

Function of the Left Atrium in the Chagas' Cardiomyopathy

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Objective

To study the function of the left atrium patients with of dilated cardiomyopathy of chagasic etiology and relate it to the diastolic function and to the functional class.

Methods

We studied 75 chagasic with cardiomyopathy from July to 1999 to May to 2001, submitted to clinical exams, electrocardiogram and transesophageal echocardiogram. The left atrium function was assessed by means of the velocities in the left atrial appendix and the atrial reverse in the pulmonary vein. The control group consisted of 20 normal patients.

Results

The age was 48 ± 13 years old and 69% were men. Most of patients (88%) were in functional classes I and II, under a conventional treatment for cardiac insufficiency. The fraction of ejection of the left ventricle was $39 \pm 13\%$. The indicators of diastolic function associate to those of systolic function and the functional class. The carriers of pseudonormal or restrictive pattern of diastolic dysfunction presented a larger diameter of the left atrium, lower flow velocities in the left atrial appendix and a longer duration of the atrial reverse. There was no difference among the patients with normal pattern and abnormal diastolic relaxation in relation to the control group.

Conclusion

The left atrial function is an important parameter in the assessment of patients with chagasic myocardopathy and it is related to the systolic and diastolic functions of the left ventricle.

Key words

chagas' disease, cardiomyopathy, left atrium and transesophageal echocardiogram

The pattern of filling of the left ventricle provides important clinical and prognostic information in patients with cardiac insufficiency¹⁻⁴. However, the diastolic function comprises a complex sequence of interrelated events and depends on several factors, such as age, heart rate and ventricular function^{1,5-7}. The left atrial function has had lower attention as a possible determinant of the dynamics of the ventricular filling, presumably due to technical difficulties to assess the size and function of such chamber.

The Doppler echocardiogram constitutes the main instrument for the non-invasive assessment of the left ventricular diastolic function⁶⁻⁸. Multiple parameters used are influenced by the ventricular load and complacence conditions, in addition to the filling pressures. The left atrium function, directly influenced by the diastolic pressure of the left ventricle, represents a stable marker of the duration and severity of the diastolic dysfunction, by showing a prognostic value⁴.

In Chagas' disease, the diastolic dysfunction can be premature, preceding the systolic compromising⁹⁻¹³. However, its pattern of ventricular filling has not been systematically studied and related to the left atrial function, at the advanced stage of chagasic cardiopathy. The present study aims at assessing the function of the left atrium in patients with chagasic myocardopathy and check its correlation with the diastolic function of the left ventricle and functional class.

Methods

Seventy-five patients with chagasic dilated cardiomyopathy were studied. They came from the Reference Ambulatory in Chagas' Disease of Hospital das Clínicas of UFMG, consecutively enrolled from July '99 to May '01. The echocardiographic exams took place at the EcoCenter - Hospital Socor, in Belo Horizonte.

Patients with a diagnostic of Chagas' disease and cardiac onset defined in the echocardiogram for the presence of dilatation of the left ventricle (diastolic diameter ≥ 55 mm or 27 mm/m²) measured at M mode and ejection fraction $\leq 55\%$, through the method of Teichholz^{14,15} were included. Those with other associated cardiopathies, hypertension, mellitus diabetes, thyroid dysfunction, pulmonary disease and alcoholism, as well as the cases with atrial fibrillation or pacemaker were excluded.

All patients were submitted to a clinical exam, aiming at determine the functional class of *New York Heart Association* (NYHA) and 12-derivation electrocardiogram.

The 20 patients (control) submitted to the transesophageal

echocardiogram were included in our service. The clinical indications of the exam were varied, as patients with cerebral ischemic event for the research of cardiac source of embolus were not included. Despite the regular values of the velocities in the appendix were established, the objective was to select a control group to identify regular values of the velocities in our service, gauged by a single examiner, and compare those measurements to those in the literature. Those patients presented or not several diseases, but they did not follow the changes of the left atrium. All of them were in a sinus rhythm in relation to the electrocardiographic monitoring during the transesophageal electrocardiogram, although the electrocardiogram had not been obtained.

