Original Article

Alterations to Tissue Doppler in Patients with Acute Form of Chagas Disease

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Summary

Background: Recently there has been an increased number of cases of acute Chagas disease primarily caused by oral transmission. Most patients have a good outcome, presenting symptoms consistent with systemic infectious process, but no significant cardiac abnormalities on physical examination, electrocardiogram and echocardiogram.

Objective: To evaluate echocardiographic changes with tissue Doppler analysis in patients with acute Chagas disease.

Methods: We evaluated patients with acute Chagas disease confirmed by cytological examination. These patients underwent a physical examination, eletrocardiogram and transthoracic echocardiography, and compared with a control group.

Results: We evaluated 12 patients with acute Chagas disease and 15 subjects in the control group. Variables that showed significant differences were waves S 'side of LV (DCA = 0.09 ± 0.02m/sec; CG = 0.11 ± 0.02 m/sec; p = 0.024); and 'side (DCA = 0.13 ± 0.03 m/sec; CG = 0.18 ± 0.03 m/sec; p = 0.001); Septal E 'LV (DCA = 0.10 ± 0.03 m/sec; CG = 0.14 ± 0.03 m/sec; p = 0.008), A' lateral LV (DCA = 0.08 ± 0.03 m/sec; CG = 0 12 ± 0.01 m/sec; p = 0,003), S wave 'RV (DCA = 0.12 ± 0.02 m/sec; CG = 0.17 ± 0.02 m/sec; p < 0.001) and TAPSE (DCA = 1,95 cm ± 0.41; CG = 2.37 ± 0.25 cm; p = 0.006).

Conclusions: In patients with acute Chagas disease, even when present benign, there may be subclinical alterations detected primarily by tissue Doppler. These changes may be important in the treatment of acute and its long-term evolution. (Arq Bras Cardiol: Imagem cardiovasc. 2016;29(4):112-117)

Keywords: Chagas Cardiomyopathy; Myocardial Contraction; Case-Control Studies, Chagas Disease.

Introduction

Chagas' disease (CD) or American trypanosomiasis is an infectious disease caused by the protozoan *Trypanosoma cruzi*. It occurs throughout the American continent, especially in the southern cone countries, where it is estimated that about 7 to 8 million people are infected.[1]

The usual form of transmission is the vector. However, there are other forms of contagion, such as oral contagion (intake of acai juice, for example), contaminated blood transfusion, organ transplant and through the placenta.[2,3]

The Chagas' disease is characterized by an acute phase lasting 4 to 6 weeks on average, during which the individual experiences nonspecific symptoms, making diagnosis difficult and highly dependent on suspicion; and a chronic phase of long latent evolution, which manifests 10 to 30 years after primary infection, whose cardiac involvement may be associated with heart failure, arrhythmia or thromboembolic events.[1-4]

The acute phase is not diagnosed in over 90% of cases of vector transmission. Acute myocarditis is clinically apparent in approximately 1% of infected individuals. It is fatal in nearly 10% of them, due to acute HF, meningitis and, rarely, sudden death.[5,6]

Echocardiographic evaluation plays an important role in the initial evaluation and whenever there is a change in the clinical status of patients with Chagas cardiomyopathy. The typical echocardiographic abnormalities found in the chronic form include segmental contractility disorders mainly compromising the inferior and posterior left ventricular wall and the apical segment, either isolated or associated with varying degrees of dilatation and systolic dysfunction. In the acute phase, special attention is given when there is pericardial effusion due to the risk of tamponade.[5]

Thorough cardiac evaluation in patients with the acute form of CD and with no ECG abnormalities and two-dimensional

echocardiography is of paramount importance for the detection of subclinical disorders that may be relevant in the long term evolution of these patients. The objective of this study was to evaluate echocardiographic abnormalities using tissue Doppler in patients with acute Chagas' disease.

