

Echocardiographic Correlation between Right Ventricular Function and Left Atrial Volume

Liz Andréa Villela Baroncini,¹ Lucas José Lira Borges,² Ana Cristina Camarozano,¹ Daniela de Castro Carmo,² Rubens Zenobio Darwich,² Jeronimo Antonio Fortunato Junior²

Instituto Saber e Aprender,¹ Curitiba, PR - Brazil

Hospital da Cruz Vermelha – Cruz Vermelha Brasileira - Filial do Estado do Paraná,² Curitiba, PR – Brazil

Abstract

Background: Few reports exist on the relationship of the left ventricular diastolic dysfunction (LVDD) with its most important features including enlargement of the left atrium and left ventricular hypertrophy (LVH), and with the right ventricular (RV) function.

Objective: To determine the correlation between the left atrial size and the RV function and dimensions in patients with and without LVDD and LVH.

Methods: Fifty patients were included, 25 (40% men) of them with LVDD, aged 67.1 ± 10.6 years (study group) and 25 without LVDD (52% men) aged 49.9 ± 16.3 years (control group). Patients underwent transthoracic echocardiography with evaluation of the left atrial size and volume (LAV), LVDD, LVH, and RV function and dimensions. P-values < 0.05 were considered statistically significant.

Results: LAV > 34 mL/m² and left atrial size > 40 mm were associated with lower absolute values of tricuspid annular plane systolic excursion (TAPSE) and RV lateral S' ($p \leq 0.001$, Pearson's correlation coefficient -0.4 and -0.38, respectively) in the study group. Patients in the study group showed higher incidence of LVH ($p = 0.02$) and greater left atrial diameter ($p = 0.03$) compared with the control group. In addition, greater left atrial diameter ($p = 0.02$) and LAV ($p = 0.01$) values were found in patients with LVDD grade II compared with LVDD grade I.

Conclusions: The present study determined, for the first time, the correlation of left atrial enlargement with progressive RV dysfunction in patients with LVDD. (Arq Bras Cardiol. 2019; 112(3):249-257)

Keywords: Ventricular Dysfunction Right; Atrial Function/Physiology; Echocardiography/Methods; Blood Pressure; Heart Failure; Stroke Volume.

Introduction

Morphological and functional interdependence between the two ventricles may be explained by three mechanisms: (1) increase in right ventricular (RV) end-diastolic pressure in response to an increase in the left ventricular (LV) volume; (2) increased LV filling pressure inducing mechanical stress of the muscle fibers common to both ventricles; and (3) humoral factors, including catecholamines, that may regulate ventricular hypertrophy in response to pressure overload of one of the ventricles.¹⁻⁴ The function and dimensions of the right ventricle are directly associated with the LV function. Dilatation of the right ventricle and reduction of its contractile strength is usually found in advanced stages of LV dysfunction, reinforcing the close relationship between the two ventricles.⁵⁻⁷ It is known that in heart failure patients with reduced LV ejection fraction both

ventricular dynamic and pressures are altered, affecting the size and function of other cardiac chambers. However, few reports exist about the relationship between heart failure with preserved LV ejection fraction and increased RV dimensions with reduced systolic function fraction.⁴ Also, there are few reports on LV diastolic dysfunction and related findings, such as enlargement of the left atrium (LA), LV hypertrophy (LVH), and their influence on systolic function and RV volume. The LA seems to reflect LV diastolic dysfunction (LVDD), since the parietal tension caused by increased filling pressures leads to dilation of the atrial chamber.⁴ In addition, there are no studies specifically evaluating the influence of LA size and LA volume on diameter and function of the right ventricle. Therefore, the aim of the present study was to evaluate the correlation of left atrial volume (LAV) and left atrial diameter with the presence of LVH and RV function and diameter in patients with and without LVDD.

