Revista da Sociedade Brasileira de Medicina Tropical
Journal of the Brazilian Society of Tropical Medicine
Vol.:52:e20180258: 2019
doi: 10.1590/0037-8682-0258-2018

Major Article

Agreement between upper endoscopy and esophagography in the diagnosis of megaesophagus in Chagas disease

***Fernando de Barros*[1], *João Carlos de Almeida Soares*[1], *Fernando Prado de Barros*[1], *Luiz Henrique Conde Sangenis*[1], *Gilberto Marcelo Sperandio da Silva*[1], *Ana Beatriz Monteiro Fonseca*[2], *Alejandro Marcel Hasslocher-Moreno*[1], *Andrea Silvestre de Sousa*[1], *Roberto Magalhães Saraiva*[1] *and Mauro Felippe Felix Mediano*[1],[3]**

[1]. Instituto Nacional de Infectologia Evandro Chagas, Fundação Oswaldo Cruz, Rio de Janeiro, RJ, Brasil.
[2]. Instituto de Matemática e Estatística, Universidade Federal Fluminense, Niterói, RJ, Brasil.
[3]. Instituto Nacional de Cardiologia, Ministério da Saúde, Rio de Janeiro, RJ, Brasil.

Abstract

Introduction: The diagnosis and classification of megaesophagus can be challenging in patients with Chagas disease. The present study aimed to evaluate the agreement between upper endoscopies and esophagographies for the diagnosis and classification of megaesophagus in Chagas disease. **Methods:** A cross-sectional study of 50 patients with Chagas disease with upper digestive symptoms was undertaken. Esophagography and upper endoscopy exams were performed to compare diagnoses. Statistical analysis included sensitivity and specificity used to evaluate the diagnostic accuracy of upper endoscopies, and measures of agreement: linearly weighted Kappa (κ_w) and Cohen`s classical Kappa (κ) coefficients with 95% confidence intervals (95% CI). **Results:** Twenty-three patients (46%) were diagnosed with megaesophagus by esophagography. The upper endoscopy sensitivity and specificity for megaesophagus diagnosis were 100% and 33.3%, respectively. Regarding megaesophagus classifications, there was a substantial agreement between the two exams (κ_w = 0.622; 95% CI: 0.498 to 0.746). Within megaesophagus groups, agreement for group I was slight (κ = 0.096; 95% CI: 0.000 to 0.403); for group II, substantial (κ = 0.703; 95% CI: 0.456 to 0.950); and for groups III and IV, inconclusive (κ = 0.457; 95% CI: 0.000 to 0.967; κ = 0.540; 95% CI: 0.035 to 1.000, respectively**).** **Conclusions**: Upper endoscopy has a high sensitivity, but a low specificity to diagnose megaesophagus. Agreement between the two exams varies depending on the megaesophagus grade. Thus, upper endoscopy can be used in the diagnostic workup of a possible Chagas disease megaesophagus, but all identified cases should undergo esophagography.

Keywords: Esophageal achalasia. Chagas disease. Esophageal motility disorder.

INTRODUCTION

Digestive involvement in Chagas disease may occur in up to 15 – 21% of patients[1,2]. However, megaesophagus is often not diagnosed due to several reasons such as a lack of information regarding the patient, health professionals missing the symptoms of Chagas disease, nonspecific symptoms, and a lack of adequate diagnostic exams in health units. This diagnostic delay directly affects the post-surgical outcome since long-term outcomes worsen with the degree of stenosis and dilatation[3].

Esophageal involvement in Chagas disease can be determined by esophagography with good accuracy according to the classification by Rezende[4]. The changes that may elucidate the diagnosis and degree of esophageal involvement include altered motility, delayed emptying velocity, changes in caliber, presence of air-fluid levels, and thinning of the esophagogastric junction. Therefore, the initial diagnostic workup of patients with a possibility of Chagas disease must include an esophagography, but in practice it is usually replaced by an upper endoscopy, which has some limitations especially for inexperienced practitioners[5]. Furthermore, the diagnostic accuracy of an upper endoscopy for megaesophagus is still

Corresponding author: Mauro Felippe Felix Mediano.
e-mail: mffmediano@gmail.com
ORCID: 0000-0001-6369-3631
Received 18 June 2018
Accepted 25 January 2019

unknown. However, an upper endoscopy is useful in the diagnosis of associated diseases such as candidiasis and to exclude the presence of malignancies.