The echocardiograms were performed by a single examiner soon after the inclusion in the study, by using a Hewlett-Packard 5500, with 2.5 and 3.5 MHz transducers and the measurements were taken in accordance to the established technique^{16,17}.

For the study of the diastolic function of the left ventricle, the velocities of the mitral flow and pulmonary veins were analyzed, in addition to the measuring the time of isovolumetric relaxation¹⁸. According to those measurements, the left ventricular filling pattern was classified as: normal, abnormal diastolic relaxation, pseudo-normal and restrictive, according to the literature⁵⁻⁷.

The transesophageal echocardiogram was performed using a Hewlett-Packard 5 MHz multiplan transducer, with standardized sequential images following the service routine¹⁹. The analysis of the flow of the pulmonary veins was made with the use of a color Doppler, by placing the volume sample 0.5cm far from the inlet opening of the upper left pulmonary vein, with a velocity of 100 m/s²⁰ (fig. 1).

The velocities in the left atrial appendix were obtained with the pulsing Doppler, by positioning the volume sample in its inlet, 1cm from the left atrial cavity²¹. The velocity of dissection of the left atrial appendix was obtained through the measurement of the positive flow that precedes the QRS of the electrocardiogram (after the atrial contraction). The filling velocity was measured through the maximum velocity of the followed negative flow (fig. 2). Both measurements were made in three consecutive cardiac cycles, using the average values from three measurements.

The function of the left atrium was assessed through the velocities of filling (V1) and ejection (V2) of the left atrial appendix (LAA) and the peak velocity of the atrial reverse flow in the pulmonary vein.

The patients with atrial fibrillation, pacemaker or important mitral regurgitation, which is subjectively defined by the assessment of the area of the regurgitant jet in relation to the left atrium area using the color Doppler, were excluded.

The continuing variables were analyzed through their descriptive statistics and the differences among the means were compared by the *t* test of Student, regarding the samples as independent. The analysis of variance (ANOVA) was employed whenever appropriate. The discreet and categorical variables were tabulated by their absolute and relative frequency. The chi-square test of Pearson was applied to test association and/or homogeneity. The relation between the clinical and Doppler echocardiographic variables was analyzed through the simple linear regression method.

Results

The average age of the patients with chagasic cardiomyopathy was 48±13 years old (26-73), without any difference in relation

to the control group (52±15 years old). The proportion of men was 69% among the chagasic and 60% in control. Most of chagasic patients were in functional class I and II (tab. I).

History of cerebral thromboembolism took place in 14 (19%) patients. There were 70 patients under the use of ECA inhibitor, 29 of amiodarone, 24 of diuretics, 13 of anticoagulants, 10 of

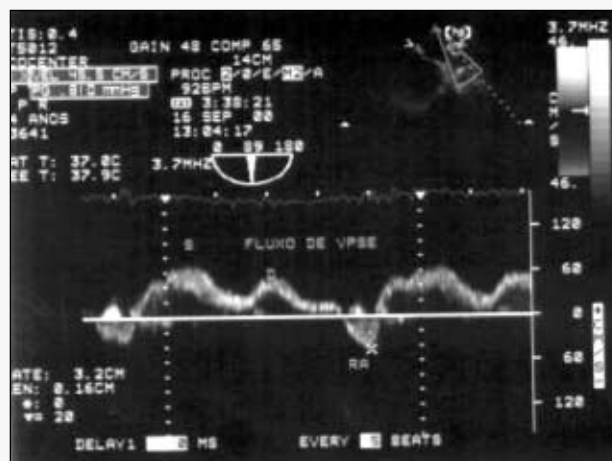


Fig. 1 - Flow of an upper left pulmonary vein, obtained at the transesophageal Doppler echocardiogram, highlighting two anterograde peaks (systolic and diastolic), followed by the atrial reverse. ULPV - upper left pulmonary vein; S - systolic peak; D - diastolic peak; AR - atrial reverse.

