

Left Atrial Function in Patients with Chronic Chagasic Cardiomyopathy

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Abstract

Background: Chagas disease is a cause of dilated cardiomyopathy, and information about left atrial (LA) function in this disease still lacks.

Objective: To assess the different LA functions (reservoir, conduit and pump functions) and their correlation with the echocardiographic parameters of left ventricular (LV) systolic and diastolic functions.

Methods: 10 control subjects (CG), and patients with Chagas disease as follows: 26 with the indeterminate form (GI); 30 with ECG alterations (GII); and 19 with LV dysfunction (GIII). All patients underwent M-mode and two-dimensional echocardiography, pulsed-wave Doppler and tissue Doppler imaging.

Results: Reservoir function (Total Emptying Fraction: TEF): ($p < 0.0001$), lower in GIII as compared to CG ($p = 0.003$), GI ($p < 0.001$) and GII ($p < 0.001$). Conduit function (Passive Emptying Fraction: PEF): ($p = 0.004$), lower in GIII (GIII and CG, $p = 0.06$; GI and GII, $p = 0.06$; and GII and GIII, $p = 0.07$). Pump function (Active Emptying Fraction: AEF): ($p = 0.0001$), lower in GIII as compared to CG ($p = 0.05$), GI ($p < 0.0001$) and GII ($p = 0.002$). There was a negative correlation of E/e'_{average} with the reservoir and pump functions (TEF and AEF), and a positive correlation of e'_{average} with s' wave (both septal and lateral walls) and the reservoir, conduit and pump LA functions.

Conclusion: An impairment of LA functions in Chagas cardiomyopathy was observed. (Arq Bras Cardiol. 2015; 105(1):28-36)

Keywords: Chagas Disease; Chagas Cardiomyopathy; Ventricular Dysfunction; Atrial Function/physiopathology; Echocardiography, Doppler/methods.

Introduction

Chagas disease, an infectious illness caused by the protozoan *Trypanosoma cruzi*, was described by Carlos Chagas in 1909, but its pathogenesis has yet to be completely elucidated¹.

Doppler echocardiography is the ideal method for cardiovascular research, especially anatomical and functional assessment, in patients with Chagas disease.

Tissue Doppler provides important additional information on cardiac function. The s' wave is related to longitudinal left ventricular (LV) systolic function, while the e' wave is related to LV diastolic function. One of the advantages of using the e' wave to assess LV diastolic function is less dependence on hemodynamic loading conditions, contrary to what occurs with the E wave of the mitral flow²⁻⁸.

The left atrial (LA) function is divided as follows:

1. Reservoir function: the left atrium stores pulmonary venous return during LV contraction and isovolumetric relaxation, getting 42% of the LV filling volume stored during these phases of the cardiac cycle⁹. Among the factors that influence it, the following must be highlighted: a) atrial contraction and relaxation, relaxation depending on contraction; b) LV contraction, which displaces the mitral annulus caudally; c) atrial stiffness and compliance; and d) right ventricular systole, which influences the flow in pulmonary veins.
2. Conduit function: the left atrium passively transfers blood to the left ventricle. It depends fundamentally on LV diastolic properties.
3. Pump function: the left atrium contracts actively during the final phase of ventricular diastole and contributes to 15%-30% of the LV end-diastolic volume. It depends on multiple factors, such as atrial contraction time, vagal stimulation, magnitude of the venous return (preload) and LV end-diastolic pressure (afterload).

When LV relaxation is abnormal, the reservoir and propulsion pump functions occupy a high percentage of the cardiac cycle, while the conduit function decreases. However, with the progressive increase in LV filling pressure

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and worsening of diastolic dysfunction, the left atrium acts predominantly as a conduit¹⁰⁻¹⁴.

The importance of assessing LA function has been highlighted in several clinical conditions, not only as part of pathophysiological mechanisms, but also as a prognostic factor¹⁵⁻²⁴.

This study aimed at finding elements for the better and earlier recognition of the following:

- changes in LA and LV functions in patients with Chagas disease;
- differences in LA function parameters;
- possible correlation between LA function data and Doppler echocardiographic parameters of LV systolic and diastolic function.

