Artigo Original

Right Ventricular Outflow Tract Acceleration Time: Correlation with Left Ventricular Diastolic Function, Sex, And Age

Tempo de Aceleração na Via de Saída do Ventrículo Direito: Correlação com a Função Diastólica do Ventrículo Esquerdo, Sexo e Idade

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Abstract

Background: Pulmonary artery acceleration time (PAAT) can be used as a parameter in the evaluation of pulmonary hypertension and aids left ventricular diastolic function (LVDF) analyses.

Objective: To assess whether there is a correlation between PAAT and LVDF parameters in individuals with a preserved left ventricular systolic function and by sex, age, and cardiovascular risk factors.

Method: Observational cross-sectional study. One hundred nineteen patients were selected (59 women [49.6%]). The subjects underwent transthoracic echocardiography including measurements of PAAT, E and A waves and E/A ratio, e′ septal and e′ lateral waves and E/e′ ratio, pulmonary artery systolic pressure (PASP), and left atrial volume.

Results: In female patients, a positive correlation (Spearman's correlation coefficient – Spearman correlation coefficient [SCC]) was found between the PAAT value and the lateral e′ (SCC, 0.47; p = 0.002), with the E/A ratio (SCC, 0.32; p = 0.04), and with septal e′ (SCC, 0.36; p = 0.023), and a negative correlation between PAAT and PASP (SCC, -0.43; p = 0.034). In men, no correlation was found between PAAT and any parameters. Lower PAAT values were found in women with systemic arterial hypertension (hypertension) than in women without hypertension (0.13 ± 0.03 s versus 0.16 ± 0.03 s; p = 0.015).

Conclusion: The present study showed a significant correlation between PAAT and some LVDF parameters in female patients only. Hypertension was correlated with lower PAAT values in women.

Keywords: Cardiac function; Cardiovascular disease; COVID-19; Echocardiography; SARS-CoV-2

Resumo

Fundamento: *O tempo de aceleração na artéria pulmonar (TAP) pode ser utilizado para avaliação da hipertensão pulmonar na análise da função diastólica do ventrículo esquerdo.*

Objetivo: *Avaliar se existe correlação entre o valor do tempo de aceleração na artéria pulmonar e parâmetros da função diastólica do ventrículo esquerdo em indivíduos com função sistólica do ventrículo esquerdo preservada e de acordo com sexo, idade e fatores de risco cardiovasculares.*

Métodos: *Estudo observacional, transversal. Foram selecionados 119 pacientes (59 mulheres; 49,6%). Os indivíduos foram submetidos ao ecocardiograma transtorácico incluindo os valores de tempo de aceleração na artéria pulmonar; ondas E e A e relação E/A ao Doppler espectral do influxo mitral; ondas e′ septal, e′ lateral e relação E/e′ ao Doppler tecidual do anel mitral; pressão sistólica na artéria pulmonar e volume atrial esquerdo.*

Resultados: *No sexo feminino, foi encontrada correlação positiva (coeficiente de correlação de Spearman) entre o valor do tempo de aceleração na artéria pulmonar e e′ lateral (coeficiente de correlação de Spearman de 0,47; p=0,002), relação E/A (coeficiente de correlação de Spearman de 0,32; p=0,04) e e′ septal (coeficiente de correlação de Spearman de 0,36; p=0,023) e uma correlação negativa entre o valor do tempo de aceleração na artéria pulmonar e pressão sistólica na artéria pulmonar (coeficiente de correlação de Spearman de -0,43; p=0,034). No sexo masculino, não foi encontrada correlação significativa. Foram encontrados menores valores de tempo de aceleração na artéria pulmonar em mulheres com hipertensão arterial sistêmica quando comparadas a mulheres sem hipertensão arterial sistêmica (0,13±0,03 segundos versus 0,16±0,03 segundos; p = 0,015).*

Conclusão: O presente estudo mostrou correlação significativa dos valores do TAP com alguns parâmetros da função diastólica do ventrículo esquerdo apenas no sexo feminino, sendo que mulheres hipertensas apresentaram menores valores de TAP.

