

Right ventricle Outflow Tract Acceleration Time: Correlation with Left Ventricular Diastolic Function

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Abstract

Background: There are no available data about the measurement of acceleration time at the right ventricle outflow tract (AcT) and its relevance in the analysis of the left ventricular diastolic function (LVDF).

Objective: To correlate AcT with echocardiographic parameters of LVDF.

Method: Eighty-seven patients (58.4±14.5 years; 52% women) submitted to transthoracic echocardiogram assessing spectral and tissue Doppler of the transmitral flow and mitral annulus, AcT, left atrial volume (LAV), and pulmonary artery systolic pressure (PASP). Patients with systolic dysfunction of the LV and grades II and III diastolic dysfunction (DD) were excluded. Main analyses were performed using the Spearman's Correlation Coefficient (SCC) and Pearson's Linear Correlation Coefficient (PLCC).

Results: A negative correlation between AcT value and age (PLCC – 0.36; Student's t-test; p <0.001) and a positive correlation between AcT and E/A ratio (SCC 0.38; p<0.001), between AcT and E/e' ratio (SCC 0.26; p=0.01), between AcT and E wave of the mitral flow (PLCC 0.36; p= 0.001) were found. LAV and PASP did not correlate with AcT. In patients with a normal diastolic function, AcT was higher when compared with the AcT in patients with Grade I DD (0.150±0.029ms versus 0.127±0.023ms; p<0.001; Student's t-test). The threshold suggested in this subgroup of patients was 0.135s.

Conclusions: The present study correlated, unprecedentedly, AcT with echocardiographic parameters of the LV diastolic function. AcT values lower than 0.135s were associated with grade I diastolic dysfunction and higher than 0.135s values were associated with normal diastole.

Key-words: diastole, Doppler echocardiography, left ventricular dysfunction, pulmonary artery

Running Title: Pulmonary Acceleration Time and Diastolic Function

Introduction

Diastole is a complex process of the cardiac cycle, dependent on the active myocardial relaxation, ventricular compliance, ventricular synchrony, ventricular diastolic suction, myocardial viscoelasticity, atrial contraction, pericardial restriction, interaction between right ventricle (RV) and left ventricle (LV) and the erectile function of the coronary arteries [1]. An altered RV-LV interaction leads to a diastolic dysfunction characterized by an increased dependence of the left ventricle filling in relation to the left atrial contraction [2]. Additionally, the diastolic function is affected by clinical factors such as age, systemic arterial hypertension and pulmonary arterial hypertension [3-4].

In this regard, at the transthoracic echocardiography (TTE), the assessment of the left ventricle diastolic function (LVDD) must be performed by integrating several techniques including the analysis of the spectral Doppler of the mitral flow, the tissue Doppler of the mitral annulus, pulmonary veins flow, the estimates of the pulmonary artery systolic pressure (PASP) and of the left atrial volume (LAV)[1]. PASP is most commonly determined by estimating the peak tricuspid regurgitant velocity, not always present, by means of the continuous wave Doppler [5], adding the right atrial pressure by assessing the inferior vena cava. An alternate option to estimate the pulmonary arterial pressure is to measure the right ventricle outflow tract acceleration time (AcT), which presented high correlation with PASP in previous studies, with a reference

value of 105ms [5-7]. Nevertheless, there are no published studies correlating its value with the conventional variables of the LV diastolic function assessed at TTE. Hence, the present study seeks to correlate AcT with the traditionally used variables at ETT to assess the LVDD, among them, E and A waves, E/A ratio, and isovolumetric relaxation time (IVRT) trough spectral Doppler of the mitral flow, septal and lateral e' waves at tissue Doppler of the mitral annulus, E/e' ratio (E/mean between septal and lateral e'), LAV and PASP.

Methods

This observational and transversal study includes 94 patients, from both genders, any ethnic background, over 18 years of age, from an outpatient cardiology unit of a public hospital, recommended by the assistant physician to undergo transthoracic echocardiogram for any clinical indication. The patients' selection did not follow any statistical criterion, but that of convenience, that is, according to their availability to participate in the research study. For each patient, a protocol form with clinical and echocardiographic parameters was completed. Analyzed demographic data included age, gender, body mass index (BMI), presence of hypertension, diabetes mellitus (DM), dyslipidemia, coronary arterial disease (CAD), history of current or former smoking, and frequent or continuous use of prescribed drugs. Diagnoses for hypertension, DM,



dyslipidemia, and CAD were recorded in the patients' medical files and/or reported by the patients themselves (referral information data).

