

DOES AORTIC STIFFNESS AFFECT THE RIGHT VENTRICULAR FUNCTIONS IN PATIENTS WITH LEFT VENTRICULAR DIASTOLIC DYSFUNCTION?

Inas Eweda¹

¹Department of Cardiology, Faculty of Medicine, Ain Shams University. Abbassia, Cairo - Egypt

Address for Correspondence:

Inas Eweda

Department of Cardiology, Faculty of Medicine, Ain Shams University. Abbassia, Cairo - Egypt

Emails: ime_1940@yahoo.com

Date Received: March 02, 2017

Date Revised: August 16, 2017

Date Accepted: October 27, 2017

Contribution

IE conceived the idea, planned the study, drafted the manuscript, collected data, did statistical analysis. The author contributed significantly to the submitted manuscript.

All authors declare no conflict of interest.

This article may be cited as: Eweda I. Does aortic stiffness affect the right ventricular functions in patients with left ventricular diastolic dysfunction? Pak Heart J 2018; 51 (01): 15-24

ABSTRACT

Objective: To determine the effect of aortic stiffness on right ventricular (RV) diastolic and systolic functions in individuals with left ventricular diastolic dysfunction (LVDD).

Methodology: Patients aged above forty years with LVDD confirmed by transthoracic echocardiography were included in this study in Ain Shams University Hospitals from January 2015 to 2016. Systolic functions of the RV and LV were assessed by two-dimensional echocardiography and pulsed wave tissue Doppler echocardiography. The diastolic diameter was obtained at the peak of QRS complex of the single lead ECG recorded by the echo machine while the systolic diameter was obtained at the maximum anterior motion of the aorta. Aortic distensibility (AD), aortic strain (AS) and aortic stiffness index (ASI) were used as aortic elasticity parameters. Blood pressure was measured with a mercury sphygmomanometer.

Results: A total of 300 consecutive patients were enrolled prospectively. This study showed that there were significant statistical differences between right ventricular diastolic function with all its states and aortic distensibility, aortic strain and aortic stiffness index. Various parameters reflecting right ventricular systolic and diastolic functions were independent predictors of AS, AD and ASI. Aortic parameters AS, AD and ASI were related to RV systolic function as the relation with TV S was 0.024, 0.002 and 0.010 respectively, also the relation with TAPSE was 0.027, 0.034 and 0.043 respectively. AS, AD and ASI were in addition related to RV diastolic function as seen with TV E/E' with p values 0.020, 0.020 & 0.000 respectively. RV DD grade was related to AS, AD & ASI with p values 0.010, 0.004 and 0.003 respectively.

Conclusions: RV systolic and diastolic parameters are independent predictors of aortic parameters reflecting aortic stiffness. This relation needs further study to verify the relation of the aorta and right ventricle although they are not in anatomical continuity with each other.

Key Words: Aorta, Right ventricular function, Doppler tissue imaging, Echocardiography.

INTRODUCTION

Increased cardiac workload is a consequence of arterial stiffness which is decreased compliance of the arterial system.¹ Among the best predictors of cardiovascular morbidity and mortality in large arteries is the presence of arterial stiffness.² Echocardiography can evaluate aortic stiffness using relatively simple noninvasive methods. The degree of aortic stiffness is reflected by aortic distensibility (AD) and aortic strain (AS) which are elasticity indexes of the aorta.³⁻⁴ Cardiac diastolic and systolic functions are affected by AS which is used as a noninvasive method clarifying the subclinical phase of atherosclerosis. Increased cardiac mortality and morbidity is reflected by AS which can be assessed by echocardiography.^{3,5,6} Cardiac systolic and diastolic functions are affected by AS which is used as a noninvasive method clarifying the subclinical phase of atherosclerosis.⁷

Left ventricular diastolic dysfunction (LVDD) is graded into three grades, grade I or mild, grade II or moderate and grade III or severe.⁸ This grading system was a very relevant prognostic tool for all the reasons of mortality in large studies.⁹

In 1616, Sir William Harvey suggested that the function of the right ventricle was to transfer blood through the lungs and not to nourish them.¹⁰ As a result, RV was profoundly underestimated for a long time and was regarded as a channel ignoring its contractile function. The importance of the RV and its role in the cardiovascular physiology have been considered since the early 1950s.¹¹

Right ventricular function plays a pivotal role in the course of heart failure, atrial fibrillation, ventricular arrhythmias and sudden death.¹²⁻¹⁴

The aim of the study was to study the impact of increased aortic stiffness on right ventricular systolic and diastolic functions in patients with LVDD.

