagia complaint was recorded from control and from indeterminate form of Chagas disease group of patients. From the remaining 91 patients, 54 (59.3%) presented dysphagia. Dysphagia as the sole symptom was seen in 25 patients, whereas dysphagia associated with other symptoms was recorded in the remaining 29 patients. In this last group, constipation was the most frequent associated symptom. The frequency of dysphagia, in patients with this complaint, has shown a direct correlation with the megaesophagus grade, but not all patients with megaesophagus presented dysphagia (Fig. 1).

The time for complete esophageal emptying has varied from 8 to 129,600seconds (36 hours), with a median of 90seconds (Figs. 2–4) When patients from all groups were pooled, patients from control and indeterminate form of the disease presented a

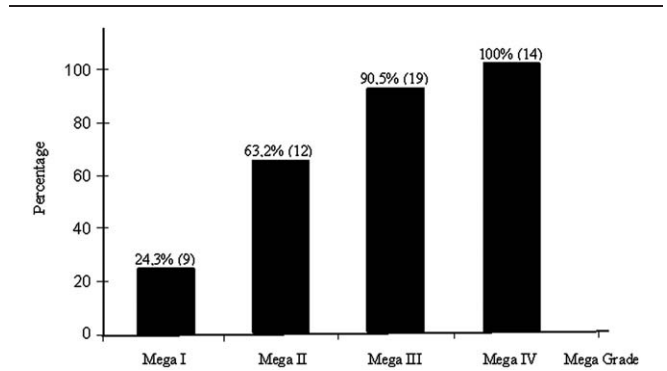


Figure 1. Correlation between frequency of dysphagia referred at actual complaint with megaesophagus grades. The columns represent the percentage of patients complaining of dysphagia. The numbers in parenthesis are the number of patients with dysphagia in the respective group.

median for esophageal emptying time of 8seconds (8–30 seconds). As the first radiograph was taken at 8seconds, this was the lowest recordable time, even if the real emptying time was <8seconds. In patients with megaesophagus but with no dysphagia, the median for esophageal emptying was 300seconds. A significant increase in the emptying time was observed in patients with both megaesophagus and dysphagia (median time, 7.200seconds, *P* <.0001 when compared to patients without dysphagia) (Table 2).

As pointed out, the transit time increased with the megaesophagus grade (Table 3).

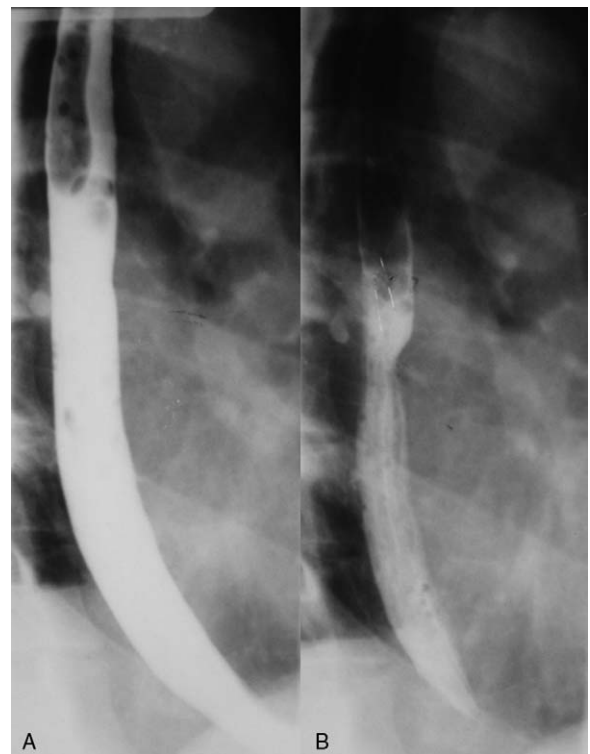


Figure 2. Illustration of esophageal emptying of a patient with chagasic megaesophagus grade I, 8seconds (A) and 30seconds (B) after barium swallow.

Table 1
Distribution of patients by megaesophagus grade, sex and age.

Grade	Sex			Age, y, descriptive measurements				
	M	F	N	Minimum	Maximum	Median	Average	SD
A, control	22	12	34	15	68	36	37.2	13.1
B, indetermin.	12	11	23	21	61	40	40.5	9.5
C, mega I	23	14	37	21	74	43	44.7	12.0
D, mega II	9	10	19	26	70	50	51.6	14.0
E, mega III	13	8	21	15	63	36	37.8	10.6
F, mega IV	7	7	14	41	76	53	55.6	10.3
Total	86	62	148	15	76	42,5	43,3	13,2

Indeterm. = indeterminate clinical form of Chagas disease. Mega = megaesophagus grade I, grade II, grade III and grade IV according to Resende Classification, N = Sum of male and female patients, SD = Standard deviation. *F* >*A*=*B*=*C*=*E*, *D*=*C* >*(A*=*B*=*E)* *P* <.001 (Kruskal-Wallis test).

