Original article

Echocardiographic Correlation Between Right Ventricular Diastolic Function and Age and Gender in Subjects With Preserved Systolic Function

Correlação Ecocardiográfica da Função Diastólica do Ventrículo Direito com Idade e Gênero em Indivíduos com Função Sistólica Preservada

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Abstract

Introduction: Right ventricular (RV) systolic and diastolic functions influence the outcomes of cardiovascular diseases. However, right chamber size and function have not been uniformly assessed by age and sex.

Objective: To evaluate RV diastolic function by age and sex in an outpatient population with preserved left ventricular (LV) and RV systolic function using transthoracic echocardiography.

Method: This observational cross-sectional study included a total of 97 patients (56 women) aged 61.5 ± 12.5 years. The assessed parameters included RV E/A ratio; peak E-wave and A-wave velocity, E-wave acceleration and deceleration time, and integral E-wave and A-wave velocity-time; and pulmonary artery systolic pressure (PASP), tricuspid reflux velocity, inferior vena cava diameter, and right atrial volume.

Results: A reduced E-wave was observed with increasing age (Pearson's correlation coefficient [PCC], -0.30; p = 0.003). The same was observed for the E/A ratio (PCC, -0.21; p = 0.035). There was a significant positive association between age and PASP results (PCC, 0.40; p = 0.004) and tricuspid reflux velocity (PCC, 0.36; p = 0.008). There was no significant intersex difference in echocardiography variables.

Conclusion: The present study showed the impact of age on RV diastolic function indices, which remained within the normal range, in subjects with preserved LV and RV function. The study did not evidence a significant difference between genders in relation to the diastolic function of the right ventricle.

Keywords: Right ventricle; Diastolic function; Echocardiography.

Resumo

Introdução: *As funções sistólica e diastólica do ventrículo direito influenciam no desfecho de doenças cardiovasculares. A avaliação sistemática das dimensões e da função das câmaras direitas, de acordo com sexo e idade, não é uniformemente realizada.*

Objetivo: *Avaliar, ao ecocardiograma transtorácico, a correlação da função diastólica do ventrículo direito com idade e sexo, em uma população ambulatorial variada, com função sistólica dos ventrículos esquerdo e direito preservada.*

Métodos: *Estudo observacional, transversal. Foram selecionados 97 pacientes, 61,5 ± 12,5 anos, sendo 56 mulheres. Foram avaliadas as seguintes medidas da função diastólica do ventrículo direito: velocidade de pico das ondas E e A, relação E/A, tempos de aceleração e desaceleração de onda E, integral velocidade-tempo da onda E, integral velocidade-tempo da onda A, além da pressão sistólica de artéria pulmonar, velocidade do refluxo tricúspide, diâmetro da veia cava inferior e volume do átrio direito.*

Resultados: *Ocorreu redução da onda E com o aumento da idade (coeficiente de correlação de Pearson de -0,30; p=0,003) e da relação E/A (coeficiente de correlação de Pearson de -0,21; p=0,035). Houve associação positiva e significativa entre idade e os resultados das variáveis pressão sistólica de artéria pulmonar (coeficiente de correlação de Pearson de 0,40; p=0,004) e velocidade do refluxo tricúspide (coeficiente de correlação de Pearson de 0,36; p=0,008). Não houve diferença significativa na comparação entre os sexos em relação a variáveis ecocardiográficas.*

Conclusão: *O presente estudo mostrou impacto da idade nos índices de função diastólica do ventrículo direito, embora ainda com valores dentro da normalidade, em indivíduos com função sistólica dos ventrículos direito e esquerdo preservada, mas sem diferença significativa entre os sexos.*

Palavras-chave: *Ventrículo direito; Função diastólica; Ecocardiografia.*

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Introduction

Cardiovascular diseases are the main cause of death in Brazil and worldwide, being responsible for about 20% of all deaths in people aged over 30 years.[1] Some noninvasive methods for the diagnosis of cardiovascular diseases, including transthoracic echocardiography, provide morphological and functional information about the cardiac chambers.

Right ventricular (RV) function influences the outcomes of cardiac and pulmonary diseases such as heart failure, pulmonary hypertension, myocardial infarction, heart valve disease, and congenital heart disease regardless of left ventricular (LV) function.[2] Although standard echocardiography can reliably assess LV function, the ultrasound assessment of RV structure and function is generally suboptimal due to its anatomical location and specific geometric configuration.