METHODOLOGY

This cross sectional study was conducted at Ain Shams University Hospitals. Patients with LVDD, aged above forty years old were enrolled. LVDD grades were confirmed by trans-thoracic echocardiography from January 2015 to January 2016. To be eligible, patients needed to be in sinus rhythm. We excluded patients with significant valvular or congenital heart disease, cardiomyopathy, congestive heart failure, left ventricular systolic dysfunction (defined by an ejection fraction < 40%), ischemic heart disease, advanced lung disease, pulmonary hypertension, bundle branch block, pericarditis, and those receiving anti-arrhythmic drugs. The study protocol was thoroughly explained for each patient followed by obtaining a written consent. Our institutional Human Research Committee reviewed and

approved the protocol of the study.

The echocardiographic examination was performed with GE Medical System Vivid 7 ultrasound machine equipped with 2-4M Hz sector transducer probe. M-mode echocardiography was obtained in the left lateral decubitus position. The traces were done at a speed of 50mm/sec and each parameter was averaged from three consecutive cycles. Routine echocardiography with the standard projections was done initially and followed by Doppler flow tracing at the level of tricuspid and mitral valves. All echo-Doppler measurements were analyzed by the average of three cardiac cycles.

In order to assess the left ventricular diastolic function, the isovolumetric relaxation time (IVRT) (ms) which was the interval from the aortic valve closure signal to the mitral valve opening signal and the following transmitral inflow parameters were measured. Pulsed wave Doppler at the tip of open mitral valve leaflets was done to obtain peak velocity of the early E-wave transmitral flow (MV E) (m/sec), peak velocity of late A-wave transmitral flow (MV A) (m/sec), and the ratio (MV E/A). The deceleration time (MV DT) (msec) defined as time elapsed between peak E velocity and the point extrapolated deceleration slope of the E velocity crosses the zero baseline was obtained. In the apical four chamber, left ventricular ejection fraction (EF) was calculated using Simpson's modified single plane method.

To assess the right ventricular diastolic function, pulsed wave Doppler was obtained at the tip of open tricuspid valve leaflets to obtain peak velocity of the early E-wave (TV E) (m/sec), peak velocity of late A-wave (TV A) (m/sec), and the ratio (TV E/A). The deceleration time (TV DT) (msec) defined as time elapsed between peak E velocity and the point where the extrapolated deceleration slope of the E velocity crosses the zero baseline, was obtained. This was done in the apical four chamber view. Right ventricular global systolic function was assessed as tricuspid annular plane systolic excursion (TAPSE), by two-dimensional difference of end-diastolic and end-systolic lines (in mm) traced between the center of the ultrasound fan origin and the junction of right ventricular lateral tricuspid annulus, in apical four-chamber view.

Using M-mode echocardiography, ascending aorta dimensions were assessed three cm above the aortic valve in the long-axis parasternal view. The diastolic diameter was obtained at the peak of QRS complex of the single lead ECG recorded by the echo machine while the systolic diameter was the one obtained at the maximum anterior motion of the aorta. Aortic distensibility, aortic strain and aortic stiffness index were used as aortic elasticity parameters. The formulas used to calculate them were:

Aortic strain (%) = (aortic systolic diameter – aortic diastolic diameter) x 100/aortic diastolic diameter

Distensibility (cm^2/dyn) = $(2 \times \text{aortic strain}) / (\text{systolic pressure} - \text{diastolic pressure})$