Mailing Address: Liz Andréa Villela Baroncini •

Rua Buenos Aires, 764, apt. 601. Postal Code 80250-070, Batel, Curitiba, PR – Brazil

E-mail: lizavb@cardiol.br, lizandreabaroncini@hotmail.com

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Methods

Patients

This was a cross-sectional cohort study. We studied a convenience sample of 50 consecutive outpatients that underwent transthoracic echocardiogram (TTE) with

quantification of LV diastolic function, left atrial diameter and LAV, and RV systolic function and diameter at public healthcare centers. Patients on both sexes, aged older than 18 years, and of any ethnicity, referred for TTE by assistant physicians for any cause were selected. Exclusion criteria were presence of global (ejection fraction < 52% for men and < 54% for women) or segmental LV systolic dysfunction, infiltrative diseases, pericardial diseases, chronic obstructive pulmonary disease, asthma, moderate-to-severe valve diseases with hemodynamic repercussion, interatrial or interventricular septal defects, conditions that impaired the analysis of LV diastolic function (valve diseases with hemodynamic repercussion, atrial fibrillation at the electrocardiogram, definite pacemaker), presence of complete left or right bundle-branch block at the electrocardiogram and patients with LV diastolic dysfunction grade III. The following clinical data were collected: age, sex, weight, height, body mass index, presence of systemic arterial hypertension (SAH), diabetes mellitus (DM), coronary artery disease (CAD), smoking status (current or former smokers) and dyslipidemia. SAH, DM, dyslipidemia and smoking status were either collected from patients' medical records or self-reported by patients. The diagnosis of SAH was defined by systolic and diastolic blood pressure ≥ 140 mmHg and 90 mmHg, respectively, on two or more occasions, or use of anti-hypertensive drugs;⁸ and DM diagnosis was confirmed by: (1) symptoms of polyuria, polydipsia, weight loss and casual (at any time of day, regardless of the time since last meal) glucose > 200 mg/dL; and (4) glycated hemoglobin A1c $\geq 6.5\%$ or use of hypoglycemic agents or insulin.⁹ Dyslipidemia was defined according to the V Brazilian Guidelines on Dyslipidemias and Prevention of Atherosclerosis¹⁰ criteria – total cholesterol > 200 mg/dL, high density lipoprotein cholesterol (HDL) < 40 mg/dL for men and < 50 for women, low density lipoprotein cholesterol (LDL) > 160 mg/dL, triglycerides > 150 mg/dL or use of lipid lowering drugs. The presence of CAD was confirmed by data from the medical records including: non-fatal myocardial infarction and surgical or percutaneous myocardial revascularization.

All patients signed the informed consent form in duplicate and kept one of the copies. The study was approved by the local ethics committee.

Echocardiographic assessment

Echocardiographic assessments with harmonic imaging were performed using the IE33™ (Phillips), Envisor™ (Phillips) and Vivid™ (GE) equipment. The tests were conducted by two echocardiographers experienced in TTE. The following parameters were collected for analysis: LV diastolic function (normal, grade I and grade II), presence of concentric or eccentric LVH, LAV, and RV systolic function measurements. Linear dimensions of the left atrial size were visualized from a parasternal long-axis window with two-dimensional and M-mode views. LAV was estimated using apical four- and two-chamber views, according to current recommendations.⁵⁻⁸ Only highly related variables were used for the LV diastolic function analysis to avoid false positive results - the peak early filling (E wave) and late diastolic filling (A wave) velocities (the E/A ratio) < 0.8; tissue Doppler imaging measured from the septal or lateral annulus (e' velocities) (septal < 7 cm/s