RV function was neglected for a long time due to its complex detection and measurement. Several researchers recently started to implement transthoracic Doppler echocardiography to assess RV diastolic function in normal subjects versus those with a variety of cardiovascular disorders.[3] Evidence of the clinical importance of RV function has increased, partly due to improved imaging techniques. RV function impacts the outcomes of patients hospitalized with heart and lung disease.[4]

In recent years, transthoracic echocardiography using Doppler ultrasound has been increasingly used to assess RV diastolic function in several pathologies. Similarly to LV diastolic dysfunction, multiple etiologies have been associated with relaxation changes that lead to RV diastolic dysfunction.[5]

Thus, this study aimed to assess RV diastolic function in terms of age and sex in an outpatient population with preserved LV and RV systolic function undergoing routine echocardiographic examinations.

Methods

Study population

This was an observational cross-sectional study. A total of 115 patients of both sexes over 18 years of age (mean age, 63.2 ± 12.1 years; 58 women) of any ethnicity who were referred by their attending physician for transthoracic echocardiography for any clinical indication were selected from the Cardiology outpatient clinic of the Red Cross Hospital of Curitiba, PR, Brazil. The patients were chosen by convenience using no statistical criteria according to their availability to participate in the research. A protocol form of clinical and echocardiographic parameters was filled out for each patient. The clinical data analyzed included age, sex, weight, height, body mass index (BMI), presence of systemic arterial hypertension (SAH), diabetes mellitus (DM), coronary artery disease (CAD), dyslipidemia, and smoking (current or previous). The diagnoses of SAH, DM, dyslipidemia, and smoking were retrieved from the patients' medical records and/or reported by the patients (referred information). The presence of CAD was confirmed by medical record data and by the patient, including non-fatal myocardial infarction and surgical or percutaneous myocardial revascularization. The regular use of drugs was also registered.

The exclusion criteria were significant valve diseases (moderate and severe), prosthetic valves, confirmed CAD and/or segmental changes in LV contraction due to ischemic heart disease or other cardiomyopathies,[7] pulmonary emphysema or chronic obstructive pulmonary disease, moderate to severe pulmonary arterial hypertension (PASP > 50 mmHg), LV contractile dysfunction (ejection fraction < 52% for men and < 54% for women), RV systolic dysfunction (tricuspid annular systolic excursion < 17 mm, tricuspid annulus peak systolic velocity < 9 cm/s, and RV fractional area < 35%), and atrial fibrillation or pacemaker rhythm.

The patients underwent complete two-dimensional transthoracic echocardiography using a Phillips IE 33, Phillips HD 11, Phillips Envisor, or ultrasound machine. Sonographic measurements were collected by two experienced echocardiographers licensed by the Department of Cardiovascular Imaging of the Brazilian Society of Cardiology.

All echocardiographic measurements of all standard acoustic windows were collected, including RV diastolic function measurements.

All patients signed two copies of the Informed Consent Form, one of which they kept. The study was approved by the local research ethics committee.

Main echocardiographic parameters analyzed in this study

The indices for calculating RV diastolic function were assessed by apical four-chamber view by positioning of the sample volume at the tips of the tricuspid leaflets during diastole. RV diastolic function was initially assessed by pulsatile spectral Doppler of the tricuspid influx. The Doppler bundle was aligned parallel to the blood flow vector. An electrocardiography tracing was included in all studies.

RV diastolic indices were calculated by tricuspid flow pulsed spectral Doppler, including E-wave peak velocity representing early filling, A-wave peak velocity representing late filling, peak ratio of early velocity at the late peak (E/A), E-wave acceleration time, E-wave deceleration time, E-wave velocity-time integral, and A-wave velocity-time integral (Figures 1 and 2). A tricuspid E/A ratio < 0.8 suggests a impaired relaxation, a tricuspid E/A ratio of 0.8–2.1 with a predominance of diastolic flow in the hepatic veins suggests a pseudo-normal filling pattern, and a tricuspid E/A ratio > 2.1 with E-wave deceleration time < 120 ms suggests a restrictive filling pattern.

The atrial filling fraction, which represents the percentage of RV filling due to atrial contraction, was calculated by the fraction of the A velocity integral compared to all tricuspid influx.