Methods

This study included patients selected consecutively at the Cardiomyopathy-Aortic Disease outpatient clinic of the Instituto do Coração, of the University of São Paulo Medical School, of both sexes, aged 18 to 55 years, who underwent clinical examination, electrocardiography, echocardiography, and laboratory tests (ELISA and immunofluorescence tests for Chagas disease, blood glucose and serum creatinine). Healthy age-matched volunteers were examined as a control group (CG).

The usual medications were maintained during the tests (angiotensin-converting-enzyme inhibitors, beta-blockers, diuretics in patients with LV systolic dysfunction).

The following exclusion criteria were considered: associated systemic diseases; ventricular arrhythmia or ventricular premature beats (≥ 10 /hour on previous Holter, or frequent on physical examination); atrial fibrillation; moderate or severe mitral regurgitation; and implanted electronic cardiac devices.

Patients with Chagas disease were divided into three groups as follows:

- Group I (GI): with the indeterminate form (asymptomatic with normal findings on electrocardiography, chest radiography and esophageal and colonic contrast studies);
- Group II (GII): with electrocardiographic abnormalities and LV ejection fraction ≥ 0.55 ;
- Group III (GIII): with electrocardiographic abnormalities and LV ejection fraction < 0.55 .

Ethics Statement

This study was registered with the approval of CAPPesq (Ethics Committee for Analysis of Research Projects of the Hospital das Clínicas of the São Paulo University - No. 0713/08). All subjects included in this study provided written informed consent in accordance with ethical regulations.

Echocardiographic study

All patients underwent M-mode and two-dimensional echocardiography, pulsed-wave Doppler and Tissue Doppler Imaging studies using a commercially available

ultrasound system (Sequoia, Acuson-Siemens, Mountain View, California, USA).

The quantitative measurements included LA e LV diameters on M-mode echocardiography, maximum, pre p-wave and minimum LA volumes (LAV_{max} , LAV_{pre} and LAV_{min} , respectively) using the modified Simpson's method on two-dimensional echocardiography with 4-chamber view, in accordance with the American Society of Echocardiography (ASE) recommendations.

The LV ejection fraction was calculated using the Teichholz method for uniformization²⁵⁻²⁷.

Transmitral velocities were also obtained in accordance with the ASE. Measurements included E wave and A wave velocities, E/A ratio, and E wave deceleration time.

Tissue Doppler imaging was performed with apical 4-chamber view. Measurements included systolic (s'), early diastolic (e') and late diastolic (a') waves, which were obtained from the lateral and septal margins of the mitral annulus, and the mean between the two sites ($e'_{average}$) was used to calculate the E/ e' ratio, which was also estimated from the LV filling pressure.

All examinations and measurements were made by one observer, and the mean of three to five consecutive cardiac cycles was used in this study.

Patients were positioned lying down on their left side, with 20° to 30° trunk inclination, and electrodes placed to obtain the electrocardiographic tracings.

All echocardiographic measurements were performed in accordance with the ASE recommendations²⁶⁻²⁸.

On two-dimensional echocardiography, the following parameters were calculated using the modified Simpson's method:

- LAV_{max} (in mL), measured at end-systole, just before the mitral valve opening;
- LAV_{min} (in mL), measured at end-diastole, just before the mitral valve closing and after the P wave;
- LAV_{pre} (in mL), measured immediately before the P wave (before atrial contraction).

The volumes and LV diastolic diameter were corrected for body surface area (BSA), which was calculated by using the Dubois' method.

Assessment of LA function

The LA reservoir function was analyzed by use of total emptying fraction (TEF), calculated according to the following formula: $TEF = (LAV_{max} - LAV_{min}) / LAV_{max}$.

The LA conduit function was examined by use of passive emptying fraction (PEF), calculated according to the following formula: $PEF = (LAV_{max} - LAV_{pre}) / LAV_{max}$.

The LA pump function was analyzed by use of active emptying fraction (AEF), calculated according to the following formula: $AEF = (LAV_{pre} - LAV_{min}) / LAV_{pre}$.

Statistical Analysis

The quantitative measures were described as means, medians, standard deviations and percentiles. Nonparametric

Kruskal-Wallis test was applied to compare those measures among the four groups. When there were significant differences, the Bonferroni correction was used for multiple comparisons among the groups.