Methodology

Cross-sectional case-control study with data collection from February 2014 to January 2015. In this period, 27 individuals were evaluated and divided into two groups: 1) Control Group (CG) - composed of 15 blood donors with negative serology for CD and no diagnosis of chronic degenerative heart diseases or illnesses, such as systemic arterial hypertension (SAH), diabetes mellitus (DM), etc.; 2) Acute Chagas' disease (ACD) - composed of 12 patients with clinical and epidemiological history and direct microscopic examination (thick blood smear) positive for CD.

Given the small number of cases of ACD today, and the scarcity of publications on the subject, the "sample N" for research was not calculated. We chose to evaluate all patients on whom it was possible to perform echocardiogram with tissue Doppler, as some patients live in areas of difficult access.

Individuals included in the study should necessarily present: 1) direct microscopic examination (thick blood smear) positive for Chagas' disease; 2) absence of clinical or laboratory evidence of any other heart disease other than Chagas' disease or other systemic disease such as hypertension, diabetes mellitus etc. These patients underwent physical examination, electrocardiography and transthoracic echocardiography scans and were compared with a control group undergoing the same procedures.

Two-dimensional transthoracic echocardiography was performed at rest complemented with M-mode and pulsed tissue color Doppler, according to the recommendations of the American Society of Echocardiography (ASE) using a GE Vivid 3 device.[7] The heart cavities were measured and the systolic and diastolic ventricular functions were evaluated.

The measures of the cavities were left ventricular diastolic diameter (LVDD), left ventricular systolic diameter (LVSD), right ventricular diastolic diameter (RVDD). Left ventricular systolic function was assessed by left ventricular ejection fraction by the Simpson's method (LVEF) and systolic velocity of the lateral mitral annulus (lateral S'). Right ventricular systolic function was assessed by the systolic velocity of the tricuspid annulus (S'_VD) and by the tricuspid annulus plane systolic excursion (TAPSE).

Left ventricular diastolic function was assessed by the E wave velocity (early ventricular filling) and A mitral wave (atrial filling wave), mitral E wave deceleration time (DT), the ratio of mitral flow E wave to lateral mitral annulus E wave on tissue Doppler (E/E' ratio) and diastolic velocity of lateral and septal mitral annulus (lateral E' and septal E'). Isovolumetric relaxation time (IRT) is an additional index of diastolic function defined as the time between the aortic valve closure and mitral valve opening.

The left and right ventricular myocardial performance index (LV MPI and RV MPI) was calculated to evaluate the global ventricular function (combination of systolic and diastolic function). This index, also known as "Tei index," was calculated using the following equation: ICT = isovolumetric contraction time + isovolumetric relaxation time/Ejection time.

To analyze the categorical variables, Fisher's exact test was used. For the quantitative analysis, all numerical variables were described as mean and standard deviation. Comparison between groups was performed using the Student's t test and if the variables did not meet the assumption of normality, the Mann-Whitney-Wilcoxon test was used. Differences were considered significant with p value <0.05. The R and Minitab software applications were used for statistical analysis.

Results

There was a higher proportion of men (CG:11, DCA:7) than women (CG: 4, ACD: 5) in both groups. There was no significant difference between the groups regarding age and gender (Table 1).

All patients with ACD were from the interior of Amazonas and 58% of them were contaminated by acai juice (oral contagion), whereas the vector form was found in 17%. In the other patients (25%), it was not possible to identify the mode of transmission (Table 1).

The most common symptoms found in patients with ACD were fever (75%), headache (58%), myalgia (25%), dizziness (17%), chills (17%), vomiting (17%), dyspepsia (8%), rashes (8%), asthenia (8%) and arthralgia (8%). No patient developed any symptoms of heart failure (Figure 1).

All patients had normal ECG and two-dimensional echocardiography with no abnormalities. However, tissue Doppler and chest echocardiography at rest of the acute CD group revealed abnormalities compared to the control group.