Palavras-chave: Artéria pulmonar; Hipertensão pulmonar; Ecocardiografia.

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Introduction

Transthoracic echocardiography (TTE) is an important tool in the investigation of several pathologies affecting the heart that analyzes the interdependence between various cardiac structures with noninvasive precision, particularly the correlation between the systolic function of the left (LV) and right ventricles (RV).[1] However, the blood flow to the lungs and its correlation with the parameters that determine LV diastolic function (LVDF) have been poorly investigated.

The RV outflow tract acceleration time, also called pulmonary artery acceleration time (PAAT), corresponds to the time the flow through the pulmonary valve takes to reach its maximum peak velocity estimated by spectral pulsed-wave Doppler in the RV outflow tract. This value is considered normal when >120 ms and abnormal when <105 ms,[2–4] suggesting the presence but not severity of pulmonary hypertension (PH). Although it is not as reliable as tricuspid regurgitation velocity, which more accurately estimates pulmonary artery systolic pressure (PASP), PAAT can also be used in this assessment.[5]

Assessing left ventricular diastolic dysfunction is a complex task based on several echocardiographic measurements and parameters, including PASP. This value cannot be estimated without adequate tricuspid regurgitation.[6–7] Therefore, the present study aimed to assess whether there is a correlation between PAAT and LVDF parameters in subjects with preserved LV systolic function in the absence of advanced LV diastolic dysfunction and by sex, age, and cardiovascular risk factors.

Methods

Study population

This was an observational cross-sectional study. A total of 119 patients aged over 18 years, including 59 women (49.6%), were selected regardless of ethnicity from the cardiology outpatient clinic of the Red Cross Hospital of Curitiba after being referred for TTE by the assistant physician for any clinical indication.

The patients were selected by convenience, without statistical criteria, according to their availability to participate in the research. A protocol form with clinical and echocardiographic parameters was completed for each patient. The clinical data collected were age, sex, weight, height, body mass index (BMI), and presence of systemic arterial hypertension (SAH), diabetes mellitus (DM), coronary artery disease (CAD), smoking (current or previous), and dyslipidemia. SAH, DM, dyslipidemia, and smoking were listed in the patients' medical records and/or reported by them. CAD was confirmed by the medical record review and the patient through a reported history of non-fatal myocardial infarction and surgical or percutaneous myocardial revascularization. Regularly used medications were also recorded.

The exclusion criteria were a) significant valvular disease (moderate or severe); b) valve prostheses; c) segmental LV contraction changes due to ischemic heart disease or other cardiomyopathies; d) pulmonary emphysema or chronic obstructive pulmonary disease; e) moderate to severe pulmonary arterial hypertension (PASP > 50 mmHg); f) left ventricular contractile dysfunction (ejection fraction < 52% for men and < 54% for women); g) infiltrative and pericardial diseases; h) congenital heart disease with increased pulmonary blood flow with or without surgical correction; i) pacemaker; j) atrial fibrillation; and k) advanced (II and III) LV diastolic dysfunction.

The patients underwent complete two-dimensional TTE using Phillips IE 33, Envisor or General Electric Vivid E echocardiography equipment. All acoustic windows and all standard echocardiographic measurements and analyses were performed for each patient. Sonographic measurements were performed by two experienced echocardiographers qualified in echocardiography by the Department of Cardiovascular Imaging of the Brazilian Society of Cardiology.

All patients signed an informed consent form. The study was approved by the institution's research ethics committee.