and lateral < 10 cm/s); average E/e' ratio > 14; LAV index obtained from four- and two-chamber views > 34 mL/m²; and peak tricuspid regurgitation velocity > 2.8m/s. Classification of diastolic dysfunction was based on the analysis of the transmitral flow. A diastolic dysfunction grade I was defined as an E/A ratio < 0.8 and an E-wave < 50 cm/s, and dysfunction grade III defined as an E/A ratio > 2. In case of an E/A ratio < 0.8 and E-wave velocity > 50 cm/s, or an E/A ratio between 0.8 and 2, other parameters were used for the evaluation: velocity of mitral regurgitation, LAV, and E/e' ratio, according to current guidelines.¹¹ LVH was categorized into concentric (increased LV mass index and increased relative wall thickness) and eccentric (increased LV mass index and normal relative wall thickness), according to relative wall thickness (normal < 0.42) and indexed LV mass (normal < 95 mg/m² for women and < 115 mg/m² for men), according to current recommendations.⁵ Diameter of the right ventricle was measured in the parasternal long-axis window between the RV anterior wall and the interventricular septum in the ventriculo-aortic junction.⁵⁻⁷ Two parameters were considered in the systolic function analysis: tricuspid annular plane systolic excursion (TAPSE) with M-mode (normal > 16 mm) and lateral S' wave velocity by tissue Doppler imaging (normal > 9.5 cm).⁵⁻⁷ Patients were then divided into two groups: individuals with normal LV diastolic function (n = 25) (control group) and individuals with LVDD grade I and II (n = 25) (study group).

Statistical analysis

Quantitative variables were described as mean and standard deviation, median and interquartile ranges. Categorical variables were described as frequency and percentages. The Student's t-test was used for two-group comparisons of quantitative variables, and the Fisher's exact test used for categorical variables. Associations between variables were determined using the Pearson correlation coefficient. Normality of distribution of quantitative variables was tested by the Kolmogorov-Smirnov test. P-values < 0.05 were considered statistically significant. All data were analyzed using the IBM SPSS Statistics software v.20.0 (Armonk, NY).

Results

Mean age of the control group was 49.9 \pm 16.3 years and 52% of the individuals were men. Mean age of the study group was 67.1 \pm 10.6 years (p < 0.001), 40% were men. A higher prevalence of SAH was seen in the study group than in the control group. Other clinical characteristics of participants are described in Table 1. The following variables showed normal distribution: TAPSE, lateral S' velocity, RV diastolic diameter, left atrial size and LAV. A higher incidence of LVH (concentric and eccentric) and a higher left atrial diameter were observed in the study group compared with the control group; no other differences were found between the groups (Tables 2 and 3). Considering the study group, patients with LVDD grade II showed significantly greater left atrial diameter and LAV compared with those with LVDD grade I, with no significant changes in the other parameters (Table 4). The type of LVH (concentric or eccentric) had no effect on the LA or other echocardiographic parameters (Table 4). There was a significant correlation of TAPSE and

Table 1 – Baseline characteristics of the study population

Variable	Classification	Group		p-value*
		Control (n = 25)	Study (n = 25)	
Age (years)	Mean ± DP	49.9 ± 16.3	67.1 ± 10.6	< 0.001
Sex	Male	13 (52%)	10 (40%)	0.571
	Female	12 (48%)	15 (60%)	
SAH	No	17 (68%)	5 (20%)	0.001
	Yes	8 (32%)	20 (80%)	
DM	No	23 (92%)	18 (72%)	0.138
	Yes	2 (8%)	7 (28%)	
Dyslipidemia	No	21 (84%)	18 (72%)	0.496
	Yes	4 (16%)	7 (28%)	
CAD	No	25 (100%)	23 (92%)	0.490
	Yes	0 (0)	2 (8%)	
Smoking	No	22 (88%)	21 (84%)	1
	Yes	3 (12%)	4 (16%)	

Results expressed as mean ± standard deviation (SD) or frequency and percentage. * Student's t-test for independent samples (age); Fisher's exact test (categorical variables); $p < 0.05$. SAH: systemic arterial hypertension; DM: diabetes mellitus; CAD: coronary artery disease

Table 2 – Baseline echocardiographic parameters in the study group and the control group