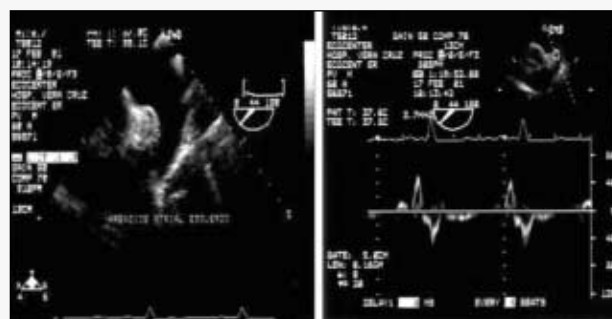


Fig. 2 - Left atrial appendix and the record of its velocities (biphasic pattern) at the transesophageal echocardiogram.

Table I - Data from the clinical exam and measures to the echocardiogram

Variables	Chagasic	Control
Clinical data		
Age (years)	47.8±13.1	53.3±15.7
Male	52 (69%)	14 (70%)
Functional class (NYHA)		
I	26 (35%)	13 (65%)
II	40 (53%)	6 (30%)
III	5 (7%)	1 (5%)
IV	4 (5%)	0
HR (bpm)	67.4±12.9	74.5±17.6
SBP (mmHg)	111.7±16.1	148.7±18.3
DBP (mmHg)	74.1±11.3	100.6±12.3
Measures		
LVD (mm)	63.1±8.7	49.3±5.6
SLV (mm)	50.7±11.3	31.5±5.9
FE (%)	39.5±12.7	66.4±7.1
FS (%)	20.2±7.5	34.5±4.7
LA (mm)	41.9±6.9	36.8±4.6

The variable are displayed in figures (%) or mean ± SD. HR - heart rate; SBP - systolic blood pressure; DBP - diastolic blood pressure; LVD - diastolic diameter of the LV; SLV - systolic diameter of the LV; FE - fraction of ejection; FS - fraction of shortening; LA - left atrium.



digital and only 3 of beta-blockers. Thirteen (18%) patients were using oral anticoagulant.

The most frequent electrocardiographic changes were the blocking of the right branch (54%) and ventricular extra-systoles (53%). The left branch blocking happened in 18% of the patients and atrial fibrillation rhythm in 5%.

The mean of the ejection fraction of the left ventricle was 39 ± 13 %. The M mode measurement can be found on table I.

The classification of patients in accordance to the diastolic function is in figure 3. The parameters used for the assessment of the diastolic function were associated to those of the systolic function and the functional class. Except for the maximum velocity of the atrial reverse flow, all other parameters employed for the assessment of the left atrial function were different in the patients with pseudonormal and restrictive pattern in relation to the others (tab. II).

The maximum velocities of the atrial reverse in the patients with pseudonormal and restrictive pattern were similar, but different in their duration.

There was no difference of V1 and V2 among the patients with normal pattern and ARR and the control group ($p=0.21$ and $p=0.46$). The atrial reverse velocity was also similar among the groups.

The velocities in the LAA correlated with the diastolic dysfunction pattern. Changes of the ventricular filling pressure, as occurred in the cases with pseudonormal and restrictive pattern, resulted in lower velocities in the LAA (fig. 3). The diameter of the left atrium was associated to the diastolic function pattern (fig. 4).

Parameters	Control ^δ	Normal/ADR	PN/Restrictive	p*
LA (mm)	36.8±4.6	37.8±3.8	45.9±66.4	p<0.00001
V1 (cm/s)	63.7±13.9	72.4±18.7	44.1±25.1	p<0.00001
V2 (cm/s)	58.0±10.9	60.6±14.4	42.6±20.3	p<0.0001
Atrial reverse				
Vmax. (cm/s)	24.7±4.2	22.7±10.5	27.2±13.2	p=0.16
Duration(ms)	121.3±23.1	120.9±36.7	167.1±34.9	p<0.0001

*Normal group/ADR in relation to the PN/Restrictive; ^δ - No difference with the normal group/ADR; ADR - abnormal diastolic relaxation; PN - pseudonormal; Vmax - maximum velocity of the atrial reverse flow.