Main echocardiographic parameters analyzed in this study

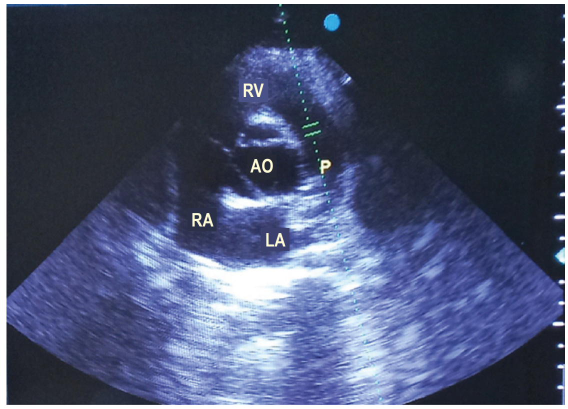
The following parameters were examined: E and A waves and E/A ratio on spectral pulsed-wave Doppler of the mitral inflow; Septal and lateral e' waves and E/e' ratio (E wave/ average between septal and lateral e' velocities) on pulsed tissue Doppler of the mitral annulus; PASP (mmHg) through the maximum tricuspid regurgitation velocity (m/s), when present, on continuous spectral wave Doppler of tricuspid regurgitation, and inferior vena cava diameter (mm); PAAT measured immediately above the pulmonary valve leaflets on spectral pulsed-wave Doppler of the RV outflow tract (Figures 1 and 2); Indexed left atrial volume (normal up to 34 mL/m^2 for women and men) measured using the modified biplane Simpson's method in four- and two-chamber orthogonal projections.

All quantifications and values considered in the present study were based on American Society of Echocardiography and European Society of Cardiovascular Imaging guidelines.[8–10]

Statistical analysis

The women and men were analyzed separately. The study results are described as mean, median, minimum and maximum value, and standard deviation for quantitative variables or as frequency and percentage for categorical variables. The association between two quantitative variables was estimated by the Pearson or Spearman correlation coefficient (PCC and SCC, respectively). Quantitative variables were compared using Student's t-test for independent samples or the non-parametric Mann-Whitney test. More than two groups were compared using one-way analysis of variance and the least significant difference test for multiple comparisons or the non-parametric Kruskal-Wallis test. The normality of the variables was evaluated by the Kolmogorov-Smirnov test. P values < 0.05 were considered statistically significant.

The data were analyzed using SPSS Statistics software v.20.0 (IBM Corp., Armonk, NY, USA).



AO, aortic valve; LA, left atrium; P, pulmonary artery; PAAT, pulmonary artery acceleration time; RA, right atrium; RV, right ventricle

Figure 1 – *Parasternal cross-sectional view at the level of the base vessels. The figure shows the pulsed-wave Doppler cursor positioned on the right ventricular outflow tract used to obtain the PAAT.*

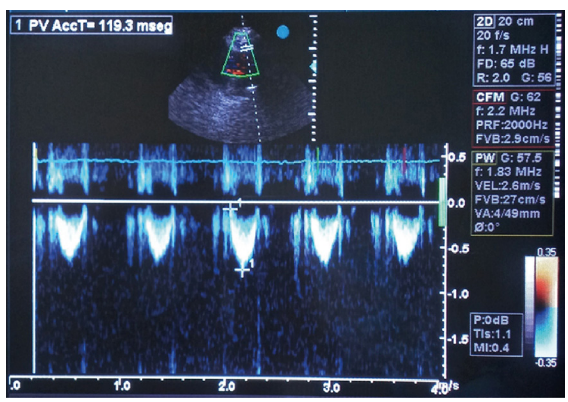


Figure 2 – *Pulsed-wave Doppler PAAT scan.*

Results

The final analysis included 119 subjects, 59 (49.6%) women (62.6 ± 16.5 years) and 60 (50.4%) men (65.1 ± 11.2 years). The clinical and epidemiological characteristics of the studied population are shown in Table 1. The baseline echocardiographic parameters of the studied population agreed with the literature.[8–10]

Women showed a positive and significant correlation between PAAT and lateral e’ (SCC, 0.47; $p = 0.002$), E/A ratio (SCC, 0.32; $p = 0.04$), and septal e’ (SCC, 0.36; $p = 0.023$); and a negative correlation between PAAT and PASP (SCC -0.43; $p = 0.034$), (Figures 3 and 4). The other variables were not correlated with PAAT, and the male participants showed no significant correlation with the analyzed parameters (Table 3).