The lateral mitral annulus systolic velocity (mitral S'), atrial filling (mitral A') and early lateral mitral annular diastolic velocity (lateral E') and septal mitral annular diastolic velocity (septal E') were lower in the ACD group compared to control. The tricuspid annular systolic velocity (tricuspid S') was lower in the acute CD group compared to control.

In addition, the tricuspid annulus plane systolic excursion (TAPSE) was also smaller in the acute CD group compared to control.

The measurements obtained on transthoracic echocardiography are described in Table 2.

Discussion

In this study, we used tissue Doppler imaging to quantify myocardial motion speeds in normal individuals and in patients with ACD. Tissue Doppler revealed significant reduction in the septal and lateral E', mitral A', lateral mitral S' and RV S' wave velocity in patients with ACD compared to normal individuals. Besides, there was a significant difference compared to TAPSE. With these results, using tissue Doppler, it was possible to detect subclinical abnormalities in myocardial velocities not perceptible on two-dimensional visual analysis, which can have great prognostic significance.

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Table 1 – Distribution of patients according to age and mode of transmission of ACD

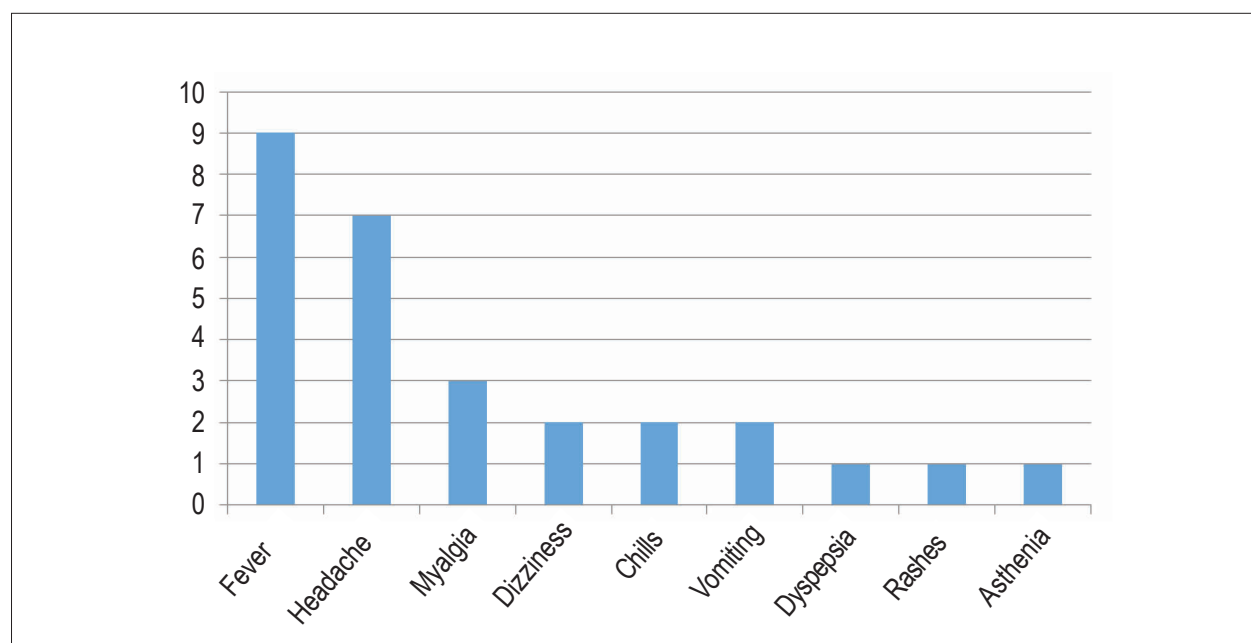| Variable	Group		
	Control Mean (± SD)	ACD Mean (± SD)	p-value
Age	43.8 (7.42)	37.5 (18.65)	0.307
Gender	N (%)	N (%)	
Male	11 (73.5)	07 (58.0)	0.447
Female	04 (26.5)	05 (42.0)	
Transmission		N (%)	
Oral		07 (58.0)	
Vector		02 (17.0)	
Unknown		03 (25.0)	