Variable	Group	n	Mean ± standard deviation	p-value*
RV TAPSE (mm)	Control	25	22.3 ± 2.0	0.103
	Study	25	21.2 ± 2.6	
RV lateral S' (cm/s)	Control	25	13.7 ± 1.8	0.295
	Study	25	13.2 ± 1.7	
RVDD (mm)	Control	25	20.9 ± 2.7	0.219
	Study	25	22.0 ± 3.2	
Left atrial size (mm)	Control	25	33.5 ± 5.1	0.016
	Study	25	37.3 ± 5.5	
Left atrial volume (ml/m ²)	Control	25	29.2 ± 5.5	0.508
	Study	25	30.3 ± 6.7	

* Student's t-test for independent samples, $p < 0.05$; RV: right ventricular; TAPSE: tricuspid annular plane systolic excursion with M-mode; RVDD: right ventricular diastolic diameter.

lateral S' of the right ventricle with LAV and size. A LAV > 34 mL/m² and left atrial size > 40 mm were associated with lower absolute values of TAPSE and RV lateral S' ($p \leq 0.001$, $r = -0.4$ and -0.38 , respectively). There was a strong positive correlation of TAPSE with RV lateral S' ($r = 0.70$, $p < 0.001$), and of LAV and left atrial size ($r = 0.89$, $p < 0.01$) (Tables 5 and 6, Figures 1 and 2).

Discussion

The role of the LAV as a sensitive index that reflects the severity of LV diastolic function and that provides prognostic information in many heart diseases has been well documented.⁴ However, its possible effect on RV performance still requires research. The present study

demonstrated a significant inverse correlation of LAV and left atrial size with absolute values of TAPSE and RV lateral S' in patients with LVDD.

In a similar study by Torii et al.,¹² 239 patients with atrial fibrillation (AF) were compared with 281 individuals with sinus rhythm; AF patients showed lower TAPSE values regardless of age, sex, heart rate, LV ejection fraction and tricuspid regurgitation velocity. No correlations were made with LAV or left atrial size. Since we did not include patients with AF, it is possible to infer that an enlarged LA, per se, affects TAPSE and RV lateral S' only. It is known that left atrial enlargement does not occur uniformly due to physical limitations imposed by the sternum and spine, which can also affect dilatation and motion of the other cardiac chambers.⁴ TAPSE reflects not only the shortening of RV free wall, but also the traction

Table 3 – Between-group comparison of baseline echocardiographic parameters in the study group and control group

Variable	Classification	Group		p-value*
		Control (n = 25)	Study (n = 25)	
LVDD	Normal	25 (100%)		
	Grade I		21 (84%)	
	Grade II		4 (16%)	-
LVH	Normal	25 (100%)	19 (76%)	
	Concentric (c)	0 (0)	5 (20%)	
	Eccentric (e)	0 (0)	1 (4%)	-
LVH	Normal	25 (100%)	19 (76%)	
	Hypertrophy (c/e)	0 (0)	6 (34%)	0.022
RV TAPSE (mm)	Normal (> 16)	25 (100%)	25 (100%)	
	Altered (≤ 16)	0 (0)	0 (0)	1
RV lateral S' (cm/s)	Normal (> 9.5)	25 (100%)	25 (100%)	
	Altered (≤ 9.5)	0 (0)	0 (0)	1
RVDD (mm)	Normal (16 a 30)	25 (100%)	25 (100%)	
	Altered (< 16 or > 30)	0 (0)	0 (0)	1
Left atrial size (mm)	Normal (< 40)	23 (92%)	16 (64%)	
	Altered (≥ 40)	2 (8%)	9 (36%)	0.037
LAV (ml/m ²)	Normal (< 34)	20 (80%)	18 (72%)	
	Altered (≥ 34)	5 (20%)	7 (28%)	0.742