PAAT was not influenced by sex, BMI, DM, dyslipidemia, CAD, or smoking (data not shown). However, lower PAAT values were found in women with versus without SAH (0.13 ± 0.03 versus 0.16 ± 0.03 s, respectively; $p = 0.015$).

Age was not significantly correlated with PAAT in either sex (SCC, -0.27, $p = 0.068$ for women; SCC, -0.31, $p = 0.065$ for men).

Discussion

The present study found a significant positive correlation between PAAT and LVDF parameters (septal and lateral e’ waves and E/A ratio) in women only, in whom the presence of SAH was associated with a lower PAAT. However, the general analysis of the studied population showed no significant PAAT differences in sex, age, or BMI.

PASP is currently the most commonly used PH data in LVDF assessments. PH degree is usually assessed by PASP estimated by tricuspid valve regurgitation. PAAT has a negative correlation with PASP (data also found in the present study). According to Granstam et al.,[11] tricuspid regurgitation may not be present or be unreliable for the correct estimation of PASP during TTE examinations. Considering this, they estimated pulmonary vascular resistance invasively, correlating it with PAAT values as a possible alternative for identifying PH. Therefore, considering those findings, it is important to have more than one method available to estimate PH in an LVDF study, especially when it is not possible to reliably estimate tricuspid regurgitation or in early cases of diastolic dysfunction that lack a significantly increased pulmonary pressure. In cases of preserved LV systolic function, the differentiation between normal and abnormal diastolic function becomes complicated due to overlapped indices obtained by Doppler. Although age structurally changes the heart and the vessels, the analysis of healthy older people by Doppler showed similar values to those of younger age groups (40–60 years of age).[12] Considering the mean age of the studied population (relatively young subjects) and that all had preserved LV systolic function, no significant differences were expected in the parameters evaluated by Doppler. However, we expected that the inclusion of PAAT values could differentiate between early stages of diastolic dysfunction when PASP is not extremely high.

A study by Baroncini et al.[13] of 87 participants also showed a negative correlation between PAAT and age and a positive correlation between PAAT and E/A ratio with no significance between other variables or the sexes. This study demonstrated that PAAT values < 0.135 s were associated with grade I diastolic dysfunction, while those > 0.135 s were associated with normal diastole. These studies suggest that PAAT correlates with parameters used to assess LVDF, even in the early stages when there are no signs of significant pulmonary arterial hypertension. At this stage,

Table 1 - Basic characteristics of the study population.

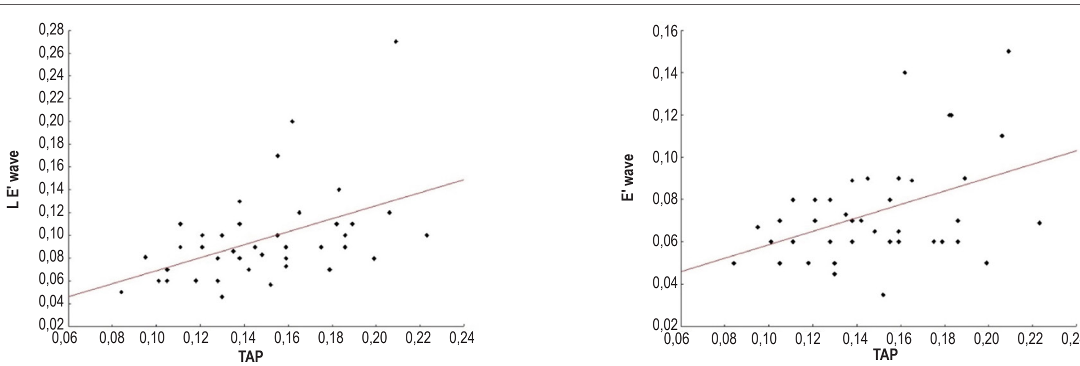
Variable	n	Women	n	Men
Age, years	59	62.6 ± 16.5	60	65.1 ± 11.2
BMI				
<30	41	72	41	68
≥30	16	28	19	32
SAH				
Yes	37	68	39	70
No	17	32	17	30
Dyslipidemia				
Yes	24	44	15	27
No	30	56	41	73
DM				
Yes	20	37	16	29
No	34	63	40	71
CAD				
Yes	11	20	21	37
No	43	80	35	62

BMI, body mass index; CAD, coronary artery disease; DM, diabetes mellitus; SAH, systemic arterial hypertension; SD, standard deviation.

