Original Article

Right Ventricle Diastolic Function: Correlation with Age

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Abstract

Introduction: **Right ventricle (RV) elasticity tends to decrease with aging and may alter its diastolic function.**

Objective: **To evaluate the correlation between echocardiographic changes in RV diastolic function and advancing age in individuals with normal biventricular systolic function.**

Methods: **This retrospective observational cohort study included 110 patients: 66 (60%) women (62 [SD, 13.7] years) and 44 (40%) men (60.6 [SD, 10.8] years). The transthoracic echocardiography data included: spectral Doppler of tricuspid inflow E wave, A wave, E/A ratio, and E wave deceleration time; tissue Doppler of lateral tricuspid annulus e' wave, a' wave, and E/e' ratio. Correlations were calculated using Pearson's and Spearman's correlation coefficients.**

Results: **Only 35.2% of the sample had RV diastolic dysfunction. Of the evaluated echocardiographic variables, the E wave was negatively correlated with age in both women (r 0.473; $p < 0.001$) and men (r -0.37, $p = 0.015$). The E/A ratio was negatively correlated with age only in women (r -0.32; $p = 0.001$), and E wave deceleration time was positively correlated with age only in women (r 0.31; $p = 0.014$). The other variables were not significantly correlated with age in men or women.**

Conclusions: **We found a significant correlation between age and echocardiographic parameters for RV diastolic dysfunction, which was more evident in women.**

Keywords: **Heart Ventricles; Heart Failure, Diastolic; Echocardiography.**

Introduction

In the last 10 years, interest in the right ventricle (RV) and its effect on clinical outcomes has increased, largely due to advancements in pharmacological treatment for pulmonary arterial hypertension.[1] However, like the left ventricle (LV), the RV is affected by numerous physiological changes inherent to age that must be distinguished from those resulting from heart disease.[2-3] Thus, more accurate assessment of both systolic and diastolic function in the RV is needed in clinical practice. The lack of studies on this chamber is likely due to its relative structural and functional complexity.[4] Unlike the LV, which has a conical shape, the RV has a hemiellipsoid shape that adheres to the LV. In clinical practice, indices of systolic performance, such as ejection fraction, reflect LV contractility as an intrinsic property of the myocardium. For the RV, systolic performance is based on analysis of ejection fraction, fractional area change, and tricuspid valve annular plane systolic excursion. These parameters are more associated with atrioventricular coupling related to elasticity, which shows the importance of RV compliance in both systolic and diastolic function.[5] In patients over 70 years of age, studies on the RV, in addition to being fewer, are incomplete, eg, the prognostic relationship between RV dysfunction and heart failure mortality is still unknown.[6] Thus, the objective of the present study was to evaluate the correlation between echocardiographic parameters of RV diastolic function with advancing age in patients with preserved biventricular function.

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Methods

Study population

This observational retrospective cohort study was based on data from the electronic medical records of 110 patients over 18 years of age of both sexes who underwent transthoracic echocardiography at the Curitiba Red Cross Hospital (Curitiba, PR, Brazil) for any clinical indication between June 2020 and August 2020.

The patient sample was chosen by convenience, rather than any statistical criteria, according to necessary echocardiographic data in the electronic medical records. For each patient, clinical and echocardiographic parameters were collected. The analyzed clinical data included: age, sex, body mass index, systemic arterial hypertension, diabetes mellitus, diabetes duration (in treatment), coronary artery disease, stroke, cerebral palsy, and smoking (current or former), in addition to regularly used medications.

The exclusion criteria were: a) medical records and reports lacking the echocardiographic values analyzed in this study, b) significant valve disease (moderate or severe), c) valve prostheses, d) segmental changes in LV contraction due to ischemic heart disease or other cardiomyopathies, e) pulmonary emphysema or overt chronic obstructive pulmonary disease, f) moderate-to-severe pulmonary arterial hypertension (pulmonary artery systolic pressure > 50 mmHg), g) left ventricular contractile dysfunction (ejection fraction < 52% for men or < 54% for women), h) infiltrative diseases or pericardiomyopathy; i) congenital heart disease with increased pulmonary flow (with or without surgical correction), and j) pacemakers.