Patients underwent a complete bidimensional transthoracic echocardiogram with the Phillips IE 33, Envisor or Vivid E General Electric models. In all acoustic views, all standard measurements and echocardiographic analyses were conducted in each patient and the sonographic analyses were performed by two experienced echocardiographers, holders of echocardiography certificates from the Cardiovascular Imaging Department of the Brazilian Society of Cardiology.

Exclusion criteria included patients with (a) significant valvular heart disease (moderate and severe); (b) prosthetic heart valves; (c) pulmonary emphysema or chronic obstructive pulmonary disease; (d) moderate to severe pulmonary arterial hypertension (PASP > 50 mmHg); (e) atrial fibrillation or pacemaker rhythm; (f) dilated cardiomyopathy or ischemic cardiomyopathy with regional wall motion abnormality or myocardial segmental thickness of left ventricle; (g) LV systolic dysfunction (ejection fraction <52% for men and <54% for women); (h) grades II and III LVDD; and (i) inappropriate acoustic window for AcT analysis.

In this study, the main echocardiographic variables assessed were: (a) at the transmitral spectral Doppler, the E wave velocity, A wave velocity, E/A ratio and isovolumetric relaxation time (IVRT); (b) from the mitral annular tissue Doppler imaging, septal e' wave velocity, lateral e' wave velocity, mean velocity between septal e' and lateral e'; (c) E/e' ratio (E wave velocity/mean velocity between septal e' and lateral e'); (d) acceleration time at the right ventricle outflow tract (AcT), measured on the short axis view toward the heart base vessels, at the tip of the pulmonary valve leaflet, from the start to the peak of the systolic flow; (e) left atrial volume (LAV) and (f) pulmonary artery systolic pressure (PASP), measured by the tricuspid regurgitation peak velocity, when present (Figures 1 and 2).

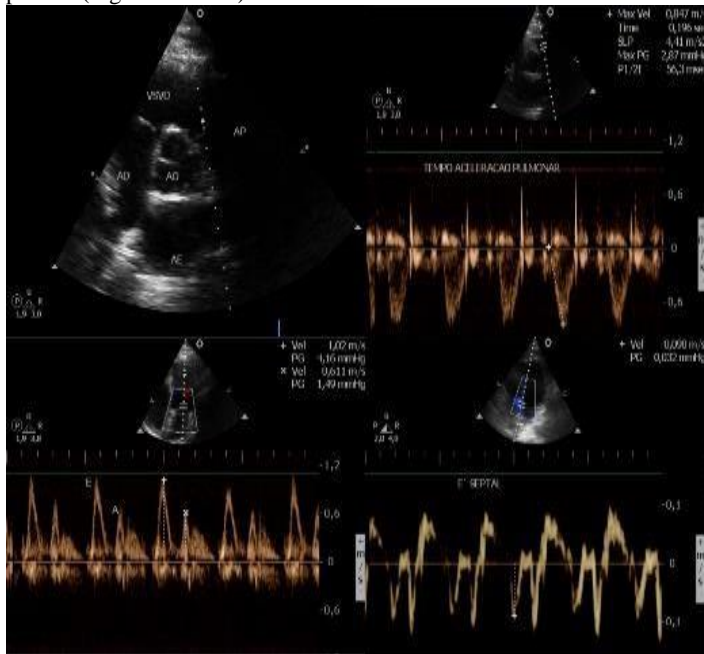


Figure 1: Upper left corner: short axis window base vessels with Doppler cursor at the tip of the pulmonary valve leaflets. Upper right corner: measurement of the acceleration time in the right ventricular outflow tract. Lower left corner: Spectral Doppler of the transmitral flow. Right lower corner: Mitral annulus tissue Doppler.