Figure 1 – *Symptoms experienced by patients with ACD.*

Echocardiography is a preparatory element of high value in the initial approach of patients with Chagas' disease, as it allows a morphological and functional assessment of the heart in a noninvasive innocuous manner at relatively low costs, besides presenting a high level of diagnostic reliability.[8]

The incorporation of tissue Doppler technique to conventional echocardiography allowed to evaluate systolic and diastolic myocardial functions in more detail and in a global and regional manner.[9,10]

The possibility of early detection of cardiac involvement, even if it is subclinical and incipient on echocardiography in Chagas' disease is extremely important. Using tissue Doppler to assess patients with normal electrocardiography

(ECG) and two-dimensional echocardiography can demonstrate subtle changes that characterize the inflammatory myocardial process and can identify a group of patients at higher risk of progressing to more advanced stages of the clinical form of Chagas' disease.

A series published in Venezuela on echocardiography in ACD includes 58 patients.[11] Abnormal two-dimensional echocardiography scans were present in 52% and pericardial effusion was seen in 42%. In 10 of the 12 patients with heart failure (HF), stroke was moderate to severe. Left ventricular ejection fraction (LVEF) was normal (63%). Apical or anterior dyskinesia was found in 21% and only 6% showed LV dilation. In two other articles,[12,13] pericardial effusion was detected in 7 out of 8 patients, 3 of whom were in tamponade.

Table 2 – Measurements obtained by transthoracic echocardiography at rest

ECHO measures	Control (n = 15) Mean ± SD	Acute CD (n = 12) Mean ± SD	*p* value
LVDD (mm)	46.90 ± 5.59	44.92 ± 4.36	0.312
LVSD (mm)	26.80 ± 4.55	24.00 ± 3.31	0.081
RVDD (mm)	16.66 ± 1.75	18.75 ± 3.57	0.083
LVEF (%)	74.66 ± 4.60	77.25 ± 4.95	0.178
E wave (m/sec)	0.74 ± 0.15	0.78 ± 0.23	0.608
A wave (m/sec)	0.53 ± 0.18	0.59 ± 0.19	0.509
EA ratio	1.45 ± 0.34	1.52 ± 0.75	1.112
IRT	83.80 ± 9.66	95.75 ± 21.73	0.229
Dec T (sec)	191.20 ± 48.53	165.83 ± 89.40	0.389
Septal E' wave (m/sec)	0.14 ± 0.03	0.10 ± 0.03*	0.008
Lateral E' wave (m/sec)	0.18 ± 0.03	0.13 ± 0.03*	0.001
Mitral A' wave(m/sec)	0.12 ± 0.01	0.08 ± 0.03*	0.003
Mitral S' wave (m/sec)	0.11 ± 0.02	0.09 ± 0.02*	0.024
EE' ratio	4.74 ± 1.41	6.05 ± 1.84	0.055
LVMPI	0.39 ± 0.11	0.37 ± 0.08	0.676
RVMPI	0.32 ± 0.11	0.38 ± 0.13	0.267
TAPSE (mm)	23.70 ± 0.25	19.50 ± 0.41*	0.006
RV_S' (m/sec)	0.17 ± 0.02	0.12 ± 0.02*	<0.001

*LVDD: left ventricular diastolic diameter; LVSD: left ventricular systolic diameter; RVDD: right ventricular diastolic diameter; LVEF: left ventricular ejection fraction, EA ratio : mitral flow E wave/A wave ratio; IRT: isovolumetric relaxation time; Dec T: mitral E wave deceleration time; Septal E': early diastolic septal mitral annular velocity; Lateral E': early diastolic lateral mitral annular velocity; Mitral A': systolic atrial contraction velocity at the mitral annulus; Mitral S' : lateral mitral annular systolic velocity; E/E' ratio : ratio of the mitral annular E wave to the lateral mitral annular E' wave; LVMPI: left ventricular myocardial performance index; RVMPI: right ventricular myocardial performance index; TAPSE: tricuspid annulus plane systolic excursion; Mitral S': systolic velocity at the lateral mitral annulus on tissue Doppler; RV_S': right ventricular systolic wave velocity; m/sec: meters per second. Values expressed as mean (±SD). * p<0.05 compared to control group.*