Aortic stiffness index = $\ln(\text{SBP}/\text{DBP}) \times (\text{aortic systolic diameter} - \text{diastolic diameter}) / \text{aortic diastolic diameter}$, where "ln" means natural logarithm.²⁰

Mitral annular velocity by pulsed-wave Doppler tissue imaging (PW-DTI): The longitudinal mitral annular velocities were stored from four LV sites (anterior, inferior, lateral and septal) by PW-DTI. This was done in the apical two and four chamber views, using the GE Vivid Seven machine supplied by 2-4 MHz transducer in addition to secondary harmonic imaging to improve the visualization of the endocardial border. Global diastolic and systolic functions were assessed by calculating the mean value of the previously mentioned four sites. A single positive systolic velocity (MV S) was used to assess the systolic function of LV. It was recorded when the mitral ring moved towards the cardiac apex. The diastolic function of the LV was assessed using two negative waves, the early diastolic wave (MV E') and the late diastolic one (MV A'). These diastolic waves were recorded when the mitral annulus moved towards the base away from the apex. In addition MV E/E' and MV E'/A' ratios were obtained. A mean of three consecutive cycles was used to calculate all echo-Doppler parameters.

Tricuspid annular velocity by pulsed-wave Doppler tissue imaging: These velocities were obtained by the same machine used in the study. The spectral pulsed Doppler signal filters were adjusted until a Nyquist limit of 15-20 cm/s and the minimal optimal gain was used. From the apical four chamber view, the longitudinal tricuspid annular velocities were recorded from lateral right ventricular site using PW-DTI. Special care was taken to ensure optimal image orientation, to avoid underestimation of velocities. The values from the above site were used to assess global systolic and diastolic function. A single positive systolic velocity (TV S) was used to assess the systolic function of RV. It was recorded when the tricuspid ring moved towards the cardiac apex. The diastolic function of the RV was assessed using two negative waves, the early diastolic wave (TV E') and the late diastolic one (TV A'). These diastolic waves were recorded when the mitral annulus moved towards the base away from the apex. Also TV E/E' and TV E'/A' ratios were obtained. A mean of three consecutive cycles was used to calculate all echo-Doppler parameters. Right ventricular diastolic dysfunction was graded according to tricuspid valve measurements TV E/A, TV E/E' and TV DT.²¹

Blood pressure measurement: Blood pressure was measured with a mercury sphygmomanometer using an appropriate cuff size. Each subject was seated quietly for 5 minutes, with his/her feet on the floor, and arm supported at heart level; the cuff bladder encircled at least 80% of the arm circumference. The cuff was inflated to 30 mm Hg above the level at which the radial pulse disappears, then deflated

slowly. The first and fifth Korotkoff sounds were recorded as systolic and diastolic blood pressure, respectively. Blood pressure was measured in both arms, and the higher value was taken. We recorded the average of three separate measurements.

Data was presented as mean \pm SD. The Chi-square test was used to compare differences between proportions. The Analysis of variance (ANOVA) test was used for analysis of continuous data. Post-Hoc test was performed for comparison between each two of the multiple variables. A probability value of $p < 0.05$ was considered statistically significant. Analyses were performed with SPSS 12.0. Differences were considered significant if the null hypothesis could be rejected at the 0.05 probability level. Multiple linear regression was done to show independent predictors of AS, AD and ASI.

RESULTS

Left ventricular diastolic dysfunction: A total of 300 patients were included in the study. Doppler and pulsed wave tissue Doppler data was obtained from the mitral valve of patients. All patients were suffering from left ventricular dysfunction while the systolic LV function was normal (Table 1).

Aortic strain, distensibility and stiffness index were compared between the three groups of patients with different grades of LV DD. The difference between groups and aortic parameters was statistically significant (Table 2).

Right ventricular diastolic function: Patient characteristics of the studied cohort according to the grade of right ventricular diastolic function with its four states, normal diastolic function, grade I, grade II and grade III diastolic dysfunction were compared by ANOVA test (table 3). The comparison among the individual groups was done by Post-Hoc test as shown in table 4. The differences between the four groups in age, weight, body mass index, SBP and DBP was statistically significant.