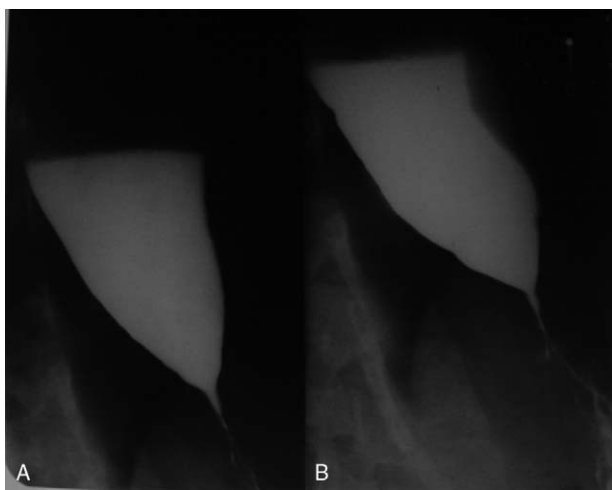


Figure 3. Esophageal emptying of a grade III chagasic megaesophagus. The film was taken 30 minutes (A) and 4 hours (B) after barium swallow.

4. Discussion

The sample used for this study is in accordance with previous reports. In Brazil, the number of younger patients with megaesophagus is decreasing and the frequency curve has shifted to older patients. This may be the result of governmental actions for prevention of infectious diseases transmission. Data from 939 patients with megaesophagus showed a median age of 55 years, the majority (86%) older than 40 years and 54% being male. The grade of megaesophagus distribution in the same publication was: 36%, 33%, 17%, and 14% corresponding to megaesophagus grades I to IV respectively.^[14]

The volume transport during clearance of the esophagus can be measured by either scintigraphy or roentgenography. The former has proven to be less invasive in terms of radioactive exposure as well as more physiological with regard to the property of the bolus. In this way, scintigraphy presents a number of advantages in

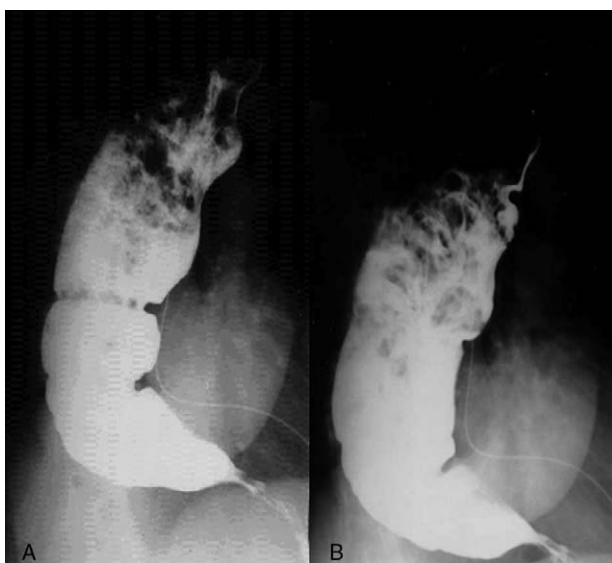


Figure 4. Illustration of chagasic megaesophagus grade IV emptying. The patient swallows the contrast and x-rays were taken 8 seconds (A) and 90 minutes (B) later. Note the image of a cardiac pacemaker wire.

Table 2

Correlation of dysphagia and esophageal emptying time (in seconds) in patients with chagasic megaesophagus.

Dysphagia	N	Emptying time, s				SD
		Minimum	Maximum	Median	Average	
Present	54	60	129,600	7200	19,855	28.1
Absent	37	60	25,200	300	1896	4.4

N=number of patients, $P < .0001$ by Kruskal-Wallis test, SD=standard deviation. Patients with the indeterminate form of Chagas disease were excluded.

comparison with roentgenography and manometry.^[23] However, the timed barium esophagogram is easily performed, inexpensive, quantitative, repeatable, comfortable for the patient, and can directly estimate the esophageal emptying.^[24] In Brazil, the initial diagnostic approach for patients with megaesophagus is barium swallow because of its low cost and because it is a method with a wide availability, even in small-community hospitals.^[9,10] The barium swallow method also allows the study of the esophageal transit time with no need for sophisticated equipments, adding important information about the esophageal function in suspected clinical chagasic megaesophagus condition.^[9,10,18]

Patients with chagasic megaesophagus present an esophageal body dilatation that worsens with time. The progression of dilatation is supported by epidemiological observation and also by demographical data in the present series, showing a significant higher age of grade IV megaesophagus patients than patients with the indeterminate form of Chagas disease or with lower grades of esophageal dilatation. Considering that all patients came from endemic areas of Chagas disease it is well possible that they were infected at early ages and showed a progressive disease during their life span.^[14,15,25] In spite of the esophageal dilatation and motility disorder seen in the chagasic megaesophagus, not all patients complain of dysphagia. A similar finding has been reported in patients with idiopathic achalasia, in which the severity of achalasia-related symptoms correlates poorly with the radiographic features.^[12] In the present study, only 59% of patients with a final diagnosis of megaesophagus presented dysphagia. This is an interesting observation if one considers that the diagnosis of chagasic megaesophagus is largely based on the clinical presentation of dysphagia along with epidemiological data.