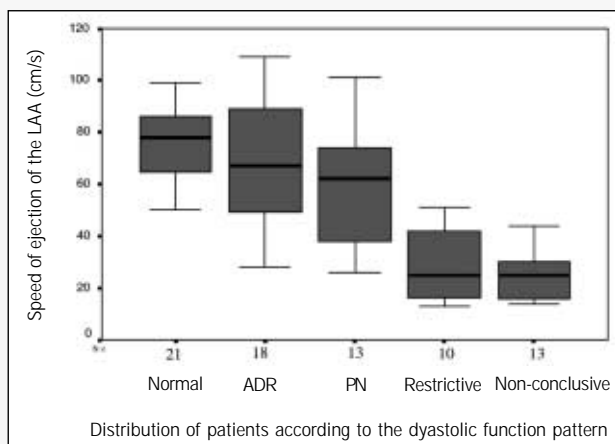


Fig. 3 - Association between the LAA ejection velocity and left ventricular diastolic function in the patients with chagasic cardiomyopathy. Normal (21 patients); ADR - Abnormal diastolic relaxation (18); PN - pseudonormal pattern (13); Restrictive (10) and non-conclusive (13).

Thrombus inside the LAA was found in four (5%) patients, and it did not associate with cerebral thromboembolism or the flow velocities, although low velocities ($V1=32.0$ cm/s) tended to be associated to thrombus ($p=0.07$). The flow velocities in the LAA correlated negatively ($r= -0.7$) with the LA diameter (fig. 5).

Discussion

Many methods have been developed to estimate the contractile function of the left atrium. Generally, they are difficult and time-consuming and they are not used in clinical practice. The velocities in the left atrial appendix appear as a clinically applicable method to estimate the atrial function¹. Our objective was to estimate the left atrial function through such technique and correlate that function with the diastolic dysfunction in the chagasic dilated cardiomyopathy.

Unlike it happens in the rheumatic mitral stenosis, in patients with sinus rhythm, there is not a clear association between the diameter of the left atrium and the velocities in the atrial appendix^{22,23}. In the patients with atrial fibrillation, the appendix flow is irregular as demonstrated in the literature. Therefore, its values were not measured in the present study²⁴⁻²⁹.

The values of the velocities in the LAA, which were obtained in our study, in the patients with normal diastolic function or abnormal diastolic relaxation, are within the limits of normality, when compared to the control group. The size of the atrium was correlated with those velocities. The atrial dilatation was more frequent in

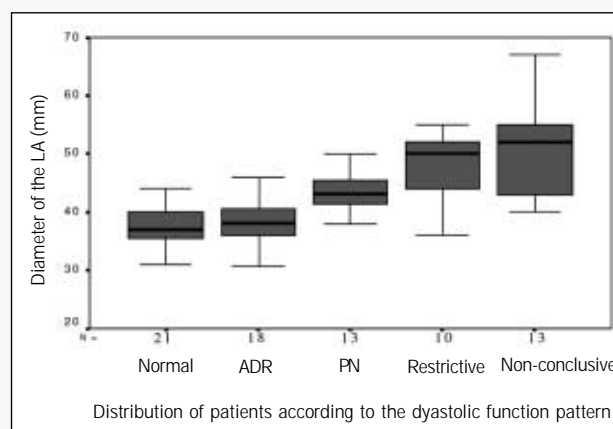


Fig. 4 - Association between the left atrium diameter and the left ventricular diastolic function in the patients with chagasic cardiomyopathy. Normal (21 patients); ADR - Abnormal diastolic relaxation (18); PN - pseudonormal pattern (13); Restrictive (10) and non-conclusive (13).