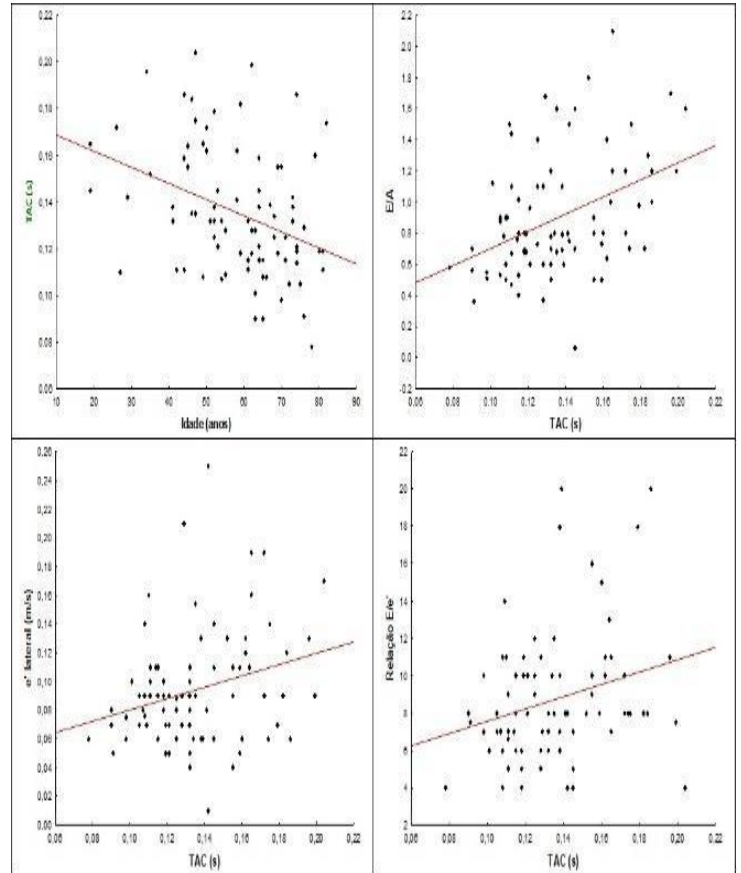


Figure 2. Upper left corner: Correlation between CAT and age (years). Upper right corner: Correlation between TAC and I / A ratio. Lower left corner: correlation between CT and lateral mitral annulus. Lower right corner: Correlation between TAC and E / e ratio.

Statistical Analysis

The results obtained were described by means, medians, minimum and maximum values, and standard deviations (quantitative variables) or by frequencies and percentages (categorical variables). To assess the association between two quantitative variables, Pearson's or Spearman's linear correlation coefficient was used. The comparison of two groups in relation to the quantitative variables was performed by the student's t test for independent samples. The one-way analysis of variance (ANOVA) was used to compare more than two groups. The Kolmogorov-Smirnov normality test examined whether the variables were normally distributed. Values of $p < 0.05$ indicated statistical significance. To determine an AcT threshold that was associated with the normal diastole versus grade I dysfunction, a ROC curve was adjusted. Data were analyzed with the IBM SPSS Statistics Software 20.0, Armonk, NY: IBM Corp.

Results

Seven patients, out of the 94 initially selected, were excluded from the study. Final analysis included 87 patients, 58.4 ± 14.5 years; 45 (52%) women. Clinical characteristics of the studied cohort are listed in Table 1.

Variable		N	%
Age (years)	58.4±14.5	87	
Gender	Male	42	48%
	Female	45	52%
Systemic arterial hypertension	No	22	30.1%
	Yes	51	69.9%
Diabetes Mellitus	No	54	64%
	Yes	19	26%
Coronary arterial disease	No	14	80.8%
	Yes	59	19.2%
Smoking	No	73	83%
	Yes	14	16%
Body Mass Index (kg/m ²)	27.9±4.9	81	

Table 1. Clinical basal characteristics of the studied population

Values from the identified echocardiographic variables corroborate those values from the available literature (Table 2).

Variable	N	Mean	Standard Deviation
Acceleration time in the pulmonary artery (s)	87	0.135	0.028
E/A ratio	87	0.894	0.382
Septal e' (m/s)	85	0.072	0.025
Lateral e' (m/s)	85	0.094	0.040
E/e' ratio	84	8.698	3.381
Isovolumetric relaxation time (s)	83	0.105	0.024
E Wave (m/s)	87	0.619	0.208
A Wave (m/s)	87	0.723	0.197
Left atrial volume (ml/m ²)	45	36.3	9.7
Systolic pressure in the pulmonary artery (mmHg)	21	28.0	5.7

Table 2. Echocardiographic variables.

A negative and significant correlation (Spearman's correlation coefficient (SCC) between AcT value and age (SCC -0.36; p = 0.001) and a tendency between AcT value and wave A (SCC -0.21; p = 0.05) were observed. Additionally, positive and significant correlations were identified between AcT value and E/A ratio (SCC 0.38; p<0.001), between AcT and lateral e' wave (SCC 0.22; p=0.04), between AcT and E/e' ratio (SCC 0.26; p=0.01) and between AcT and E wave (SCC 0.36; p= 0.001). The other variables did not correlate with AcT (Table 3, Figure 3).