The *T. cruzi* infection has an estimated duration of 20 to 30 years and even in patients with the asymptomatic indeterminate chronic phase of Chagas disease and in spite of no dysphagia nor esophageal dilatation, >50% have some grade of intramural denervation with impaired esophageal motility and hypertensive LES, as demonstrated by manometry.^[26]

Considering patients with huge esophageal dilatation, a striking aspect of our results is the long esophageal emptying time. They can manage to survive possibly by adapting their alimentary habits to their clinical condition, in which the esophageal transit time for a definite meal might last for up to 36 hours.

The study has also shown a correlation between the severity of dilatation with the increase in esophageal transit time and with the frequency of dysphagia. However, some patients with grade III megaesophagus may not complain dysphagia by the time of consultation, although this symptom was said by them to be present long time ago.

Furthermore, the esophageal emptying time, as demonstrated by barium swallow, varies among patients with similar esophageal dilatation.

Table 3**Esophageal transit time (in seconds) according to the study groups.**

Grade	N (%)	Esophageal transit time descriptive measurement, s		Esophageal transit time analysis, s		
		Minimum	Maximum	Median	Average	SD
A, control	34 (23)	8	30	8	15.3	10.4
B, indeter	23 (16)	8	30	8	9.9	6.3
C, mega I	37 (25)	60	7200	300	831.9	1679.9
D, mega II	19 (13)	60	25,200	1,800	4781.1	7136.7
E, mega III	21 (14)	900	86,400	7200	18,685.7	25,150.0
F, mega IV	14 (9)	7200	129,600	33,300	44,485.7	33,663.3
Total	148 (100)	8	129,600	90	7698.2	19,367.3

Mega = megaesophagus grade I, grade II, grade III and grade IV according to Resende Classification, N (%) = Number and percentage of patients, SD = standard deviation. $F > E > D > C > (B = A)$, $P < .001$ (Kruskal-Wallis test).

What seems to be important in the study is the finding of patients with severe dysphagia complaint with low grade of esophageal dilatation, as well as patients with grade III megaesophagus with no dysphagia complaint. So, it was not possible to establish a direct clear-cut correlation between grade of megaesophagus and dysphagia what might have important clinical implication as far as indication for surgical treatment is concerned. The progressive esophageal denervation may lead to lack of sensory perception of food delivery to the stomach. The data do not allow the correlation between the esophageal transit time and the tendency to progress into more advanced stages of megaesophagus. However, it was clear that in patients with more advanced grades of mega esophagus the transit time increases.

It might well be possible that the slow progression of lesions induces an adaptation of patients to this condition over the long years of evolution of chagasic megaesophagus. It is also possible that a more pronounced neuronal destruction seen in more severe grades of megaesophagus might lead to desensitization to food-induced dilatation with consequent lack of conscious perception (or adaptation) of the swallowing difficulty. If no dysphagia complaint is referred, one may postulate that the incidence of megaesophagus in the population living in endemic areas of Chagas disease might be higher than we are aware of. Therefore, lack of dysphagia complaint may not exclude by itself the diagnosis of megaesophagus and further investigations mainly in patients from endemic areas or presenting other signs of Chagas disease are needed.

In spite of showing a functional aspect of the megaesophagus resulting in longer esophageal transit time, the present data were unable to show any practical advantage over the classical static roentgenography. This was mainly because of the fact that the degree of esophageal dilatation keeps a correlation with the emptying time and also with the occurrence of dysphagia, although about 40% of patients with radiological evidences of esophageal involvement by Chagas disease do not refer dysphagia.

Patients with the indeterminate form of the disease show neural plexus destruction without macroscopically detected esophageal dilatation.^[20,22] These patients did not complain of dysphagia. This fact seems to indicate that large amounts of plexus destruction need to occur before any functional or gross anatomic alteration of the esophagus can be detected.^[5,16,17] The other indication that can be withdrawn from this study is that the lesions are progressive and a long delay may be expected before any anatomic impairment to function can cause symptoms.^[20,22]

5. Conclusions

Patients with Chagas disease may present megaesophagus. The cases classified as indeterminate clinical form present neither dysphagia nor esophageal dilatation.

The dilation of the esophagus in patients with a final diagnosis of megaesophagus in general correlates with the severity of dysphagia. However, dysphagia only occurs in 60% of patients. The remaining 40% even with advanced degree of dilatation may not report dysphagia.

The esophageal transit time in patients with the indeterminate form of the disease is not different from normal control non-chagasic patients. Patients with megaesophagus have an esophageal transit time longer than control individuals. Also in patients with more pronounced megaesophagus, the esophageal transit time tends to be longer than those with less severe megaesophagus, in spite of a wide range variation of transit time in patients with the same grade of megaesophagus.

Patients with grade IV megaesophagus are older than other groups of graded patients, suggesting that the severity of esophageal dilatation increases with time.

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