The relation between measures was assessed by Spearman correlation coefficient. When it was significant, a positive correlation coefficient (r) indicated that higher values of the variable x correspond to higher values of the variable y . If r was negative, the relation was reverse and higher values of the variable x correspond to smaller values of the variable y . According to the absolute r values, the correlations between variables were as follows: $r < 0.3$, weak correlation; $r \geq 0.3$ and < 0.7 , moderate correlation; and $r \geq 0.7$, strong correlation.

The significance level adopted was "p" value $< 5\%$. The Statistical Package for the Social Sciences (SPSS) software, version 19, was applied^{29,30}.

Results

This study included 85 individuals as follows: CG, 10 individuals; GI, 26; GII, 30; and GIII, 19. The groups did not differ regarding the following parameters: mean age ($p = 0.107$); weight ($p = 0.815$); height ($p = 0.880$); BSA ($p = 0.791$); heart rate ($p = 0.164$); and sex ($p = 0.492$) (Table 1).

The baseline LA and LV echocardiographic parameters were as follows:

• Left atrium

There was a significant difference between groups in relation to LAV_{max} ($p < 0.0001$). The mean value was higher in GIII as compared to CG ($p = 0.001$), GI ($p = 0.0001$) and GII ($p = 0.012$). Similarly, the mean values in GIII were higher when compared to GII and CG ($p = 0.03$). There was no significant difference between CG and GI.

There was a significant difference between groups in relation to LAV_{pre} ($p < 0.0001$). The mean value was higher in GIII as compared to CG ($p = 0.0004$), GI ($p = 0.0003$) and GII ($p = 0.012$). Similarly, the mean values were higher

when compared to GII and CG ($p = 0.012$). There was no significant difference between CG and GI.

There was a significant difference between groups in relation to LAV_{min} ($p < 0.0001$). The mean value was higher in GIII as compared to CG ($p = 0.0003$), GI ($p < 0.0001$) and GII ($p = 0.0007$). There was no significant difference in GI and GII as compared to CG, and between GI and GII (Table 2).

• Left ventricle

There was a significant difference between groups regarding LV diastolic diameter ($p < 0.0001$). The mean value was higher in GIII as compared to CG ($p = 0.001$), GI ($p < 0.0001$) and GII ($p < 0.0001$), and in GII as compared to CG ($p = 0.05$). There was no significant difference between CG and GI (Table 2).

Parameter of LV systolic function

• Ejection fraction

There was a significant difference between groups regarding LV ejection fraction ($p < 0.0001$). The mean value was lower in GIII as compared to CG ($p = 0.001$), GI ($p < 0.0001$) and GII ($p < 0.0001$). There was no significant difference between CG, GI and GII when compared to each other (Table 3).

Parameters of LV diastolic function:

• Mitral flow

There was no statistically significant difference between groups regarding E wave ($p = 0.76$), A wave ($p = 0.09$), E/A ratio ($p = 0.22$) and E wave deceleration time ($p = 0.18$) (Table 3).

• Tissue Doppler

There was a significant difference between groups ($p = 0.0004$) regarding e'_{lat} evaluation on tissue Doppler. The mean value was lower in GIII as compared to CG ($p = 0.0076$), GI ($p = 0.001$) and GII ($p = 0.036$). There was no significant difference of mean values between CG, GI and GII.

Table 1 – Age, anthropometric characteristics, blood pressure and heart rate of the subjects included in the study

Variables	CG (n = 10)	GI (n = 26)	GII (n = 30)	GIII (n = 19)	p
	mean \pm SD	mean \pm SD	mean \pm SD	mean \pm SD	
Age (years)	40 \pm 6	46 \pm 6	43 \pm 8	43 \pm 7	0.11
Weight (kg)	68 \pm 13	68 \pm 12	68 \pm 11	71 \pm 13	0.82
Height (cm)	162 \pm 8	163 \pm 7	162 \pm 9	164 \pm 10	0.88
BSA (m ²)	1.70 \pm 0.2	1.72 \pm 0.2	1.70 \pm 0.2	1.80 \pm 0.2	0.79
SBP (mm Hg)	109 \pm 9	114 \pm 10	118 \pm 12	109 \pm 10	0.05
DBP (mm Hg)	70 \pm 9	73 \pm 8	72 \pm 8	67 \pm 8	0.14
HR (bpm)	68 \pm 10	70 \pm 9	67 \pm 9	64 \pm 10	0.16

CG: control group; GI: indeterminate form; GII: electrocardiographic abnormalities and LV ejection fraction ≥ 0.55 ; GIII: electrocardiographic abnormalities and LV ejection fraction < 0.55 ; SD: standard deviation; BSA: body surface area; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart rate.