Variables	n	Correlation Coefficient*	P
Age vs BMI (kg/m ²)	86	-0.04	0.735
Age vs E/A Ratio	85	-0.52	<0.001
Age vs Septal e' (m/s)	83	-0.40	<0.001
Age vs Lateral e' (m/s)	83	-0.57	<0.001
Age vs E/e' Ratio	82	0.03	0.775
Age vs IVRT (s)	81	0.34	0.002
Age vs E Wave (m/s)	85	-0.33	0.002
Age vs A Wave (m/s)	85	0.49	<0.001
Age vs Left Atrial Volume	43	0.45	0.002
Age vs PASP	21	0.39	0.082

Table 3. Correlation between age and LV diastolic function. * Spearman's correlation coefficient (E/A, lateral e' and E/e' ratio) or Pearson's linear correlation coefficient (other variables).

BMI = Body Mass Index; IVRT = Isovolumetric Relaxation Time; PASP = Pulmonary Artery Systolic Pressure.

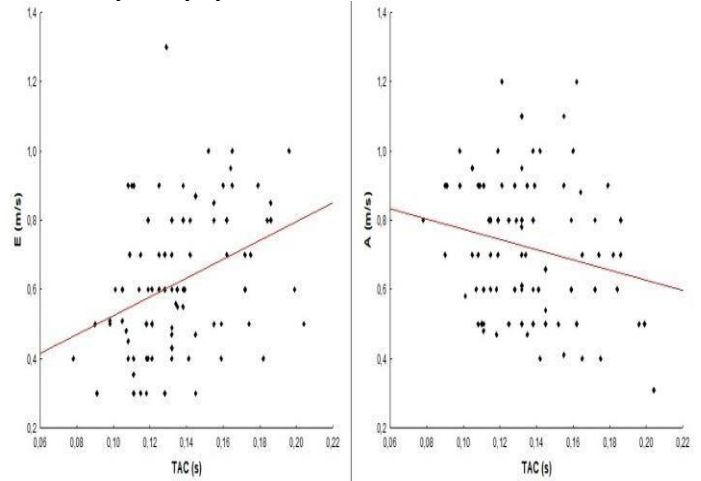
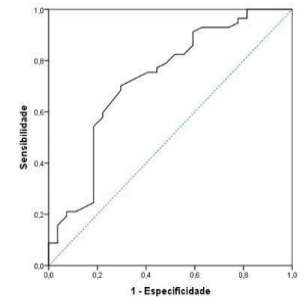


Figure 3: Left side: Correlation between CT and E-wave mitral flow. Right side: correlation between CT and mitral flow wave A.

Only 5 patients presented AcT values lower than 105ms and these values did not correlate with PASP increase or with any other variable (data not shown). AcT value was not influenced by gender, BMI, presence hypertension, DM, dyslipidemia, CAD or smoking (data not shown). Lower AcT values were identified in patients affected by LVDD grade I when compared to patients with preserved LVDD (0.127±0.023 versus 0.150±0.29ms; p<0.001). The threshold suggested by the ROC curve adjustment was 0.135s. Hence, AcT values lower than 0.135s were associated with the presence of a LVDD grade I and values higher than 0.135s with normal diastole, with sensitivity and specificity thresholds estimated in 70.2% and 70.4%, respectively. (Figure 4).

TAC	DIÁSTOLE	
	Normal	DD1
≥ 0,135	19 70,4% (especif)	17 29,8%
< 0,135	8 29,6%	40 70,2% (sensib)
Total	27	57



Sensibilidade: probabilidade do TAC ser <0,135 dado que a diástole é DD1

Especificidade: probabilidade do TAC ser ≥ 0,135 dado que a diástole é normal

Figure 4. ROC curve for the value of CT and left ventricular diastolic function.

Age presented a negative and significant correlation with E/A ratio (SCC -0.54; p <0.001), with lateral e' wave (SCC -0.59; p <0.001), with septal e' wave (Pearson's correlation coefficient - PCC - 0.40; p<0.001) and with E wave (PCC -0.34, p=0.001). Age also showed positive and significant correlation with IVRT (PCC 0.38; p=0.001) and A wave (PCC 0.51; p <0.001); however, it did not correlate significantly with E/e' ratio (p=0.78) (Table 4).