Results expressed as frequency and percentage. Fisher's exact test (categorical variables); $p < 0.05$. LVDD: left ventricular diastolic dysfunction; LVH: left ventricular hypertrophy; RV: right ventricular TAPSE: tricuspid annular plane systolic excursion with M-mode; RVDD: right ventricular diastolic diameter; LAV: left atrial volume

of the right ventricle resulting from LV contraction and effects of heart translation in the chest.¹³ Left atrial enlargement due to pressure and volume overload causes structural changes in the other chambers, including concomitant tricuspid annulus dilation, increased mobility of the tricuspid leaflets and tricuspid regurgitation.^{14,15} One hypothesis is that tricuspid annular dilatation, as a consequence of enlarged LA, could change TAPSE and lateral S' due to displacement of mitral annulus. This would result in RV remodeling and affect RV longitudinal shortening, as the site used for TAPSE and S' measurements is the lateral insertion site of the tricuspid valve. However, we cannot rule out the possibility that such changes in cardiac chambers induced by the enlargement of the LA could also affect the ultrasonic angle beam, leading to changes in tissue Doppler imaging results. One interesting finding was that although the linear dimension of the LA was greater in the study group than in controls, LAV was practically normal in both groups. It is known that this linear measure of the LA has low accuracy and reproducibility due to technical limitations including the angle of the ultrasound beam, and the left atrial irregular geometry.⁴

It is also worth pointing out that the reference values for LAV are derived from international studies involving individuals with higher height; no study involving LAV measurements in a large Brazilian population has been performed so far.¹⁶ However, even small changes in the LAV caused changes in both TAPSE and RV lateral S' values.

Due to the strict exclusion criteria, no signs of RV dysfunction were expected in either study or control group. This was confirmed by the normal values of TAPSE and lateral S' of the right ventricle in all participants. In the study by Bruhl et al.¹⁷ evaluating 51 healthy individuals, with no past history of cardiac disease, found that TAPSE, mitral annular plane of systolic excursion (MAPSE), and tissue Doppler imaging measurements of the right and left ventricles were stable across age, gender, and body surface area. These findings illustrate the ventricular relationship and systolic interdependence. RV size and function correlate with the symptoms and physical capacity of patients with many clinical conditions. An accurate echocardiographic assessment of the right ventricle allows early detection of cardiac diseases, improves risk stratification and may indicate the right moment to start drug therapy.^{18,19} Zakir et al.,²⁰ addressed, appropriately and in detail, the correlation of LV diastolic function with RV systolic dysfunction, based on the invasive measurement of the pulmonary venous system. LV diastolic dysfunction causes an increase in left atrial filling pressure, which can be transmitted backwards, leading to pulmonary arterial hypertension and RV pressure overload. According to Simon et al.²¹ the first stage of RV dysfunction is pulmonary hypertension, which causes RV hypertrophy and ultimately right systolic dysfunction. However, in the present study, even patients with LVDD grade II showed normal TAPSE and RV lateral S'. In addition, difficulties in the analysis of the RV function may also result from RV

Table 4 – Echocardiographic parameters in the study group by left ventricular diastolic dysfunction grade and presence of concentric (c) and eccentric (e) left ventricular hypertrophy

Variable	LVDD	n	Mean ± standard deviation	p-value*
RV TAPSE (mm)	Grade I	21	21.2 ± 2.5	0.832
	Grade II	4	21.5 ± 3.5	
RV S' (cm/s)	Grade I	21	13.2 ± 1.7	0.604
	Grade II	4	12.8 ± 1.7	
RVDD (mm)	Grade I	21	21.5 ± 3.2	0.085
	Grade II	4	24.5 ± 1.9	
Left atrial (mm)	Grade I	21	35.9 ± 4.6	0.002
	Grade II	4	44.5 ± 4.4	
LAV (ml/m ²)	Grau I	21	29.0 ± 5.5	0.017
	Grau II	4	37.5 ± 8.9	
Variable	LVH	n	Mean ± standard deviation	p-value*
RV TAPSE (mm)	Normal	19	20.8 ± 2.5	0.176
	LVH (c/e)	6	22.5 ± 2.8	
RV S' (cm/s)	Normal	19	13.1 ± 1.7	0.580
	LVH (c/e)	6	13.5 ± 1.8	
RVDD (mm)	Normal	19	21.5 ± 3.3	0.185
	LVH (c/e)	6	23.5 ± 2.8	
Left atrial (mm)	Normal	19	36.3 ± 5.2	0.104
	LVH (c/e)	6	40.5 ± 6.0	
LAV (ml/m ²)	Normal	19	29.7 ± 6.2	0.413