Table 2 – Baseline echocardiographic parameters corrected for body surface, with respective means, standard deviations (SD) and p values (Kruskal-Wallis test)

Variables	CG (n = 10)	GI (n = 26)	GII (n = 30)	GIII (n = 19)	p
	mean ± SD	mean ± SD	mean ± SD	mean ± SD	
LVDD (mm/m ²)	25 ± 2.1	25.9 ± 2.3	28.4 ± 3.3#	37.1 ± 5.0*	< 0.0001
LAV _{max} (ml/m ²)	23 ± 4.5	27 ± 6.4	31 ± 8.7#	42 ± 12.1*	< 0.0001
LAV _{pre P} (ml/m ²)	14 ± 3	17 ± 4.21	21 ± 6.5#	32 ± 12*	< 0.0001
LAV _{min} (ml/m ²)	8.5 ± 2	9.8 ± 2.9	12.3 ± 5.9	24 ± 10.9*	< 0.0001

* GIII values significantly different from those of other groups

GI values significantly different from CG values

CG: control group; GI: indeterminate form; GII: electrocardiographic abnormalities and LV ejection fraction ≥ 0.55 ; GIII: electrocardiographic abnormalities and LV ejection fraction < 0.55 ; LVDD: left ventricular diastolic diameter; LAV_{max}: maximum left atrial volume; LAV_{pre P}: pre-P-wave left atrial volume; LAV_{min}: minimum left atrial volume.

Table 3 – Mitral flow variables used to assess LV diastolic function and LV ejection fraction, with respective means, standard deviations (SD) and p values (Kruskal-Wallis test)

Variables	CG (n = 10)	GI (n = 26)	GII (n = 30)	GIII (n = 19)	p
	mean ± SD	mean ± SD	mean ± SD	mean ± SD	
E wave (cm/s)	74.2 ± 12.7	71.9 ± 14.4	71.2 ± 17.4	68 ± 19.4	0.7635
A wave (cm/s)	54.1 ± 4.9	62.5 ± 7.9	59.7 ± 12.0	58.9 ± 16.9	0.0949
E/A	1.4 ± 0.2	1.2 ± 0.3	1.2 ± 0.4	1.3 ± 0.6	0.2279
DTE (ms)	174.4 ± 18.1	198.8 ± 30.7	198.9 ± 33.1	210 ± 64.6	0.1836
LVEF	0.67 ± 0.05	0.66 ± 0.04	0.67 ± 0.06	0.41 ± 0.07*	< 0.0001

* GIII values significantly different from those of other groups

CG: control group; GI: indeterminate form; GII: electrocardiographic abnormalities and LV ejection fraction ≥ 0.55 ; GIII: electrocardiographic abnormalities and LV ejection fraction < 0.55 ; E wave: E wave in mitral flow; A wave: A wave in mitral flow; E/A: E wave/A wave ratio; DTE: E wave deceleration time; LVEF: left ventricular ejection fraction.

There was a significant difference between groups ($p < 0.001$) regarding e'_{sep} evaluation on tissue Doppler. The mean value was lower in GIII as compared to CG ($p = 0.0004$), GI ($p < 0.001$) and GII ($p = 0.0001$). There was no significant difference of mean values when comparing CG, GI and GII.

A significant difference between groups was found ($p < 0.001$) regarding $e'_{average}$ evaluation on tissue Doppler. The mean value was lower in GIII as compared to CG ($p < 0.001$), GI ($p < 0.001$) and GII ($p < 0.001$). There was no significant difference of mean values between CG, GI and GII.

Regarding $E/e'_{average}$, there was a significant difference between groups ($p < 0.001$). The mean value was significantly higher in GIII as compared to CG ($p = 0.009$), GI ($p = 0.0001$) and GII ($p = 0.007$). There was no significant difference of mean values between CG, GI and GII (Table 4).