PASP was estimated by tricuspid reflux continuous spectral Doppler in millimeters of mercury (Figure 3) using the maximum tricuspid regurgitation speed (m/s), when present, added to the diameter of the inferior vena cava (mm) to determine the right atrial (RA) pressure.[6-7]

Right atrium (RA) was analyzed in the apical transthoracic four-chamber window. The RA area was estimated from this window by planimetry considering a reference limit of 18 cm^2. Indexed RA volume, the most accurate way to assess chamber size, was calculated as a reference value of 32 mL/m^2 for men and 27 mL/m^2 for women (Figure 4).

All quantifications and values considered in the present study were based on American Society of Echocardiography and of the European Association of Cardiovascular Imaging guidelines.[8-12]

Statistical analysis

The results of this study are described as mean, median, minimum and maximum values, or standard deviation for quantitative variables and as frequency and percentage for categorical variables. Student's t-test for independent samples was used to compare the echocardiographic variables between the sexes. The association between age and echocardiographic variables was assessed by estimating Pearson's correlation coefficient (PCC). A univariate linear regression model was adjusted for each echocardiographic variable (response variable), including age, sex, BMI, SAH, DM, dyslipidemia, and smoking as explanatory variables. Subsequently, a multivariate linear regression model was adjusted for each echocardiographic variable of age and sex (as they are the main interest of the study) and the variables with values of $p < 0.10$ in the univariate analysis (univariate model).

The normality of the quantitative variables was assessed by the Kolmogorov-Smirnov test. P values < 0.05 were considered statistical significance. The data were analyzed using Stata/SE software v.14.1 (Statacorp LP, USA).

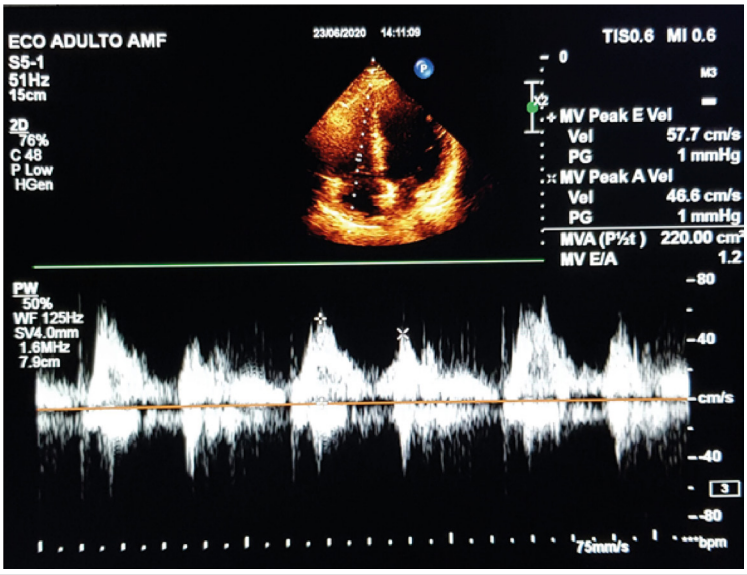


Figure 1 – *Pulsatile spectral Doppler ultrasound image of the tricuspid flow used to assess right ventricular diastolic function.*