The objectives of this study were to evaluate the accuracy of upper endoscopies for the diagnosis of megaesophagus and to evaluate the agreement between upper endoscopies and esophagographies for the classification of megaesophagus in patients with Chagas disease.

METHODS

Study population

This was a cross-sectional study of patients with Chagas disease who were followed at the Evandro Chagas National Institute of Infectious Diseases from the Oswaldo Cruz Foundation (INI/Fiocruz) and presented with continuous or intermittent dysphagia for liquids or solids. The diagnosis of Chagas disease was confirmed by two simultaneous serological tests (an enzyme-linked immunosorbent assay and an indirect immunofluorescence assay). The study was approved by the Research Ethics Committee at the INI/Fiocruz under number 832.303.

Participants included in the study underwent a clinical evaluation performed by a single surgeon who assessed symptoms compatible with megaesophagus during medical appointments. Afterwards, patients underwent endoscopy, by a single endoscopist, followed by esophagography (6 months maximum interval between exams).

To date, there are no defined endoscopic criteria and parameters for the classification of megaesophagus published in the literature. Therefore, to evaluate the degree of involvement, the reports of the Endoscopy Service were subjectively based on the following findings:

1. Group I - Greater salivary retention, presence of reduced peristaltic waves and no dilatation;
2. Group II - Mild dilation with greater retention of liquids and possibly food residue;
3. Group III - Upstream dilatation with difficulty of passage of the endoscope through the cardia; and
4. Group IV - Clear esophageal tortuosity mainly in the distal third of the esophagus.

The parameters used for assessment and classification of megaesophagus during esophagography were determined according to the classification of Rezende[4] as follows (**Figure 1**):

1. Group I – Esophagus apparently with a normal caliber to the radiological examination. Slow traffic. Small retention on radiography taken one minute after ingestion of barium sulfate;
2. Group II – Esophagus with small to moderate increase in caliber. Appreciable contrast retention. Frequent presence of tertiary waves, with or without association with hypertonia of the esophagus;
3. Group III - Esophagus with a great enlargement of diameter. Reduced motor activity. Hypotonia of the lower esophagus. Great contrast retention; and
4. Group IV - Dolicomegaesophagus. Esophagus with great retention capacity, stretched, bending over the diaphragmatic.

Statistical analysis

Endoscopic validity for detecting megaesophagus was evaluated through sensitivity and specificity measurements, considering esophagography as the gold standard[6]. The analysis of agreement between esophagography and endoscopy was performed using the linearly weighted Kappa (κ_w)[7], since they have an ordinal scale with 5 levels (normal and groups I, II, III, and IV). When there are 5 categories, the weights in the linear set used to calculate κ_w, are: 1, 0.75, 0.50, 0.25, and 0 when there is a difference of 0 (total agreement) or 1, 2, 3, and 4 categories between esophagography and endoscopy diagnostics, respectively. Cohen´s classical Kappa (κ) coefficient was used for concordance analysis, by collapsing the original 5 x 5 contingency table into five 2 x 2 tables where each category is compared with all others[8]. We used the scale presented in the work of Landis and Koch for interpretation of all Kappa coefficients where 0 to 0.20 is slight, 0.21 to 0.40 is fair, 0.41 to

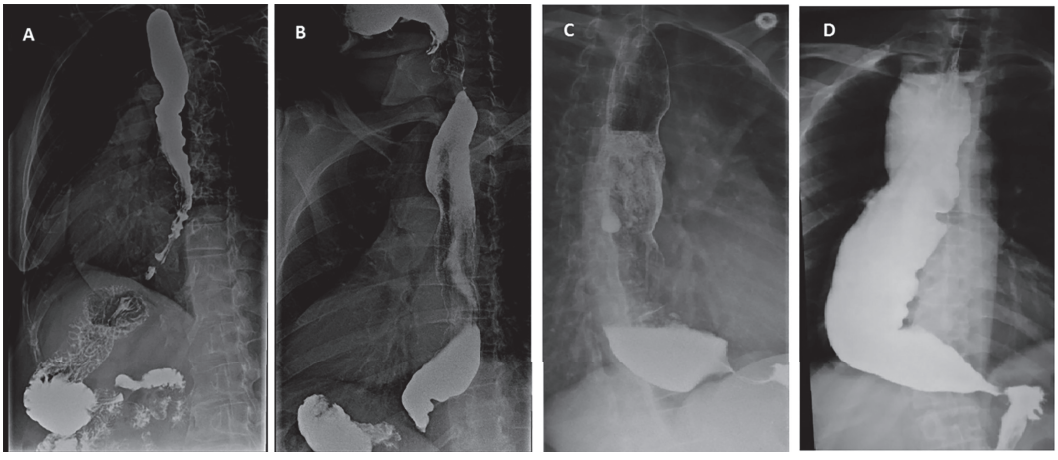

FIGURE 1: A = Group I, B = Group II, C = Group III, D = Group IV.