Parameters of LA function

• Reservoir function

The TEF significantly differed between groups ($p < 0.0001$). The mean values were significantly lower in

GIII as compared to CG ($p = 0.003$), GI ($p < 0.001$) and GII ($p < 0.001$). The mean values did not significantly differ between CG, GI and GII (Table 5).

• Conduit function

The PEF significantly differed between groups ($p = 0.004$). The mean value was lower in GIII, but with no statistical significance, when comparing GIII and CG ($p = 0.06$), GI and GII ($p = 0.06$), and GII and GIII ($p = 0.07$) (Table 5).

• Pump function

The AEF significantly differed between groups ($p = 0.0001$). The mean value was lower in GIII when compared to CG ($p = 0.05$), GI ($p < 0.0001$) and GII ($p = 0.002$) (Table 5).

Analysis of the correlations

There was a negative correlation of $E/e'_{average}$ with the reservoir and pump functions (TEF and AEF), and a positive correlation of $e'_{average}$ with s' (both septal and lateral walls) and the reservoir, conduit and pump functions. Table 6 describes the correlations among variables.

Discussion

This study reveals important features and details of the relationship and interdependency of the systolic and diastolic functions of the left ventricle and left atrium.

The LA function has been extensively studied in recent decades, with great interest in the pathophysiological and prognostic implications and interrelation with LV systolic and diastolic functions. It has been investigated in several clinical situations and diseases. A hemodynamic study with simultaneous recording of pressure and volume curves is ideal to allow the assessment of LA relaxation and compliance,

which directly influence LA filling. However, it is an invasive and costly exam, being reserved almost exclusively to experimental studies.

Echocardiography is a good alternative, being currently the method of choice for non-invasive LA analysis. Alterations in diastolic function properties or in any of LA functions (reservoir, conduit or pump) may interfere in LV filling. In addition to some cardiovascular diseases, the aging process modifies the LA size and some functions, especially the passive and active emptying.³¹

It is intuitive that all mechanisms involved in the process of LV filling and LA emptying are interdependent; therefore,

Table 4 – Tissue Doppler variables used to assess LV diastolic function, with respective means, standard deviations (SD) and p values (Kruskal-Wallis test)

Variables	CG (n = 10)	GI (n = 26)	GII (n = 30)	GIII (n = 19)	p
	mean ± SD	mean ± SD	mean ± SD	mean ± SD	
s' _{lat}	11.4 ± 2.2	13.2 ± 2.0	13.5 ± 2.7	8.0 ± 1.9*	< 0.0001
e' _{lat}	15 ± 2.3	15.1 ± 3.2	13.3 ± 3.1	9.8 ± 3.7*	0.0004
s' _{sep}	9.2 ± 2.8	10.6 ± 1.5	10.5 ± 2.0	7.3 ± 1.8*	< 0.0001
e' _{sep}	11.0 ± 2.1	10.5 ± 2.3	9.7 ± 1.8	7 ± 1.5*	< 0.0001
e' _{average}	13 ± 1.6	12.8 ± 2.5	11.3 ± 2.5	8.1 ± 2.6*	< 0.0001
E/e' _{average}	5.8 ± 1.5	5.7 ± 0.8	6.6 ± 2.3	9.6 ± 3.4*	< 0.0001

* GIII values significantly different from those of other groups

CG: control group; GI: indeterminate form; GII: electrocardiographic abnormalities and LV ejection fraction ≥ 0.55; GIII: electrocardiographic abnormalities and LV ejection fraction < 0.55; s'_{lat}: s wave in lateral wall (Tissue Doppler); e'_{lat}: e wave in lateral wall (Tissue Doppler); s'_{sep}: s wave in septal wall (Tissue Doppler); e'_{sep}: e wave in septal wall (Tissue Doppler); e'_{average}: the mean between e'_{lat} and e'_{sep}; E/e'_{average}: E wave/e' average ratio.