Transthoracic echocardiography was performed with a Phillips IE 33, Phillips HD 11, Phillips Envisor (Koninklijke Philips N.V., Amsterdam, Netherlands), or GE Vivid IQ Premium (General Electric, Boston, MA, USA) ultrasound machine. To be included in the analysis, the echocardiographic reports had to contain all standard acoustic windows (with all echocardiographic measurements) and a complete assessment of RV diastolic function.

All ultrasound measurements were performed by experienced echocardiographers qualified in echocardiography by Brazilian Society of Cardiology's Department of Cardiovascular Imaging. This study was approved by the institutional research ethics committee.

Main echocardiographic parameters analyzed in this study

- Spectral Doppler of the tricuspid inflow: E and A waves, E/A ratio and E wave deceleration time
- Tissue Doppler of the free wall of the tricuspid annulus: waves e' and a'
- E/e' ratio
- Cavity diameters in the two-dimensional echocardiography of the right chambers
- RV systolic function through analysis of fractional area change, tricuspid valve annular plane systolic excursion
- S' wave in lateral tissue Doppler of the tricuspid annulus.

These parameters were not used in the final data analysis. Patients with any signs of RV contractile dysfunction, such as fractional area change < 35%, tricuspid valve annular plane systolic excursion < 17 mm, or S' wave < 10 cm/s, were excluded from the study.

RV diastolic dysfunction was classified according to the following criteria: a tricuspid E/A ratio < 0.8 suggests relaxation (Grade I), a tricuspid E/A ratio of 0.8-2.1 with predominant diastolic flow in hepatic veins suggests a "pseudonormal" (Grade II) filling pattern, and a tricuspid E/A ratio > 2.1 with an E wave deceleration time < 120 ms suggests a restrictive filling pattern (Grade III).[7-11]

All quantifications and values used in the present study were based on American Society of Echocardiography and European Society of Cardiovascular Imaging guidelines.[7-11]

Statistical analysis

The analysis was performed separately for women and men. The results were described as means, medians, minimum and maximum values, and SD for quantitative variables or as frequencies and percentages for categorical variables. Pearson's or Spearman's correlation coefficients were estimated for age and echocardiographic variables. The normality of continuous variables was assesses with the Kolmogorov-Smirnov test. P-values < 0.05 were considered statistically significant. The data were analyzed in IBM SPSS Statistics 20.0 (IBM, Armonk, NY, USA).

Results

The analysis included data from 110 patients, 66 (60%) women with a mean age of 62.6 (SD, 13.70] years (median 64 [18-90] years), and 44 (40%) men with a mean age of 60.6 (SD, 10.8) years (median 62.5 [37-85] years). The sample's clinical characteristics are shown in Table 1. Baseline echocardiographic parameters (Table 2) were in agreement with literature.[7]

Regarding RV diastolic dysfunction (Table 3): 70 patients (64.8%) were normal, 18 (16.7%) had grade I dysfunction, 19 (17.6%) had grade II dysfunction, and only 1 patient (male) had grade III dysfunction.

In the correlation analysis (Table 4), the E wave was negatively correlated with age in both women (r -0.473, p < 0.001) and men (r -0.37, p = 0.015). The E/A ratio was negatively correlated with age only in women (r -0.36; p = 0.004), and E wave deceleration was only positively correlated with age only in women (r 0.31, p = 0.014) (Figures 1 and 2). The other variables were not significantly correlated with age in men or women.

Discussion

Most individuals in the sample (mean age 62 years) had normal RV diastolic function. We also found that the echocardiographic parameters, such as E wave, E/A ratio, and E wave deceleration of the tricuspid valve change more with advancing age in women than men in the same age group. In a similar population, Lasari Melo et al.[12] also found a significant decrease in RV E wave and E/A ratio with age, but no significant sex differences. One reason that age-related RV diastolic dysfunction was more prevalent in women could be the significant drop in estrogen levels after menopause. It is known that estrogen receptors in female hearts can act protectively against heart failure with preserved ejection fraction, which is more common in women. Estrogen causes reduced angiotensin-converting enzyme activity, a reduction in angiotensin-II, and increased production of angiotensin-I, which has an antioxidant and anti-inflammatory effect, among other benefits.[13]

The sample of Lasari Melo et al.[12] had normal diastolic function. Despite having similar populations, approximately 35% of our sample had diastolic dysfunction (Table 3). Nevertheless, we consider this a very low degree of diastolic dysfunction, which raises the question of whether this low level of diastolic dysfunction was related to the fact that we used LV diastolic dysfunction criteria to assess the RV.