Table 2 – Echocardiographic and hemodynamic parameters of the study population.

Variable	n	Mean	SD	p*
E wave				
Female	45	0.75	0.27	0.070
Male	43	0.65	0.27	
A wave				
Female	41	0.80	0.20	0.484
Male	39	0.77	0.24	
E/A ratio				
Female	41	0.97	0.44	0.234
Male	39	0.92	0.65	
Lateral e' wave				
Female	43	0.10	0.04	0.835
Male	42	0.09	0.03	
Septal e' wave				
Female	43	0.08	0.03	0.509
Male	42	0.07	0.03	
E/e' ratio				
Female	43	10.0	4.7	0.150
Male	41	8.6	2.7	
PASP				
Female	31	28.8	11.7	0.346
Male	29	29.7	9.0	
AE volume				
Female	35	36.7	19.3	0.772
Male	42	35.1	14.0	
PAAT				
Female	45	0.15	0.04	0.404
Male	37	0,14	0,03	

**Student's t-test for independent samples or non-parametric Mann-Whitney test, p < 0.05. LA, left atrium; PAAT, pulmonary artery acceleration time; PASP, pulmonary artery systolic pressure; SD, standard deviation.*



TAP: tempo de aceleração na pulmonar.

Figure 3 – *Correlation between pulmonary artery acceleration time (PAAT) and lateral E' and medial e' waves in women.*

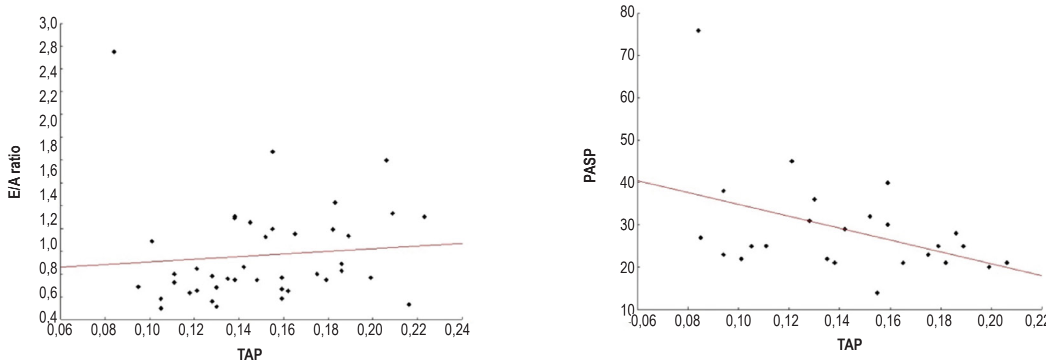


Figure 4 – *Correlation between pulmonary artery acceleration time (PAAT), E/A ratio, and pulmonary artery systolic pressure (PASP).*

Table 3 – Correlation between PAAT and diastolic function parameters.

Variable	n	r	p
PAAT × E/A ratio			
Female	41	0.32	0.040
Male	35	0.32	0.061
PAAT × septal e' wave			
Female	40	0.36	0.023
Male	35	0.30	0.081
PAAT × E/e' ratio			
Female	40	-0.13	0.436
Male	35	-0.04	0.822
PAAT × PASP			
Female	25	-0.43	0.034
Male	19	-0.21	0.380
PAAT × LAV			
Female	28	-0.08	0.701
Male	29	-0.11	0.577

LAV, left atrial volume; PAAT, pulmonary artery acceleration time; PASP, pulmonary artery systolic pressure; r, Spearman correlation coefficient.

the E/e′ ratio is still low and the PAAT values are within the normal range (>120 ms).[14,15]

In a study of a larger number of participants, Marra et al.[16] analyzed 1,029 healthy subjects and reported no differences in PAAT values between men and women. However, they noticed a small reduction in this parameter with advancing age, increasing BMI, and higher systolic and diastolic systemic blood pressure. Similar to our findings, they also found a positive correlation between PAAT and E/A ratio; however, they did not discuss this last finding, suggesting the need for further studies in the area.