Table 5 – Assessment of left atrial function with respective means, standard deviations (SD) and p values (Kruskal-Wallis test)

Variables	CG (n = 10)	GI (n = 26)	GII (n = 30)	GIII (n = 19)	p
	mean ± SD	mean ± SD	mean ± SD	mean ± SD	
AEF (mL)	0.38 ± 0.05	0.44 ± 0.08	0.42 ± 0.11	0.27 ± 0.11*	0.0001
TEF (mL)	0.63 ± 0.09	0.63 ± 0.08	0.62 ± 0.10	0.44 ± 0.13*	< 0.0001
PEF (mL)	0.39 ± 0.12	0.35 ± 0.10	0.35 ± 0.10	0.23 ± 0.12	0.004

* GIII values significantly different from those of other groups

CG: control group; GI: indeterminate form; GII: electrocardiographic abnormalities and LV ejection fraction ≥ 0.55; GIII: electrocardiographic abnormalities and LV ejection fraction < 0.55; AEF: active emptying fraction; TEF: total emptying fraction; PEF: passive emptying fraction.

Table 6 – Correlations

	E/e' _{average}	e' _{average}	LVEF	s' _{sep}	s' _{lat}
TEF	r = -0.26	r = 0.53	r = 0.35	r = 0.33	r = 0.28
	p = 0.02	p < 0.001	p = 0.003	p = 0.003	p = 0.003
PEF	r = -0.09	r = 0.49	r = 0.42	r = 0.197	r = 0.118
	p = 0.44	p < 0.001	p < 0.001	p = 0.135	p = 0.378
AEF	r = -0.36	r = 0.39	r = 0.35	r = 0.37	r = 0.34
	p = 0.002	p = 0.001	p = 0.003	p = 0.004	p = 0.01

AEF: active emptying fraction; TEF: total emptying fraction; PEF: passive emptying fraction; s'_{lat}: s wave in lateral wall (Tissue Doppler); s'_{sep}: s wave in septal wall (Tissue Doppler); e'_{average}: the mean between e'_{lat} and e'_{sep}; E/e'_{average}: E wave/e' average ratio; LVEF: left ventricular ejection fraction.

the interpretation and importance of each of the influencing factors must be carefully analyzed.

For these reasons, in this study, patients with moderate or severe mitral dysfunction were excluded, as were those older than 55 years, although this criterion finds no support in the literature.^{32,33}

Regarding Chagas cardiomyopathy, most published studies involve patients with LV systolic dysfunction, and use LA size as a prognostic marker, showing that individuals with higher volumes had more cardiovascular events. The LV diastolic dysfunction degree is also related to the LA volume, and most significant changes in this parameter occur when there is greater LV diastolic and systolic dysfunction.

Some studies of patients with Chagas cardiomyopathy and preserved LV systolic function have suggested that there is a higher risk of atrial fibrillation when the atrial diameter is high. Other authors, studying various degrees of systolic impairment, including a group of patients with Chagas disease's indeterminate form and others without Chagas disease, have analyzed LA size and volume, and reported no significant differences between those groups regarding diastolic function. However, atrial functional parameters have not been considered.

In Brazil, Nunes et al.³³ have highlighted the importance of assessing LA function, relating it to LV systolic and diastolic functions. More recently, Mancuso et al.³⁴ have studied LA function, assessed by using LA total and active emptying fractions, and concluded that both decreased more in patients with Chagas cardiomyopathy than in those with idiopathic dilated cardiomyopathy^{34,35}.

The indeterminate form of Chagas disease has usually no symptoms, or only electrocardiographic alterations. The same occurs when there is a mild systolic dysfunction. Clinical manifestations could vary and depend on the degree and type of the predominant involvement.

Functional capacity depends on cardiac output. Stroke volume results from the difference between LV systolic and end-diastolic volume. The LV end-diastolic volume depends on diastolic function and blood supply, being directly related to LA anatomical and functional properties^{36,37}.

According to the disease classification criteria, GIII patients had significantly lower LV ejection fraction values as compared to the other groups. The mean value of this parameter in GIII (0.41) suggests moderate systolic function impairment.

Significantly lower values of the s wave in this group strengthen the evidence of myocardial damage, because this variable is related to longitudinal LV systolic function³⁸.

The positive correlations of those two variables with TEF and AEF shown in this study corroborate the decrease in the reservoir function in chagasic patients with LV systolic dysfunction probably by reducing the caudal displacement of the mitral annulus during ventricular systole and the effect of suction at the beginning of diastole. Moreover, the decrease in the propulsion pump function may be related to impaired myocardial function.