0.60 is moderate, 0.61 to 0.80 is substantial, and 0.81 to 1.00 is perfect[9]. The 95% confidence intervals (95% CI) for κ_w and κ coefficients were also presented. The analyses were performed using the R language, the vcd package, and the Kappa and confint functions.

RESULTS

Altogether 50 patients (33 women and 17 men) with a mean age of 49 years with Chagas disease and dysphagia symptoms were analyzed. Twenty-three patients (46%) were diagnosed with megaesophagus by esophagography. Since all patients with megaesophagus were detected by both exams, the upper endoscopy sensitivity for megaesophagus diagnosis was exactly 100%. On the other hand, only 9 patients (out of twenty-seven) were considered negative for megaesophagus by both methods, resulting in 33.3% specificity. Among 18 normal subjects by esophagography, 17 were misdiagnosed with grade I megaesophagus and 1 subject was misdiagnosed with grade II megaesophagus by upper endoscopy (**Table 1**).

Twenty-five patients (50%) had esophagography results concordant with upper endoscopy as shown in Table 1. Using linearly weighted Kappa coefficients, a substantial concordance (K_w = 0.622; 95% CI: 0.498 – 0.746) between these diagnostic methods was observed. **Table 2** summarizes the comparison of the samples according to the diagnostic method (upper endoscopy vs. esophagography). Regarding the concordance analysis by group using classical Kappa coefficients within each category, 27 patients (54%) had a normal result report according to esophagography vs. only 9 (18%) according to endoscopy with fair agreement (κ = 0.315; 95% CI: 0.062 – 0.568). In group I, 7 (14%) cases were found using esophagography vs. 21 (42%) using endoscopy with slight agreement (κ = 0.096; 95% CI: 0.000 – 0.403). In group II, 8 (16%) vs. 13 (26%) cases were found by these diagnostic methods, respectively, with substantial agreement (κ = 0.703; 95% CI: 0.456 – 0.950). In group III, 4 (8%) vs. 4 (8%) cases, with inconclusive agreement were found due to a wide 95% CI (κ = 0.457; 95% CI: 0.000 – 0.967). Finally, in group IV, 4 (8%) vs. 3 (6%) cases, also with inconclusive agreements due to a wide 95% CI (κ = 0.540; 95% CI: 0.035 – 1.000), were observed by esophagography and endoscopy, respectively.

DISCUSSION

Chagas disease is a chronic and progressive disease and serious lesions can affect the digestive tract[10]. However, most health professionals are not appropriately trained in the clinical management, diagnosis, and treatment of this condition as it is a neglected disease. Thus, delay or even non-diagnosis can allow irreversible digestive tract injuries requiring more invasive operations as the disease progresses.

Chagas megaesophagus is the most common form of gastrointestinal involvement, affecting any age, sex, and stage of the disease. Initial symptoms may be quite nonspecific such as nocturnal coughing, hypersalivation, coughing sensation after eating, and weight loss which further complicates the diagnosis[11]. More classic signs and symptoms include dysphagia

TABLE 1: Agreement results between methods for all 50 patients with dysphagia included in the study.