The echo-Doppler and pulsed-wave tissue Doppler data obtained from the right side was compared by ANOVA test and Post-Hoc test respectively are shown in table 5 and 6. The systolic function of RV was impaired significantly in patients with grade III RVDD ($p = 0.001$). Similarly in patients with grade III RV DD the measurements of aortic elasticity showed statistically significant impairment as shown in Table 5.

AS, AD and ASI among the groups divided according to right ventricular diastolic function, there was statistically significant difference. This significant difference was also evident by Post-Hoc test between normal individuals and those suffering from grade II and grade III right ventricular diastolic dysfunction (Table 6).

Table 1: Doppler Data of the Studied Group According to the Degree of Left Ventricular Diastolic Dysfunction Grade (n=300)

LV Parameters	LV DD Grade I	LV DD Grade II	LV DD Grade III	p-value
MV E (CM/SEC)	51.84±11.44	65.07±13.61	107.86±40.03	0.000
MV A (CM/SEC)	78.69±14.52	62.74±13.17	47.08±19.00	0.000
MV E/A	0.66±0.08	1.06±0.23	2.36±0.36	0.000
MV DT (MSEC)	243.36±41.64	218.06±49.40	126.58±22.43	0.000
IVRT (MSEC)	107.11±12.92	98.76±14.88	57.19±9.55	0.000
MV S (CM/SEC)	9.05±2.55	8.87±2.40	8.39±1.70	0.402
MV E'(CM/SEC)	7.44±1.87	7.93±1.81	6.33±2.37	0.000
MV A'(CM/SEC)	10.28±2.43	9.47±2.37	6.86±1.50	0.000
MV E/E'	7.20±1.62	8.55±2.26	17.17±1.97	0.000
E/A'	0.74±0.19	0.87±0.21	0.95±0.39	0.000
LV EF (%)	64.72±5.34	65.89±6.41	64.13±5.75	0.191

LV=left ventricle, DD=diastolic dysfunction, MV E=mitral valve E wave, MV A=mitral valve A wave, MV E/A=mitral valve E/A ratio, MV DT=mitral valve deceleration time, IVRT=isovolumetric relaxation time, MV S=mitral valve positive peak systolic velocity, MV E'=mitral valve negative early diastolic velocity, MV A'=mitral valve negative late diastolic velocity, MV E/E' =mitral valve E/E' ratio, MV E/A' =mitral valve E/A' ratio, EF=ejection fraction

p > 0.05: NS, p < 0.05: S, p < 0.01: HS

Table 2: Comparison between Aortic Parameters According to Left Ventricular Diastolic Dysfunction Grades (n=300)

AORTIC PARAMETERS	LV DD Grade I	LV DD Grade II	LV DD Grade III	p-value	p1	p2	p3
AS (%)	14.81±4.37	12.22±4.80	5.79±0.36	0.000	0.000	0.000	0.000
AD (CM ² /DYN)	0.65±0.25	0.51±0.27	0.17±0.01	0.000	0.000	0.000	0.000
ASI	0.03±0.01	0.04±0.02	0.09±0.01	0.000	0.000	0.000	0.000

LV=left ventricle, DD=diastolic dysfunction, AS=aortic strain, AD=aortic distensibility, ASI=aortic stiffness index

p1: Comparison between left ventricular diastolic dysfunction grade I group and grade II group.

p2: Comparison between left ventricular diastolic dysfunction grade I group and grade III group.

p3: Comparison between left ventricular diastolic dysfunction grade II group and grade III group.

p > 0.05: NS, p < 0.05: S, p < 0.01: HS

Table 3: Comparison between the Demographic Data According to Right Ventricular Function by ANOVA Test (n=300)