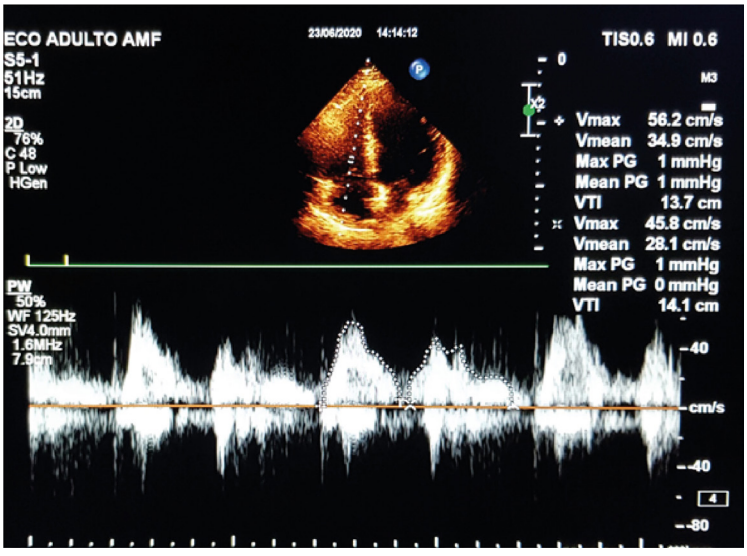


Figure 2 – *Determination of right ventricular diastolic function.*

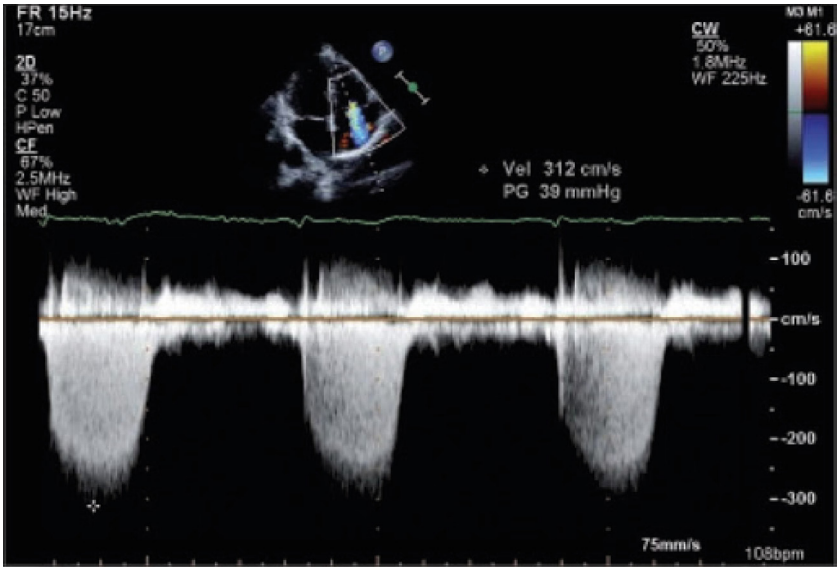
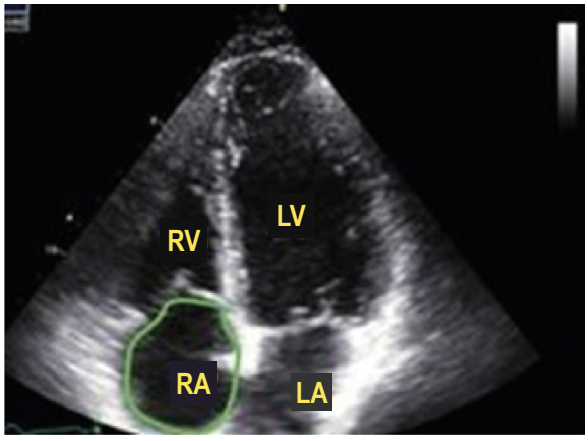


Figure 3 – *Determination of estimated pulmonary artery systolic pressure using continuous spectral Doppler ultrasound of the tricuspid reflux (in mmHg).*



RV: right ventricle; LV: left ventricle; LA: left atrium; RA: right atrium.

Figure 4 – *Determination of right atrial volume.*

RESULTS

Eighteen patients were excluded from the study according to the selected parameters. The characteristics of the remaining 97 subjects are shown in Table 1. The mean participant age was 61 ± 12.5 years; 56 (57%) were women. The echocardiographic variables found in the sample are shown in Table 2.

There was no significant intergroup difference in the echocardiographic variables (Table 3).

Tricuspid influx E/A ratio values were within the normal range, indicating preserved diastolic RV function. PASP was also within the normal range in all subjects. However, the echocardiographic E-wave peak velocity variables decreased with increasing age (PCC, -0.30; p = 0.003). The same was observed for the E/A ratio (PCC, -0.21; p = 0.035). There was a significant positive association between age and PASP variables (PCC, 0.40; p = 0.004) and tricuspid velocity (PCC, 0.36; p = 0.008) (Figure 5). The other parameters showed no significant correlation with age. The presence of comorbidities did not influence the results (Table 4).

Uni- and multivariate analyses showed decreasing E-wave and E/A ratio values (coefficient, -0.003, p = 0.003, R^2 = 7.1%; and coefficient, -0.005, p = 0.004, R^2 = 3%, respectively) and increasing PASP and tricuspid reflux velocity values (coefficient, 0.21, p = 0.004, R^2 = 14.5%; and coefficient, 0.01, p = 0.009, R^2 = 10%, respectively) with increasing age. A-wave and A-wave integral values increased (coefficient, 0.009, p = 0.0001; and coefficient, 0.112; p = 0.005, respectively) while the E/A ratio decreased

Table 1 – General descriptive statistics of the study population.