Esophagogram	Endoscopy	Match
NORMAL	GROUP I	No
NORMAL	NORMAL	Yes
GROUP II	GROUP II	Yes
NORMAL	GROUP I	No
GROUP III	GROUP II	No
NORMAL	GROUP I	No
NORMAL	GROUP I	No
GROUP II	GROUP II	Yes
NORMAL	NORMAL	Yes
NORMAL	GROUP I	No
GROUP I	GROUP I	Yes
NORMAL	NORMAL	Yes
NORMAL	GROUP I	No
GROUP I	GROUP II	No
GROUP III	GROUP III	Yes
GROUP II	GROUP II	Yes
GROUP IV	GROUP IV	Yes
NORMAL	GROUP I	No
GROUP IV	GROUP III	No
NORMAL	GROUP I	No
GROUP IV	GROUP III	No
NORMAL	GROUP I	No
GROUP II	GROUP II	Yes
GROUP II	GROUP II	Yes
NORMAL	NORMAL	Yes
NORMAL	GROUP I	No
GROUP I	GROUP I	Yes
GROUP I	GROUP II	No
NORMAL	NORMAL	Yes
GROUP III	GROUP III	Yes
GROUP III	GROUP IV	No
NORMAL	GROUP I	No
NORMAL	NORMAL	Yes
NORMAL	GROUP I	No
NORMAL	GROUP II	No
GROUP IV	GROUP IV	Yes
NORMAL	GROUP I	No
NORMAL	NORMAL	Yes
NORMAL	NORMAL	Yes
NORMAL	GROUP I	No
NORMAL	NORMAL	Yes
GROUP II	GROUP II	Yes
GROUP I	GROUP II	No
GROUP I	GROUP I	Yes
NORMAL	GROUP I	No
GROUP II	GROUP II	Yes
GROUP I	GROUP I	Yes
NORMAL	GROUP I	No
NORMAL	GROUP I	No
GROUP II	GROUP II	Yes
	YES	25
	NO	25

TABLE 2: Comparative results between upper endoscopy vs. esophagography.

	Upper Endoscopy					
	Normal	**Group I**	**Group II**	**Group III**	**Group IV**	**Total**
Esophagography						
Normal	9	17	1	0	0	27
Group I	0	4	3	0	0	7
Group II	0	0	8	0	0	8
Group III	0	0	1	2	1	4
Group IV	0	0	0	2	2	4
Total	**9**	**21**	**13**	**4**	**3**	**50**

for liquids or solids, weight loss, odynophagia, choking, and even recurrent pneumonia making a diagnostic workup mandatory in such cases[12].

The diagnostic assessment usually begins with an upper endoscopy due to the availability of this exam in most hospitals, but this is an operator-dependent examination without a standardized, validated grading scale for megaesophagus. However, symptomatic Chagas disease patients must undergo this exam since diseases associated with or mimicking achalasia, such as neoplasms, infections, and other mucosal changes, need to be excluded. Although the use of endoscopy, along with high-resolution manometry for the diagnosis and classification of achalasia has been proposed to evaluate patient candidates for peroral endoscopic myotomy[13], there is no endoscopic classification to assess the degree of megaesophagus due to Chagas disease by endoscopic methods.

In our study, we found that upper endoscopy has a high sensitivity for the diagnosis of chagasic megaesophagus, but a very low specificity. This may be due to the criteria we used to diagnose and estimate the classification of megaesophagus by endoscopy which includes the absence of peristalsis during the examination, non-relaxation of the lower esophageal sphincter, non-passage of the endoscope to the stomach, salivary or food retention, and dilation. During the endoscopy, a moderate amount of air is injected so that there is sufficient space for the examination, which will slightly distend the organ. In addition, the image generated by the device is slightly increased and can result in an inaccurate diameter estimate of the megaesophagus. The endoscopy device itself is thicker than the contrast used to do the esophagography and therefore more difficult to get in the stomach. All of these factors might justify the high number of false positives on endoscopy seen in megaesophagus and the low concordance between an upper endoscopy and an esophagography for megaesophagus grade I classifications. Therefore, whenever Chagas disease megaesophagus, especially grade I, is diagnosed using endoscopy, the diagnostic workup should include an esophagography in order to avoid misdiagnoses. Moreover, manometry should also be included in the diagnostic workup as it has the sensitivity to identify the problem according to its pathophysiology (nerve and muscle injury of the lower esophageal sphincter) and is considered a diagnostic gold standard[14]. Manometry is essential for pre-operative evaluations since the type of operation is defined depending on the function of the esophagus thus avoiding very tight anti-flow valves that lead to dysphagia or incompetent valves that will lead to gastroesophageal reflux after myotomy[15]. However, many health institutions do use manometry, which delays a correct diagnosis.