Baseline parameters	Normal	RV DD grade I	RV DD Grade II	RV DD Grade III	p-value
Age	55.12 ± 10.50	55.17 ± 10.23	57.61 ± 9.01	67.75 ± 5.19	0.035
Height	168.35 ± 9.13	165.91 ± 9.71	165.46 ± 7.30	167.50 ± 5.00	0.272
Weight	82.15 ± 14.15	87.39 ± 12.40	90.11 ± 12.27	80.00 ± 0.01	0.004
BMI	29.35 ± 5.30	31.98 ± 4.88	32.95 ± 5.08	28.57 ± 1.75	0.000
SBP	129.38 ± 18.47	136.87 ± 18.85	153.86 ± 16.24	160.01 ± 1.26	0.000
DBP	85.65 ± 10.89	93.36 ± 8.28	95.02 ± 5.77	87.05 ± 11.17	0.000
Pulse	77.96 ± 7.31	75.85 ± 7.89	76.16 ± 6.73	80.25 ± 7.89	0.233

RV=right ventricle, DD=diastolic dysfunction, BMI=body mass index, SBP=systolic blood pressure, DBP=diastolic blood pressure

p > 0.05: NS, p < 0.05: S, p < 0.01: HS

Table 4: Comparison Between the Four Studied Groups As Regards Demographic Data According to Right Ventricular Function by Post Hoc Test (n=300)

Baseline Parameters	RV N VS I	RV N VS II	RV N VS III	RV I VS II	RV I VS III	RV II VS III
Age	0.976	0.161	0.015	0.101	0.013	0.048
Weight	0.011	0.001	0.743	0.153	0.253	0.123
BMI	0.001	0.000	0.764	0.194	0.182	0.090
SBP	0.010	0.000	0.001	0.000	0.012	0.507
DBP	0.014	0.000	0.013	0.000	0.076	0.757

RV=right ventricle, N=normal right ventricular diastolic function, vs=versus, I=grade I right ventricular diastolic dysfunction, II= grade II right ventricular diastolic dysfunction, III= grade III right ventricular diastolic dysfunction, BMI=body mass index, SBP=systolic blood pressure, DBP=diastolic blood pressure

P > 0.05: NS, P < 0.05: S, P < 0.01: HS

Table 5: Comparison between the echo-Doppler Parameters of the Right Side of the Heart and Aortic Parameters According to the Right Ventricular Diastolic Function (n=300)

Parameters	Normal	RV DD Grade I	RV DD Grade II	RV DD Grade III	p value
TV E (cm/sec)	49.72 ± 8.74	45.20 ± 9.94	64.90 ± 12.96	81.25 ± 2.50	0.000
TV A (cm/sec)	44.18 ± 10.41	62.49 ± 14.47	60.27 ± 13.87	41.00 ± 0.01	0.000
TV E/A	1.15 ± 0.18	0.73 ± 0.11	1.09 ± 0.20	1.98 ± 0.06	0.000
TV DT (msec)	221.88 ± 70.99	226.86 ± 63.84	189.18 ± 60.68	116.25 ± 2.50	0.000
TV S (cm/sec)	14.04 ± 4.87	13.81 ± 4.76	11.89 ± 4.78	7.01 ± 0.01	0.001
TV E' (cm/sec)	12.30 ± 2.34	12.02 ± 3.63	8.73 ± 1.53	8.01 ± 0.02	0.000
TV A' (cm/sec)	13.56 ± 3.26	13.62 ± 3.78	12.40 ± 4.04	11.02 ± 0.03	0.082
TV E/E'	4.15 ± 0.92	4.01 ± 1.24	7.49 ± 1.18	10.15 ± 0.13	0.000
TV E'/A'	0.95 ± 0.27	0.92 ± 0.30	0.75 ± 0.20	0.73 ± 0.01	0.000
TAPSE	2.56 ± 0.35	2.54 ± 0.32	2.53 ± 0.35	2.70 ± 0.27	0.785
AS (%)	14.53 ± 5.07	12.96 ± 4.91	8.37 ± 3.13	5.69 ± 0.33	0.000
AD (cm ² /dyn)	0.65 ± 0.29	0.55 ± 0.28	0.29 ± 0.15	0.18 ± 0.01	0.000
ASI	0.04 ± 0.01	0.04 ± 0.02	0.07 ± 0.02	0.09 ± 0.01	0.000