Classification	Men		Women	
Age (years)	41	62.5 ± 10.9	56	60.8 ± 13.6
Body mass index (kg/m²)	41	27.1 ± 4.4	56	27.5 ± 4.2
Systemic arterial hypertension				
No	15	36.6	22	39.3
Yes	26	63.4	34	60.7
Diabetes mellitus				
No	33	80.6	45	80.4
Yes	8	19.4	11	19.6
Dyslipidemia				
No	24	58.5	43	76.8
Yes	17	41.5	13	23.2
Smoking				
No	25	61.0	48	85.7
Yes	16	39.0	8	14.3

SD, standard deviation.

Table 2 – Baseline echocardiographic parameters in the study population.

Variable	n	Mean	Standard deviation
E-wave (m/s)	97	0.48	0.12
A-wave (m/s)	97	0.43	0.12
E/A ratio	97	1.18	0.33
E-wave deceleration (ms)	97	178.1	61.6
E-wave integral	92	7.49	2.46
A-wave integral	92	4.85	1.60
Pulmonary artery systolic pressure (mmHg)	50	26.1	7.0
Vena cava (mm)	94	11.4	2.1
Right atrial volume (mL/m²)	97	19.5	6.1
Tricuspid velocity (m/s)	53	2.22	0.45
Right atrium area (cm²)	94	8.08	2.02
Atrial filling fraction (%)	92	39.5	9.6

(coefficient, -0.003, $p < 0.001$) with increasing BMI. SAH, diabetes, dyslipidemia, and sex did not influence the analyzed variables (data not shown).

Discussion

The present study found a significant correlation between RV diastolic function and age similar to what occurs with LV diastolic function. Innelli P et al.[13] demonstrated that the E/A ratio on spectral Doppler ultrasound of the tricuspid influx decreases about 0.1 point per decade of life. That study[13] found a significant negative correlation between age and RV tricuspid influx E-wave peak velocity and a positive correlation between age and A-wave peak velocity. The data presented here corroborate these results since the E-wave peak velocity progressively decreased with age but remained within the normal range,[12] indicating the influence of the aging process on relaxation of the RV base. Likewise, Lindqvist P et al.[14] reported a decreased tricuspid influx E/A ratio on Doppler ultrasound with increasing age.

Table 3 – Correlation between sex and echocardiographic variables.

Variable	n	Mean	Standard deviation	p*
E-wave (m/s)				
Male	41	0.48	0.12	
Female	56	0.48	0.12	0.992
A-wave (m/s)				
Male	41	0.44	0.11	
Female	56	0.43	0.13	0.752
E/A ratio				
Male	41	1.15	0.30	
Female	56	1.20	0.34	0.451
E-wave deceleration (ms)				
Male	40	179.4	50.8	
Female	56	177.2	68.7	0.861
E-wave integral (cm)				
Male	37	7.26	2.49	
Female	55	7.64	2.45	0.467
A-wave integral (cm)				
Male	37	4.95	1.60	
Female	54	4.79	1.62	0.630
PASP (mmHg)				
Male	19	27.3	8.4	
Female	31	25.3	6.1	0.327
Inferior vena cava (mm)				
Male	40	11.9	2.0	
Female	54	11.1	2.2	0.063
Right atrial volume (ml/m²)				
Male	40	19.9	6.9	
Female	56	19.1	5.4	0.534
Tricuspid reflux velocity (ms)				
Male	19	2.3	0.5	
Female	34	2.2	0.4	0.522
Right atrial area (cm²)				
Male	38	8.2	2.4	
Female	56	8.0	1.7	0.714
Atrial filling fraction (%)				
Male	37	40.7	9.7	
Female	54	38.6	9.6	0.321

**Student's t-test for independent samples, p < 0.05. PASP, pulmonary artery systolic pressure.*

The RV may present relaxation changes due to collagen deposition with increased local fibrosis. In addition, calcium uptake from the cardiomyocytes leads to incomplete relaxation and worsening diastolic function in aged hearts.[15] This reduced RV diastolic function can decrease the heart's tolerance of structural diseases and functional conditions that affect RV filling.[16-17] However, the data presented here show no significant influence of comorbidities such as SAH, DM, dyslipidemia, and smoking on the evaluated parameters. It is worth mentioning that the American Society of Echocardiography[12] recommendations for echocardiographic evaluation of the right chambers did not establish reference values for normality based on body surface area and height since it was a compilation of several independent studies including those of patients with several systemic pathologies.