Based on our findings, esophagography should still be the exam chosen to classify megaesophagus, as the concordance between exams for megaesophagus classification varies from slight to substantial depending on the megaesophagus group. The dynamics and the number of variables evaluated by esophagography provide more information than just an upper endoscopy. With real-time radioscopy or recorded movies, esophagography allows visualization of important changes such as motility disorders, the presence of tertiary waves, delayed emptying of the esophagus, changes in caliber, the presence of barium and liquid levels, and the presence of the "bird's beak" signal, which is a distal and symmetrical tapering contrast sign[16]. Nonetheless, in cases of megaesophagus groups III or IV, the endoscopist might have a higher percentage of correct grading responses as some parameters are better identified using endoscopy such as lack of peristalsis in the esophageal body, tortuosity, large amounts of retained food, and the non-passage of the endoscope to the stomach.

CONCLUSION

Upper endoscopy has a high sensitivity, but a low specificity for the diagnosis of megaesophagus due to Chagas disease in comparison to esophagography. Moreover, the agreement between endoscopy and esophagography for megaesophagus classifications has a wide variation depending on the megaesophagus grade. Therefore, an upper endoscopy can be used in the diagnostic workup of Chagas disease patients with possible megaesophagus, but confirmatory exams are needed whenever a case is identified, especially, if the case is classified as a grade I or II by endoscopy. Therefore, after a possible megaesophagus is identified using endoscopy, esophagography should also be performed to confirm the diagnosis and grade.

Acknowledgments: The authors thank the Evandro Chagas National Institute of Infectious Diseases for clinical and administrative support.

Conflicts of Interest: The authors declare no conflicts of interest.

Financial Support: This study was supported by the Evandro Chagas National Institute of Infectious Diseases.

REFERENCES

1. Pinazo MJ, Lacima G, Elizalde JI, Posada EJ, Gimeno F, Aldasoro E, et al. Characterization of digestive involvement in patients with chronic T. cruzi infection in Barcelona, Spain. PLoS Negl Trop Dis. 2014;8(8): e3105. e Collection 2014 Aug.
2. Prata A. Clinical and epidemiological aspects of chagas disease. Lancet Infect Dis. 2001;1(2):92-100.
3. Downs DJ, Jadick G, Swaid F, Ross SB, Rosemurgy AS. Age and Achalasia: How Does Age Affect Patient Presentation, Hospital Course, and Surgical Outcomes? Am Surg. 2017;83(9):952-61.
4. Rezende JM. Classificação radiológica do megaesôfago. Rev Goiana Med. 1982;28:187-91.
5. Uppal DS, Wang AY. Update on the endoscopic treatments for achalasia. World J Gastroenterol. 2016;22(39):8670-83.
6. Bland M. An Introduction to Medical Statistics, 2000. 3rd. Edition, Oxford, Oxford University Press.
7. Kvalseth TO. An alternative interpretation of the linearly weighted Kappa coefficients for ordinal data. Psychometrika 2018; 83(3):618-27.
8. Spitzer RL, Cohen J, Fleiss JL, Endicott J. Quantification of agreement in psychiatric diagnosis. Archives of General Psychiatry 1967;17:83-7.
9. Landis, J.R., Koch, G.G. The measurement of observer agreement for categorical data. Biometrics. 1977;33(1):159-74.
10. Pérez-Molina JA, Molina I. Chagas disease. Lancet 2018;391(10115): 82-94.
11. de Oliveira RB, Troncon LE, Dantas RO, Menghelli UG. Gastrointestinal manifestations of Chagas' disease. Am J Gastroenterol. 1998;93(6):884-9.
12. Boeckxstaens GE, Zaninotto G, Richter JE. Achalasia. Lancet. 2014;383: 83-93.
13. Zhang WG, Linghu EQ, Chai NL, Li HK. Ling classification describes endoscopic progressive process of achalasia and successful peroral endoscopy myotomy prevents endoscopic progression of achalasia. World J Gastroenterol. 2017;23(18):3309-14.
14. Smith I, Kahaleh M. An Update on Current Management Strategies for Achalasia and Future Perspectives. J Clin Gastroenterol. 2018;52(4):277-86.
15. Sato H, Takahashi K, Mizuno KI, Hashimoto S, Yokoyama J, Hasegawa G, et al. Esophageal motility disorders: new perspectives from high-resolution manometry and histopathology. J Gastroenterol. 2018;53(4):484-93.
16. Krill JT, Naik RD, Vaezi MF. Clinical management of achalasia: current state of the art. Clin Exp Gastroenterol. 2016;9:71-82.