In another series of 233 cases of ACD from Pará, Amapá and Maranhão, pericardial effusion occurred in almost half the cases,[13] demonstrating the need to conduct echocardiography to rule out a rapidly treatable cause of pericardial effusion and evaluate systolic dysfunction during phase acute. However, none of these studies highlighted the echocardiographic analysis of tissue Doppler in patients with ACD.

In the state of Amazonas, in recent years, there are reports of ACD,[4,14] where patients presented some disorders like right bundle branch block, anterior divisional block, atrial fibrillation, ventricular extrasystole, left ventricular systolic dysfunction and pericardial effusion. However, most of these cases were reversed with medical treatment and benign evolution.

Our group evaluated 62 cases of ACD from 2007 to 2015, of which 32 were subjected to two-dimensional echocardiography, of which 84% were normal. This shows a benign evolution in most patients in the study group. However, in this group, tissue Doppler was not analyzed for a more detailed assessment of subclinical disorders. This analysis is important for the diagnosis of acute phase, once the treatment at this stage allows healing and prevents progression to a chronic form, completely modifying the natural history of the disease and long-term prognosis.[14]

In patients with chronic CD, Silva et al.[15] used tissue Doppler through myocardial strain to quantify the contractility percentage of different myocardial segments in patients with chronic Chagas' disease and found that the contraction percentage of the different myocardial segments is greater in normal individuals than in patients with the chronic and indeterminate form of Chagas' disease, and the indeterminate form behaved in an intermediate way between the normal and dilated form of chronic Chagas' cardiomyopathy, proposing a progressive character of myocardial impairment in these patients.

The Brazilian scientific community should be aware of this emerging disease in the Amazon region in order to enhance preventive measures of control. Recently, there has been an increased number of acute cases of Chagas' disease, most often caused by oral transmission and a greater incidence in the Amazon region. Most patients have a good outcome with symptoms consistent with systemic infection, but no significant cardiac abnormalities on physical examination, electrocardiography and transthoracic echocardiography.

The limitations of this study include lack of new technologies such as strain/strain rate, currently useful in the assessment of regional systolic function, diastolic dysfunction and myocardial

contractility. Besides, the difficult access to some patients living in the countryside of the state of Amazonas limited the sampling number. Finally, there are few publications with echocardiography in patients with acute Chagas' disease, especially with evaluation by tissue Doppler. Current knowledge in this area comes mostly from studies of the chronic phase.

Conclusion

In this study, tissue Doppler imaging allowed to detect, in patients with ACD, even when they present benign evolution and normal ECG, early subclinical abnormalities. This reinforces the need for further prospective studies that may evaluate the natural history of patients by influencing the treatment of the acute phase and its evolution in the long term.

Authors' contributions

Research creation and design: Sedlacek EC, Barbosa-Ferreira JM; Data acquisition: Sedlacek EC, Pereira BVM, Barbosa MGV, Guerra JAO, Barbosa-Ferreira JM; Data analysis and interpretation: Sedlacek EC, Barbosa-Ferreira JM; Statistical analysis: Sedlacek EC, Barbosa-Ferreira JM; Funding: Barbosa-Ferreira JM; Manuscript drafting: Sedlacek EC, Antunes AF, Silva PRL, Barbosa-Ferreira JM; Critical revision of the manuscript as for important intellectual content: Sedlacek EC, Antunes AF, Nobre MN, Hosannah e Silva MR, Barbosa MGV, Guerra JAO, Barbosa-Ferreira JM.

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