*Student's t-test for independent variables, $p < 0.05$. RV: right ventricular; TAPSE: tricuspid annular plane systolic excursion with M-mode; RVDD: right ventricular diastolic diameter; LA: left atrium; LAV: left atrial volume

geometric and the complex correlation of the right ventricle with the LV septum. This could lead to delayed diagnosis of RV systolic dysfunction, which is generally detected in severe disease states. Therefore, serial analysis of the LAV and of TAPSE and lateral S' of the right ventricle in patients with LVDD or heart failure with preserved ejection fraction may provide initial evidence of deterioration of the RV function.

The other findings of the study were in accordance with literature data. In our study group, LVDD patients were older, showed higher incidence of LVH and greater left atrial size, and higher prevalence of SAH when compared with the control group.²²⁻²⁴ Patients with altered diastolic function had larger LA, which was positively associated with the degree of diastolic dysfunction. This is in line with the study by El Aouar et al.¹⁶

Regarding the high prevalence of SAH in the study group, it is well known that SAH can cause not only LVH but also RV hypertrophy^{25,26} that, in turn, was not assessed in our study. The fact that we did not find significant differences in echocardiographic measures between the groups can be explained by the strict exclusion criteria; it also reflects the fact that the analysis and referral values of echocardiographic parameters used in the assessment of the RV function is a matter of considerable debate in the literature, with wide variability within and between observers.^{6,7} In this sense, there is not a gold standard method, but rather a set of

group that should be sequentially interpreted considering the clinical conditions of each patient. Thus, subtle changes in the variables used for RV function analysis in our study, as well as their correlation with left atrial enlargement can serve as a basis for future studies in this field. It is pertinent to consider the use of the speckle tracking technique (strain [ε] and strain rate [SR or s⁻¹]) for assessment of the RV function in future studies. The ε and s⁻¹ indexes evaluate regional and global myocardial deformation with advantages over the use of the strain measure obtained from tissue Doppler, especially a lower variability within and between observers. The use of two-dimensional speckle tracking echocardiography allows the analysis of longitudinal, circumferential and radial strain, with not influence of the angle.²⁷

Finally, this study has important limitations that should be considered: (1) the small number of the sample; studies involving larger sample sizes would be needed to confirm our findings; (2) the groups were not perfectly matched, especially in terms of age; (3) the lack of adequate or precise information about the time of hypertensive disease and its treatment, as well as on medications used by the patients; and (4) we did not analyze the variables tricuspid annulus diameter and right atrial volume, which could provide more information on the RV remodeling. In addition, patients with LVDD was composed of older individuals compared with the control group. This may have

Table 5 – Echocardiographic parameters in the study group by left atrial size (mm) and left atrial volume (mL/m²)

Variable	Left atrial size	n	Mean ± standard deviation	p-value*
RV TAPSE (mm)	Normal (< 40)	16	21.9 ± 2.4	0.103
	Altered (≥ 40)	9	20.1 ± 2.6	
RV lateral S' (cm/s)	Normal (< 40)	16	13.6 ± 1.8	0.111
	Altered (≥ 40)	9	12.4 ± 1.2	
RVDD (mm)	Normal (< 40)	16	21.7 ± 3.2	0.584
	Altered (≥ 40)	9	22.4 ± 3.3	
LAV (ml/m ²)	Normal (< 40)	16	26.8 ± 3.8	< 0.001
	Altered (≥ 40)	9	36.7 ± 6.2	
Variable	LAV	n	Mean ± standard deviation	p-value*
RV TAPSE (mm)	Normal (< 34)	18	22.2±2.4	< 0.001
	Altered (≥ 34)	7	18.9 ± 0.9	
RV lateral S' (cm/s)	Normal (< 34)	18	13.7 ± 1.7	0.001
	Altered (≥ 34)	7	11.9 ± 0.7	
RVDD (mm)	Normal (< 34)	18	21.7 ± 3.3	0.565
	Altered (≥ 34)	7	22.6 ± 3.2	
Left atrial size (mm)	Normal (< 34)	18	34.7 ± 3.6	< 0.001
	Altered (≥34)	7	43.9 ± 4.0	

*Student's t-test for independent samples, $p < 0.05$. RV: right ventricular TAPSE: tricuspid annular plane systolic excursion with M-mode; RVDD: right ventricular diastolic diameter; LAV: left atrial volume.