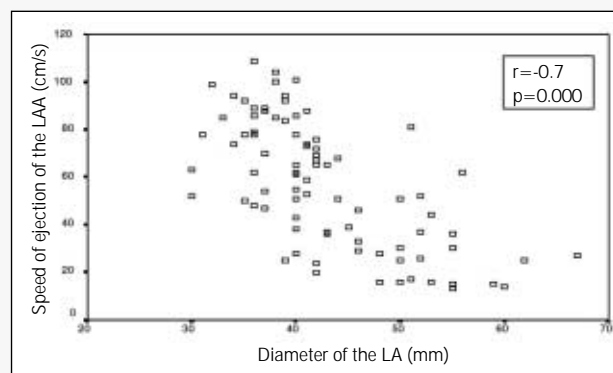


Fig. 5 - Correlation between the LA diameter and ejection velocity of the LAA.

the patients with an intense compromising of the left ventricular contractile function, showing advanced diastolic function and depressed ejection fraction, with the changes associated to the dysfunction of the LAA. Agmon et al. considered that the contractility of the appendix is affected by the systolic and/or diastolic dysfunction, primarily due to the rising of the ventricular filling pressure²². Triposkiadis et al.³⁰, on the other hand, suggested that there is a left atrial myopathy in the dilated cardiomyopathy, which contributes to the depression of the atrial function. That can precede, develop simultaneously or follow the ventricular the myopathic process.

Ito et al.³¹ have made clear that the function of the LAA improves after the treatment of the cardiac insufficiency and demonstrated a correlation between the fraction of ejection of the left ventricle and the velocity of dissection of the atrial appendix ($r=0.8$, $p<0.0005$).

The outline of the pulmonary venous flow is another strategy currently employed for the study of the left atrium function. The analysis of the record of the atrial reverse can be limited to the transthoracic, even with the evolution of the transducers³². The transesophageal stays as a useful strategy, allowing for a clear tracing and accurate measurements of the velocities of the pulmonary venous flow. Hoit and Gabel³³, in an experimental study, demonstrated that the reverse flow, during the atrial systole, was absent in the cases of isolated or combined atrial dysfunction, and showed increased velocity after isolated left ventricular dysfunction. In the chagasic cardiomyopathy, the loss of the effective atrial systole can cause the decrease of the cardiac output, which can explain the differences in the clinical evolution of the patients and an unfavorable diagnostic.

The left atrium is directly exposed to the diastolic pressure of the left ventricle. Therefore, its dimension is determined by the same factors that influence the diastolic filling. It is regarded as a more stable indicator, which reflects the duration and severity of the diastolic function⁴. The chronic rising of the left atrial pressure in the carriers

of restrictive pattern of diastolic dysfunction can cause atrial mechanic failure, which leads to the decrease of the velocity of the atrial reverse, as it occurred in the present study, without any difference among the patients with milder ways of onset of diastole⁷.

The increase of the size of the left atrium is associated to a cardiovascular disease and represents a risk factor for atrial fibrillation, cerebrovascular accident and death^{34,35}. Moller et al.⁴ demonstrated that the increase of the left atrial volume was a strong mortality predictor after acute myocardial infarction. The prognostic value persisted after stratification for clinical predictors of events and for conventional Doppler echocardiographic indexes of systolic and diastolic function of the left ventricle. Those authors also verified the association between the volume and size of the left atrium ($p<0.001$). The volume of the left atrium was not analyzed in the present study.

In another study, Tsang et al.³⁶ showed that the size of the left atrium was a predictor of development of a nonvalvular atrial fibrillation. The chronic diastolic function reflects the extent of the changes in the atrial substratum, which predisposes electrophysiological abnormalities and development of arrhythmias. That mechanism can also contribute for thromboembolic complications, which are classically associated with the cardiac insufficiency of chagasic etiology. So, patients with a restrictive pattern of diastolic dysfunction show a greater predisposition for the occurrence of atrial fibrillation and thromboembolic events. However, in the present study, the patients with restrictive pattern were not homogenous concerning the atrial function. The atrial reverse velocity in those patients varied from increased, suggesting atrial function preserved and diastolic dysfunction, to normal or reduced, in the presence of atrial dysfunction.

Concluding, the left atrial function constitutes an important parameter in the assessment of the patients with chagasic cardiomyopathy, and it is related to the systolic and diastolic functions of the left ventricle.

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