Table 1 – Descriptive statistical analysis of comorbidities, stratified by sex

Variable	Grade	Sex		General
		Female	Male	
ECG	Sinus	28 (96.6%)	25 (96.2%)	53 (96.4%)
	Non-sinus	1 (3.5%)	1 (3.9%)	2 (3.6%)
SAH	No	30 (45.5%)	12 (27.3%)	42 (38.2%)
	Yes	36 (54.6%)	32 (72.7%)	68 (61.8%)
DM	No	46 (69.7%)	28 (63.6%)	74 (67.3%)
	Yes	20 (30.3%)	16 (36.4%)	36 (32.7%)
Dyslipidemia	No	45 (68.2%)	16 (36.4%)	61 (55.5%)
	Yes	21 (31.8%)	28 (63.6%)	49 (44.5%)
Previous AMI	No	63 (95.5%)	33 (75.0%)	96 (87.3%)
	Yes	3 (4.6%)	11 (25.0%)	14 (12.7%)
Previous CAD	No	58 (87.9%)	29 (65.9%)	87 (79.1%)
	Yes	8 (12.1%)	15 (34.1%)	23 (20.9%)
History of smoking	No	53 (81.5%)	32 (72.7%)	85 (78.0%)
	Yes	12 (18.5%)	12 (27.3%)	24 (22.0%)
HF	No	65 (98.5%)	40 (90.9%)	105 (95.5%)
	Yes	1 (1.5%)	4 (9.1%)	5 (4.5%)
Valve disease	No	66 (100.0%)	43 (97.7%)	109 (99.1%)
	Yes	0 (0.0%)	1 (2.3%)	1 (0.9%)
COPD	No	63 (95.5%)	42 (95.5%)	105 (95.5%)
	Yes	3 (4.6%)	2 (4.6%)	5 (4.5%)
Chronic kidney disease	No	64 (97.0%)	44 (100.0%)	108 (98.2%)
	Yes	2 (3.0%)	0 (0.0%)	2 (1.8%)
Arrhythmias	No	63 (95.5%)	40 (90.9%)	103 (93.6%)
	Yes	3 (4.6%)	4 (9.1%)	7 (6.4%)

ECG: electrocardiogram; SAH: systolic arterial hypertension; DM: diabetes mellitus; AMI: acute myocardial infarction; CAD: coronary artery disease; HF: heart failure; COPD: chronic obstructive pulmonary disease.

Table 2 – Descriptive statistical analysis of echocardiographic variables

Variable	N	Mean (SD)	Median (min-max)
RV – E wave (m/s)	110	0.49±0.13	0.5 (0.1-0.8)
RV – A wave (m/s)	108	0.42±0.13	0.4 (0.18-0.8)
RV – E/A ratio	108	1.22±0.44	1.2 (0.5-2.7)
RV – e' lateral (m/s)	110	0.14±0.17	0.1 (0.02-0.9)
RV – A´ (m/s)	108	0.18±0.16	0.14 (0.03-0.9)
RV – E/e´	110	4.95±2.24	4.9 (0.5-11)
RV – E deceleration (ms)	109	204.71±75.96	194.0 (84-690)

RV: right ventricle; SD: standard deviation.

Table 3 – Descriptive statistical analysis of right ventricular diastolic dysfunction

Variable	Grade	Sex		General
		Female	Male	
RV diastolic dysfunction	0	41 (63.1%)	29 (67.4%)	70 (64.8%)
	1	15 (23.1%)	3 (7.0%)	18 (16.7%)
	2	9 (13.8%)	10 (23.3%)	19 (17.6%)
	3	0 (0.0%)	1 (2.3%)	1 (0.9%)

RV: right ventricle.