In the present study, an increased PASP was also correlated

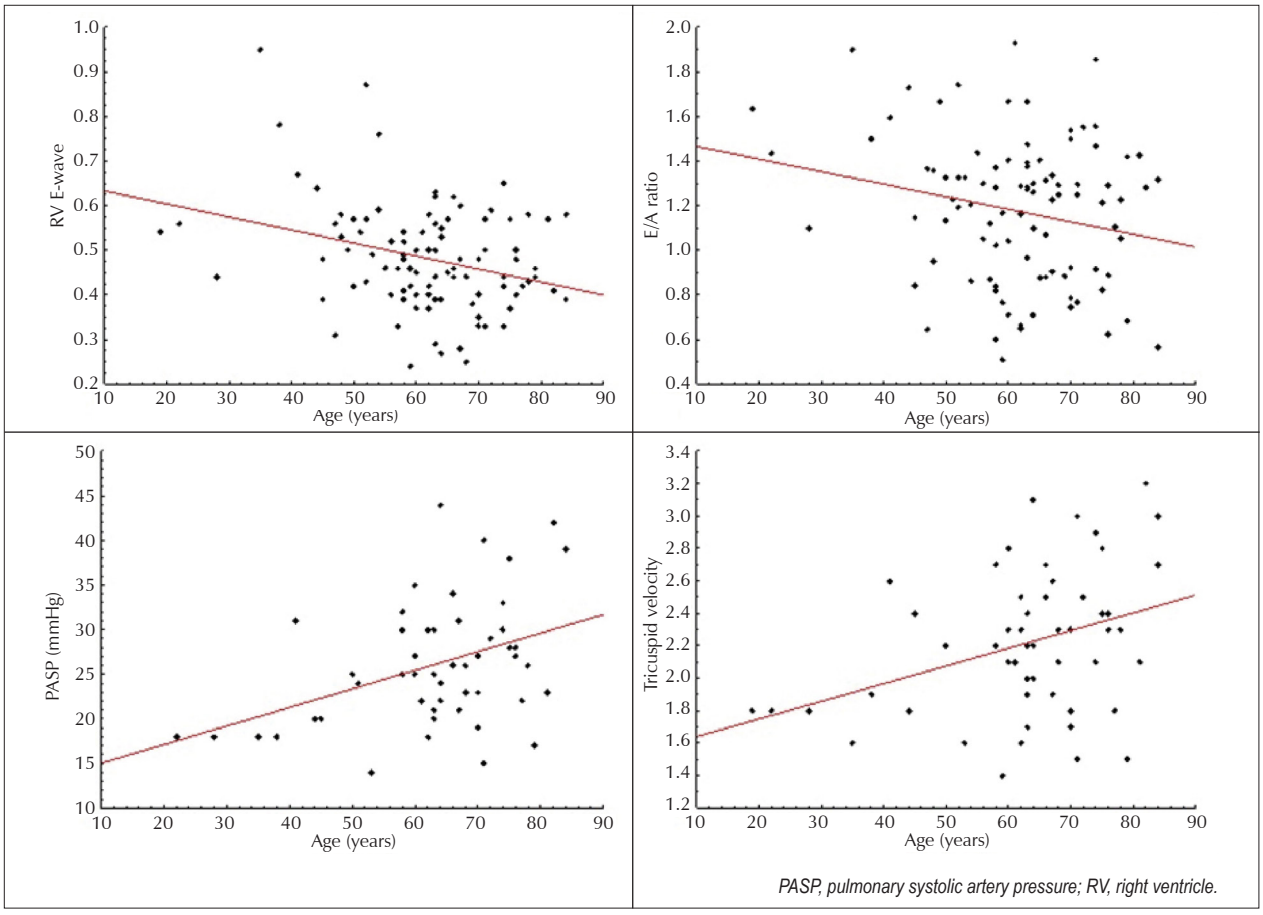


Figure 4 – *Correlation between age and E-wave, E/A ratio, PASP, and tricuspid reflux.*

Table 4 – Correlation between age (years) and echocardiographic variables.