Table 6 – Correlations between quantitative variables in the study group

Variables	n	Pearson's correlation coefficient	p-value
Age × RV TAPSE	25	-0.22	0.281
Age × RV lateral S'	25	-0.42	0.035
Age × RVDD	25	0.04	0.866
Age × left atrial size	25	0.31	0.134
Age × LAV	25	0.40	0.050
RV TAPSE × RV lateral S'	25	0.70	< 0.001
RV TAPSE × RVDD	25	0.33	0.106
RV TAPSE × left atrial size	25	-0.33	0.107
RV TAPSE × LAV	25	-0.40	0.047
RV lateral S' × RVDD	25	0.40	0.051
S' lateral VD × left atrial size	25	-0.26	0.216
RV lateral S' × LAV	25	-0.38	0.063
RVDD × left atrial size	25	0.30	0.149
RVDD × LAV	25	0.23	0.271
Left atrial size × LAV	25	0.89	< 0.001

TAPSE: tricuspid annular plane systolic excursion with M-mode; RVDD: right ventricular diastolic diameter; LAV: left atrial volume.

influenced the results, particularly the LAV. Also, the prevalence of SAH increases with age and differently in men and women.^{28,29} Although the study group and the control group were not perfectly matched, the proportion of men and women was not different between the groups; yet, we did not find any significant difference between men and women in the study variables.

Conclusions

The present study determined, for the first time, a correlation of the increase in LAV with progressive RV functional changes in patients with LVDD. However, further studies are needed to confirm these findings.

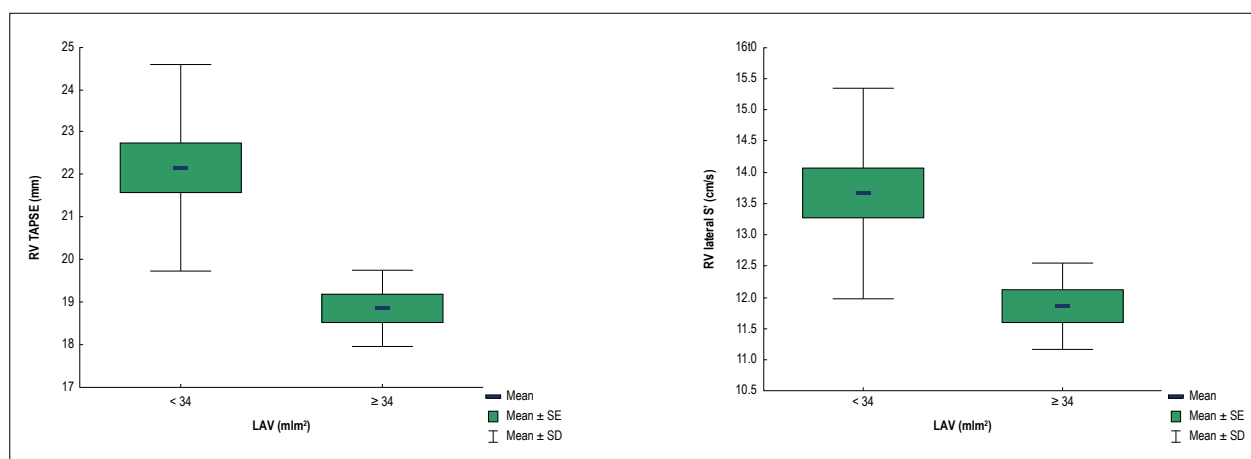


Figure 1 – Correlation between right ventricular tricuspid annular plane systolic excursion (RV TAPSE) and left atrial volume (LAV) (left panel; $p < 0.001$), and between lateral S' of the right ventricle and LAV (right panel; $p < 0.001$). RV: right ventricular; LA: left atrium; SE: standard error; SD: standard deviation; Student's t-test for independent samples; $p < 0.05$.