The shortening and lengthening of the RV are greater longitudinally than radially, unlike the LV, in which radial torsion is greater. Thus, pulsed tissue Doppler can be considered an ideal technique for assessing changes in age-related RV function.[9] Changes that occur in the myocardium with aging include increased deposition of extracellular matrix, cardiomyocyte loss and, consequently, hypertrophy of the remaining cells, leading to myocardial stiffness.[13] Homeostasis between extracellular matrix synthesis and degradation is the key factor in maintaining cardiac structure and function.[14] However, especially in women, there is an excessive increase in the synthesis of type I and III collagen with aging, which leads to increased myocardial thickness and rigidity, causing heart failure with preserved LV ejection fraction.[15-16] In our data, tissue Doppler of the tricuspid annulus did not change significantly with age. Corroborating these findings, Lindqvist et al.[17] (255 healthy patients) and Alam et al.[18] found that systolic myocardial velocities were preserved with aging. In Lindqvist et al.,[17] the E/A ratio decreased over time, similar to our findings in the present study.

Inneli et al.[19] divided a sample of 298 healthy individuals into 7 decade-based age groups, finding a significant positive correlation between the E/e' ratio and aging and a negative correlation between e' wave and age. However, this appears to be the only study to date that has found such correlations.

Our findings reinforce the hypothesis that E wave velocity and RV E/A ratio (indicators of diastolic function change) decrease with age, and this decrease was more pronounced in women.

Our study's main limitation was its small sample size and the fact that it was conducted retrospectively by analyzing medical records. Another relevant factor was the exclusion of patients with significant pulmonary arterial hypertension, making it impossible to assess diastolic dysfunction in this condition.[20] However, our main objective was to assess RV diastolic function in isolation according to age.

Conclusions

The present study demonstrated that age influenced the progression of RV diastolic dysfunction, which was more evident in women. However, more studies are needed to confirm these findings.

Table 4 – Descriptive statistical analysis of the association between age and echocardiographic variables

Variable	General			Women			Men		
	n	r	p	n	r	p	n	r	p
Age (years) x RV – E wave (m/s)	107	-0.43	< 0.001	64	-0.47	< 0.001	43	-0.37	0.015
Age (years) x RV – E/A Ratio	107	-0.32	0.001	64	-0.36	0.004	43	-0.23	0.145
Age (years) x RV – E/e'	107	-0.01	0.925	64	-0.13	0.315	43	0.19	0.234
Age (years) x RV – E deceleration (ms)	107	0.14	0.139	64	0.31	0.014	43	-0.03	0.841
Age (years) x RV – A wave (m/s)	108	0.00	0.964	65	0.01	0.924	43	-0.07	0.651
Age (years) x RV – e' lateral (m/s)	110	-0.14	0.135	66	-0.16	0.212	44	-0.19	0.209
Age (years) x RV – H' (m/s)	108	0.18	0.057	65	0.13	0.306	43	0.18	0.237

**r: Pearson's or Spearman's correlation coefficient, p < 0.05. RV: right ventricle*

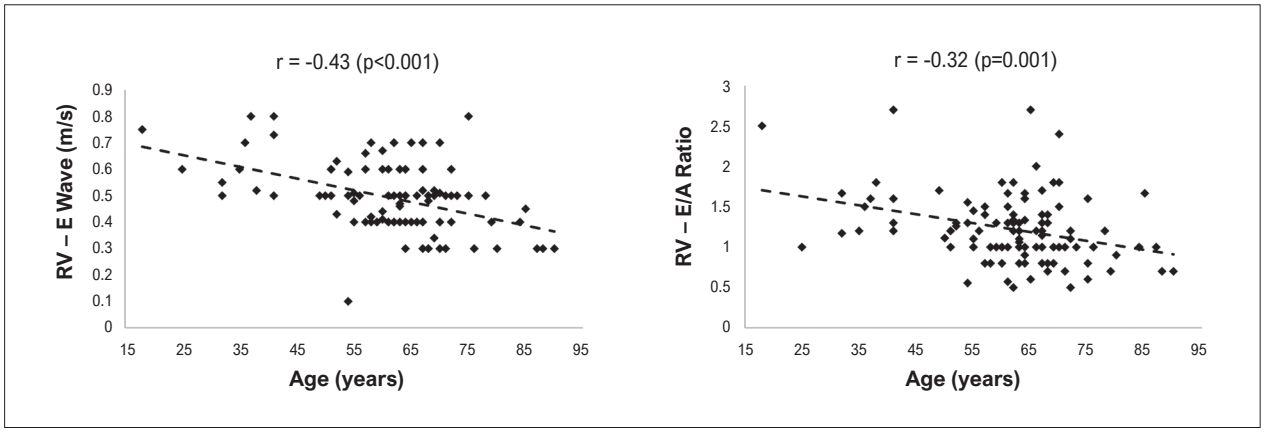

Figure 1 – *Correlation between age, E wave, and E/A ratio among men. RV: right ventricle; r: Pearson's or Spearman's correlation coefficient.*