Variable	n	PCC	p
Age × E-wave (m/s)	97	-0.30	0.003
Age × A-wave (m/s)	97	0.01	0.961
Age × E/A ratio	97	-0.21	0.035
Age × E-wave deceleration (ms)	96	0.15	0.148
Age × E-wave integral (cm)	92	-0.15	0.157
Age × A-wave integral (cm)	91	-0.02	0.859
Age × pulmonary artery systolic pressure (mmHg)	50	0.40	0.004
Age × inferior vena cava (mm)	94	0.15	0.147
Age × right atrial volume (mL/m²)	96	0.16	0.124
Age × tricuspid velocity (m/s)	53	0.36	0.008
Age × right atrial area (cm²)	94	0.12	0.260
Age × atrial filling fraction (%)	91	0.09	0.423

PCC, Pearson's correlation coefficient.

with age, although it remained within the normal range, due to increased arterial stiffness of the pulmonary vessels.[18] The pulmonary blood flow decreases with age, with increased mean pulmonary arterial pressure and pulmonary resistance, which is probably related to decreased lung compliance. Likewise, high left atrial pressures occur frequently in older people since LV stiffness increases, often leading to diastolic dysfunction.[19-20]

The data presented here showed no intersex differences in any of the analyzed parameters. Previous studies[21-25] demonstrated significant differences in both contractile and diastolic RV function in men versus women. These differences should be considered to avoid potential errors in the assessment of RV systolic and diastolic function.

Considering the above, the limitations of the present study must be clarified. First, the strict exclusion criteria resulted in no significant changes in the analyzed data; however, they enabled a homogeneous sample of relatively healthy subjects. The small number of participants (97) was also a determining factor in the results, for example, it limited the finding of a possible parameter difference between men and women. Another factor was the exclusion of subjects with any sign of RV contractile dysfunction AND ALSO having been excluded the data regarding the size and volume of the RV. A joint analysis of RV systolic-diastolic function could have added further interesting findings. It was also not computed whether heart rate (HR) variations would influence the findings presented here. In previous studies, Berman GO et al.[26] evaluated a population of only 41 people, reporting an influence of HR on RV diastolic function assessed by tricuspid influx spectral pulsed Doppler ultrasound; however, without clarifying which parameters were actually affected

by the HR variation. Yu CM et al.[27] studied 106 patients and determined that an increased HR influences the A-wave, therefore influencing the E/A ratio on mitral influx spectral Doppler ultrasound. However, RV velocity was analyzed with tricuspid annulus tissue Doppler ultrasound, which presented a small variation with HR. Similarly, Zoghbi et al.[28] studied 50 volunteers and presented no significant HR differences on spectral pulsed Doppler ultrasound of the mitral or tricuspid inflows. There are few studies to date on this topic.

We were unable to find a study with an older population and the same number of participants without cardiovascular comorbidities such as SAH, DM, dyslipidemia, and smoking as controls, which influences the echocardiographic variables used to assess LV and RV function.[12]

Therefore, no tissue Doppler ultrasound data were collected from the tricuspid annulus. The RV walls include superficial layers in which the fibers are arranged circumferentially in a direction parallel to the atrioventricular groove as well as deep layers where the fibers are aligned longitudinally.[9] Therefore, an echocardiographic evaluation using tissue Doppler ultrasound can be considered ideal for assessing RV diastolic function changes since it measures both longitudinal shortening and elongation of this chamber.

Studies worldwide have demonstrated changes in the population pattern. An increased incidence of heart failure and cardiovascular diseases, in which the RV plays an important role, has been documented. Thus, the careful monitoring of RV changes is both necessary and relevant.

Conclusions

The present study showed the significant impact of age on RV diastolic function indices in subjects with preserved LV and RV systolic function analyzed by transthoracic echocardiography. Although the values remained within the normal range, the observed changes suggest a progressive RV diastolic function deficit with aging; however, no significant intersex differences were noted.

Authors' contributions

Data collection: Baroncini LAV, Melo LL, Camarozano AC, Carmo DC, Fortunato JA, Darwich RZ, Sá CRF; data analysis: Baroncini LAV, Melo LL, Camarozano AC, Carmo DC; data design: Baroncini LAV, Melo LL, Camarozano AC, Carmo DC; manuscript writing: Baroncini LAV, Melo LL, Camarozano AC, Carmo DC, Fortunato JA, Darwich RZ, Sá CRF; critical review of the manuscript for important intellectual content: Baroncini LAV, Melo LL, Camarozano AC.

Conflict of interest

The authors have declared that they have no conflict of interest.

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