Variables	n	Correlation Coefficient*	p
AcT (s) vs Age (years)	85	-0.36	<0.001
AcT (s) vs BMI (kg/m ²)	85	-0.03	0.757
AcT (s) vs E/A	87	0.38	<0.001
AcT (s) vs Septal e' (m/s)	85	0.09	0.437
AcT (s) vs Lateral e' (m/s)	85	0.21	0.055
AcT (s) vs E/e' Ratio	84	0.26	0.019
AcT (s) vs IVRT (s)	83	-0.12	0.273
AcT (s) vs E Wave (m/s)	87	0.36	0.001
AcT (s) vs A Wave (m/s)	87	-0.21	0.055
AcT (s) vs Left Atrial Volume	45	0.05	0.731
AcT (s) vs PASP	21	0.06	0.793

Table 4. Correlation between the acceleration time (AcT) in the pulmonary artery and LV diastolic function variables. * Spearman's correlation coefficient (E/A, lateral e' and E/e' ratio) or Pearson's linear correlation coefficient (other variables).

BMI = Body Mass Index; IVRT = Isovolumetric Relaxation Time; PASP = Pulmonary Artery Systolic Pressure.

Discussion

The present study presented unprecedented correlation of AcT absolute values with echocardiographic variables representatives of LV diastolic function. Concomitantly, the same values have shown to change with age increase. Previous studies report that LV diastolic function changes and progresses with age[11-12], independent of a LV preserved systolic function, and may even lead to heart failure with normal LV ejection fraction[13-15]. Similarly, the systolic pressure in the pulmonary artery progressively increases with age both at rest and during exercise[16-17]. AcT values identified in this study follow the same alterations. The rigid exclusion criteria applied enabled the assessment of the LV diastolic function and AcT without the influence of other factors, such as the presence of a significant pulmonary arterial hypertension, systolic dysfunction or advanced grades of LV diastolic dysfunction, which might lead to different interpretations. These same criteria determined homogeneity in the studied cohort. Hence, it was possible to observe that correlation of E/A ratio at mitral spectral Doppler decreases with age (following the decrease of wave E velocity and increase of A wave). Values of septal and lateral e' waves of the mitral annulus at tissue Doppler also decreased. These findings corroborate former studies involving a larger cohort of patients[18-19]. Similarly, AcT values followed the same values obtained for the LV diastolic function variables used in this study: the age increase correlated with AcT lower values, the lower AcT values correlated significantly with lower values of the E/A ratio, with lower values of E and lateral e' waves. However, E/e' ratio presented a positive correlation with AcT value, specifically, lower AcT values correlated with lower values of the E/e' ratio. This finding may be accounted for by analyzing the behavior of lateral and septal e' waves that decrease with age (about 10 to 15 years earlier) when compared with E wave of spectral Doppler, which decreases at a late stage, as described by Kadappu KK et al. In the present study, a stronger negative correlation of age with septal and lateral e' waves in relation to E wave of the spectral Doppler was observed. Hence, in an early stage of the diastolic dysfunction, without the increase of the filling pressures of the left atrium (LA), the E/e' ratio is still low, as is the AcT value, since e' waves decrease more sharply than E wave in this phase. Similar explanation is provided for the lack of correlation between IVRT and Act values. It is known that IVRT prolongs with age; however, when there is an increase in the filling pressures, IVRT shortens²¹. The selected severe exclusion

criteria also enabled assessment of AcT in quasi-normality conditions. PASP mean value was 28mmHg and its maximum value was 40mmHg, values considered to be within normality for the age range in the studied population[22]. Hence, a correspondence between AcT and PASP would only be expected in the presence of significant pulmonary hypertension, which was not the purpose of this study. However, when patients with a normal LV diastolic function and those with grade I diastolic dysfunction were compared, the latter presented lower AcT values, suggesting an increase in the pulmonary arterial pressure in this group, although still within their normal values. AcT values below 105ms are considered abnormal or reveal an increase in the pulmonary arterial pressure (PAH) [23]. Conversely, by excluding patients with a significant pulmonary arterial hypertension from the studied cohort, AcT values below 105ms were not expected. However, in an unprecedented way, it was possible to identify an alteration in AcT value in patients without a significant PAH, with an initial alteration of the LV diastolic function when compared with a preserved LV diastolic function. Some limitations of this study include the small number of participants, lack of data about the size and function of the right chambers and lack of analysis of the intra- and inter-observer measurement variability in relation to AcT, as errors may occur, considering that AcT values are affected by heart rates, cardiac output, RV systolic function and technical difficulties such as the angle of the ultrasonic beam[5].

Conclusions

The present study correlated significantly and unprecedentedly AcT with echocardiographic parameters of the LV diastolic function, presenting lower values in individuals with grade I diastolic dysfunction. The threshold suggested by the ROC curve was 0.135s, with AcT values lower than 0.135s associated with grade I diastolic dysfunction and higher than 0.135s values associated with normal diastole.

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