Author Contributions

Conception and design of the research, writing of the manuscript and critical revision of the manuscript for intellectual content: Moura AN, Camarozona AC, Fortunato JA, Baroncini LAV; acquisition of data, analysis and interpretation of the data and statistical analysis: Moura AN, Camarozona AC, Sá CRF, Carmo DC, Fortunato JA, Darwich RZ, Baroncini LAV.

Potential Conflict of Interest

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

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Study Association

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Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Universidade Positivo under the protocol number 5.582.981. 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.

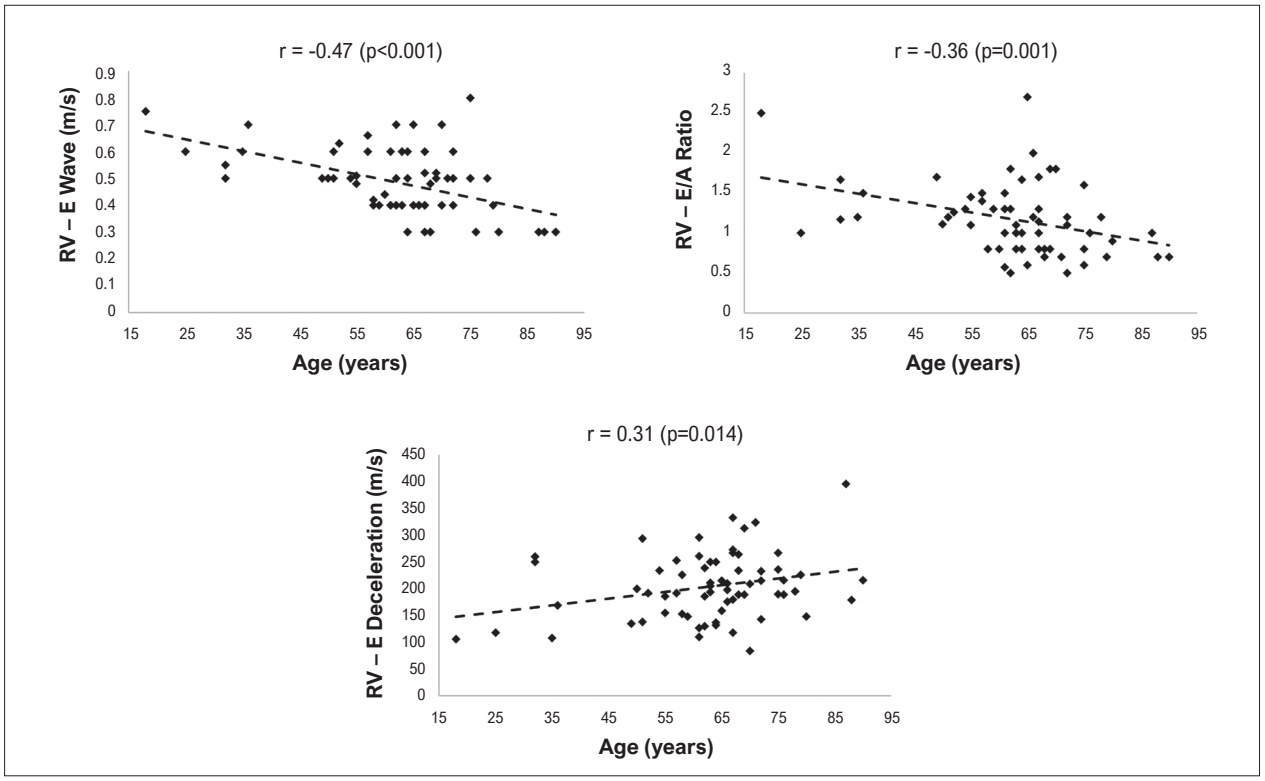

Figure 2 – *Correlation between age and E wave, E/A ratio, and E wave deceleration among women. RV: right ventricle; r: Pearson's or Spearman's correlation coefficient.*

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