A study by Zabalgoitia et al.[17] prospectively analyzed LV mass, relative wall thickness, and systolic and diastolic interaction in 508 hypertensive patients aged 50–80 years according to age and sex. In men, most measures were similarly distributed. Nevertheless, women aged 65 years and older presented smaller LV systolic dimensions, greater ventricular thicknesses, greater fractional shortening, and less end-systolic wall stress, i.e., structural and functional changes were more pronounced in women.

In the present study, statistically significant findings, particularly in women, correlated with the findings by Zabalgoitia et al.,[17] indicating the importance of further studies on systolic ventricular function, diastolic function, possible hormonal influence, and SAH behavior in the female heart. Previous studies already reported hormonal influence in pre- and postmenopausal women and a higher incidence of heart failure with preserved ejection fraction in women.[18,19] Likewise, SAH causes different structural changes in ventricular geometric patterns in men and women, with possible deleterious effects that are more pronounced in women.[20]

A study by Alecrin et al.[21] with postmenopausal hypertensive women showed that hormone replacement therapy with oral estradiol for 12 weeks significantly improved LVDF on TTE. Mohamed et al.[22] correlated diastolic dysfunction with age and arterial hypertension and concluded that arterial hypertension duration, systolic and diastolic arterial hypertension level, and age are important prognostic indicators for predicting the development of diastolic dysfunction in hypertensive patients. A better understanding of these particularities may improve the treatment of hypertension and congestive heart failure.

Liebson et al.[23] evaluated a large population of men (n=511) and women (n=333) with mild primary hypertension and found a substantial percentage of participants with left ventricular hypertrophy diagnosed on echocardiography. In that study, left ventricular mass indices were positively correlated with systolic blood pressure, BMI, urinary sodium excretion, and smoking, with no significant difference between the sexes. Also, similar to findings presented here, they found a positive correlation between the PAAT and E/A ratio, without, however, discussing the later finding, suggesting further studies in this area.

The main limitation of the present study is the small number of participants (N=119), especially compared to other studies, thus increasing the chances of outliers that may have influenced the final results presented here. Another relevant factor was the exclusion of patients with more advanced degrees of diastolic dysfunction (DD), hindering the assessment of PAAT behavior in these situations. However, the main objective was to evaluate PAAT behavior in the initial stages of left ventricular

DD. Echocardiographic measurement intra- and inter-observer variability is also possible,[24] but this analysis was not performed in the parameters evaluated here. However, none of the studies cited in the discussion presented this PAAT analysis. Likewise, heart rate and blood pressure were also not measured concomitantly. According to Marra et al.,[16] who analyzed eight previous studies with 1,029 healthy subjects, PAAT values were weakly influenced by both heart rate and blood pressure.

Conclusions

The present study correlated PAAT with signs of early left ventricular DD in women only. Among the cardiovascular risk factors, the presence of SAH influenced PAAT in women only.

Authors' contributions

Data collection: Coimbra RM, Baroncini LAV, Camarozano AC, Carmo DC, Sá CRF, Fortunato JA, Darwich RZ; Data analysis: Coimbra RM, Baroncini LAV, Camarozano AC, Carmo DC; Data design: Coimbra RM, Baroncini LAV, Camarozano AC; Manuscript writing: Coimbra RM, Baroncini LAV, Camarozano AC, Carmo DC, Sá CRF, Fortunato JA, Darwich RZ; Critical review of the manuscript for important intellectual content: Coimbra RM, Baroncini LAV, Camarozano AC.

Conflict of interest

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

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