The mitral flow variables, usually used to assess LV diastolic function, showed no significant difference

between groups. However, when analyzed on tissue Doppler, some considerations should be highlighted.

Patients with normal LV ejection fraction (CG, GI and GII) had normal values of e'_{sep} , e'_{lat} , $e'_{average}$ and $E/e'_{average} < 8$, indicating normal LV filling pressure. In contrast, GIII patients showed signs of LV diastolic dysfunction, when analyzed regarding the same variables, with values of e'_{sep} and e'_{lat} lower than normal for age range according to the ASE criteria.

The values of $E/e'_{average}$ were significantly higher in GIII (mean = 9.6). However, this result should be analyzed carefully. Values greater than 15 are indicative of increased LV filling pressure, while those lower than 8 are considered normal. When there are intermediary values, such as in GIII, the conclusion requires association with other data. In addition, E/e' is not adequate to assess LV filling pressure in individuals without significant heart disease.

The LA volume, although significantly higher in GIII, can be interpreted in this study as a diastolic dysfunction parameter and there is chronic elevation of LV filling pressure³⁹.

The absence of other variables that point to significant diastolic dysfunction, such as mitral flow behavior, indicates that patients in GIII have mild diastolic dysfunction, with probably normal LA filling pressure, consistent with clinical features (all in NYHA functional class II when evaluated). Drug action should also be considered in these results, because all patients in this group were on optimized medical treatment.

Reservoir, conduit and pump functions can be evaluated more consistently by analyzing the LA volume variation: the reservoir function, by using TEF; the conduit function, by using PEF; and the pump function, by using AEF.

The results of this study demonstrate that patients with LV dysfunction (GIII) had decreased LA reservoir and pump functions, which does not occur in patients with the indeterminate form and those with electrocardiographic alterations only.

The decrease in LA pump function is probably related to the LA involvement in chagasic myopathy, with consequent contractile injury and lower ejection during atrial systole, therefore, with larger atrial volume at the end of this phase of the cardiac cycle.

According to the definition of the two functions and the way they are calculated, in this study, the reservoir function deterioration might be related only to the LA and LV contractile function impairment. Other factors analyzed in this study that significantly contribute to the reservoir function (relaxation, stiffness and compliance) showed no significant differences.

Some facts regarding LA reservoir and pump functions should be considered. The negative correlations of $E/e'_{average}$ and these two parameters of atrial function demonstrate the influence of LV filling pressure (LA pressure or LV diastolic pressure) on LA filling and emptying.

Another highlight is the positive correlation of these two roles (reservoir and pump) with LV diastolic function, specifically with myocardial relaxation evaluated by using e' wave.

The parameter used to assess conduit function (PEF) was lower in GIII, with statistical significance. The positive correlation of the e' wave with the conduit function highlights the importance of diastolic dysfunction in LA passive emptying.

Usually, the clinical and pathophysiological mechanisms involved in heart failure have their focus on higher LV systolic and diastolic dysfunction. The present study demonstrates that LA can play a critical role in this process. Determining the functional boundary of each structure in this context is still a big challenge.

Conclusion

In patients with Chagas cardiomyopathy and LV systolic dysfunction, there was an impairment in LA reservoir, conduit and pump functions. Those with normal systolic function showed no alterations in these parameters. There was a correlation between LA function and LV systolic and diastolic functions assessed on tissue Doppler imaging.

Author contributions

Conception and design of the research: Fragata CS, Matsumoto AY, Ramires FJA, Fernandes F, Buck PC, Salemi

VMC, Mady C, Ianni BM. Acquisition of data: Fragata CS, Matsumoto AY, Ramires FJA, Fernandes F, Buck PC, Mady C, Ianni BM. Analysis and interpretation of the data: Fragata CS, Matsumoto AY, Ramires FJA, Fernandes F, Buck PC, Nastari L, Mady C, Ianni BM. Statistical analysis: Fragata CS, Mady C, Ianni BM. Obtaining financing: Fragata CS. Writing of the manuscript: Fragata CS, Matsumoto AY, Buck PC, Salemi VMC, Nastari L, Mady C, Ianni BM. Critical revision of the manuscript for intellectual content: Fragata CS, Matsumoto AY, Fernandes F, Buck PC, Salemi VMC, Nastari L, Mady C, Ianni BM.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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