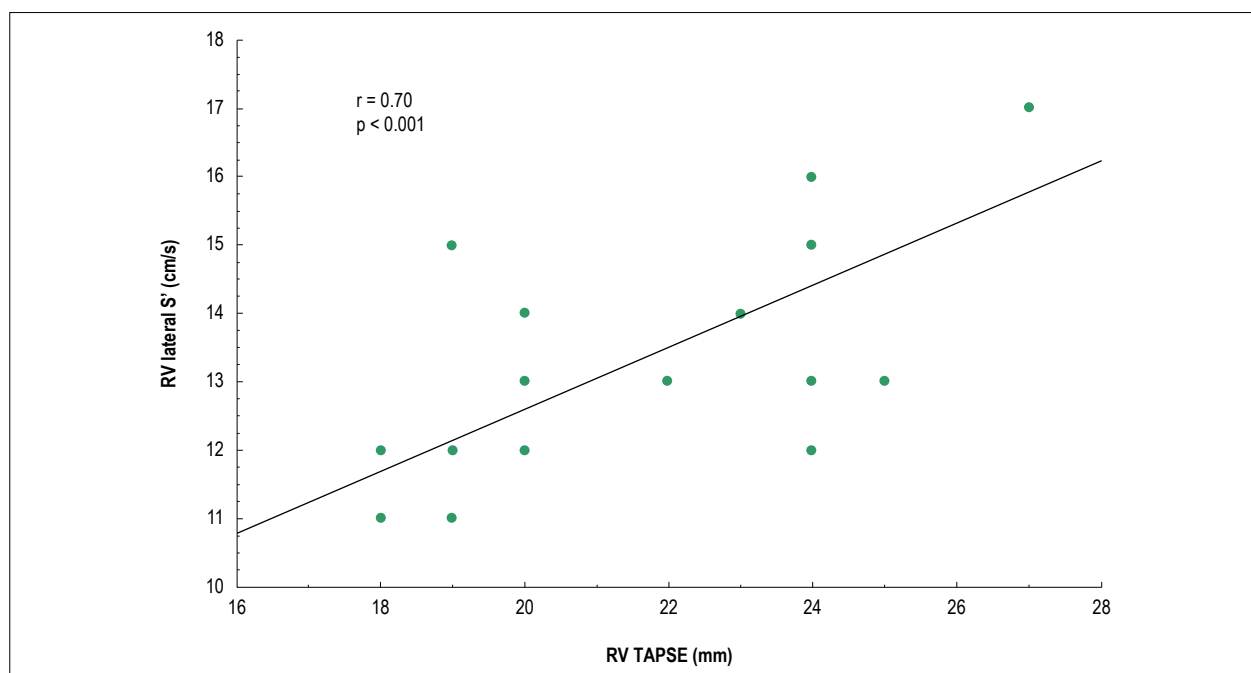


Figure 2 – Correlation between right ventricular tricuspid annular plane systolic excursion (RV TAPSE) and right ventricular S' lateral.

Author contributions

Conception and design of the research, acquisition of data and analysis and interpretation of the data: Baroncini LAV, Borges L JL, Camarozano AC, Carmo DC, Darwich RZ, Fortunato Junior JÁ; statistical analysis: Baroncini LAV; writing of the manuscript: Baroncini LAV, Darwich RZ, Fortunato Junior JÁ; critical revision of the manuscript for intellectual content: Baroncini LAV, Borges L JL, Camarozano AC, Carmo DC.

Potential Conflict of Interest

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

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Universidade Positivo under the protocol number 2331223. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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