RV=right ventricle, DD=diastolic dysfunction, TV E=tricuspid valve E wave, TV A=tricuspid valve A wave, TV E/A=tricuspid valve E/A ratio, TV DT=tricuspid valve deceleration time, TV S=tricuspid valve positive peak systolic velocity, TV E' =tricuspid valve negative early diastolic velocity, TV A'=tricuspid valve negative late diastolic velocity, TV E/E' =tricuspid valve E/E' ratio, TV E'/A' =tricuspid valve E'/A' ratio, TAPSE=tricuspid annular plane systolic excursion AS=aortic strain, AD=aortic distensibility, ASI=aortic stiffness index

p > 0.05: NS, p < 0.05: S, p < 0.01: HS

Table 6: Comparison between the Four Studied Groups as Regards the Echo-Doppler Parameters of the Right Side of the Heart and Aortic Parameters According to the Right Ventricular Diastolic Function by Post Hoc Test (n=300)

Parameters	RV N vs I	RV N vs II	RV N vs III	RV I vs II	RV I vs III	RV II vs III
TV E (cm/sec)	0.008	0.000	0.000	0.000	0.000	0.003
TV A (cm/sec)	0.000	0.000	0.647	0.270	0.002	0.006
TV E/A	0.000	0.057	0.000	0.000	0.000	0.000
TV DT (msec)	0.628	0.005	0.002	0.000	0.001	0.028
TV S (cm/sec)	0.771	0.012	0.005	0.007	0.005	0.047
TV E' (cm/sec)	0.554	0.000	0.004	0.000	0.006	0.623
TV E/E'	0.428	0.000	0.000	0.000	0.000	0.000
TV E'/A'	0.613	0.000	0.104	0.000	0.135	0.860
TAPSE	0.822	0.667	0.403	0.786	0.356	0.322
AS (%)	0.029	0.000	0.000	0.000	0.002	0.247
AD (cm ² /dyn)	0.012	0.000	0.000	0.000	0.004	0.356
ASI	0.050	0.000	0.000	0.000	0.000	0.012

Relations between aortic parameters and various parameters: Multiple linear regression was done to show the independent predictors of AS, AD and ASI regarding the baseline characteristics (Table 7). The SBP and DBP showed relation with all the aortic parameters, while height, weight and BMI showed relation with ASI only.

According to left side measurements, AS was related to MV A and MV E/A. AD was related to MV A and MV S. The

situation was different for ASI where it was related to MV A, MV E/A, IVRT, EF and LV DD grade as shown in Table 8.

The right sided measurements and aortic parameters like AS, AD and ASI were related to TV S, TAPSE, TV E/E' and RV DD grade indicating that aortic stiffness is related to systolic function of RV.

Table 7: Multiple linear regression showing independent predictors of AS, AD and ASI regarding baseline data (n=300)

Model	AS	AD	ASI
Age	0.867	0.573	0.519
Sex	0.991	0.416	0.214
Height	0.519	0.467	0.027
Weight	0.298	0.372	0.014
BMI	0.317	0.386	0.011
SBP	0.001	0.000	0.000
DBP	0.043	0.000	0.000
Pulse	0.396	0.425	0.093

AS=aortic strain, AD=aortic distensibility, ASI=aortic stiffness index, BMI=body mass index, SBP=systolic blood pressure, DBP=diastolic blood pressure.

p > 0.05: NS, p < 0.05: S, p < 0.01: HS

Table 8: Multiple linear Regression Showing Independent Predictors of AS, AD and ASI Regarding Left side Measurements (n=300)

Model	AS	AD	ASI
MVE	0.093	0.107	0.102
MVA	0.008	0.010	0.010
MV E/A	0.031	0.103	0.017
MV DT	0.053	0.523	0.114
IVRT	0.772	0.423	0.019
MV S	0.060	0.020	0.994
MV E'	0.461	0.162	0.829
MV A'	0.675	0.712	0.212
MV E/E'	0.153	0.075	0.122
MV E'/A'	0.369	0.830	0.269
LV EF	0.965	0.149	0.015
LV DD Grade	0.342	0.207	0.015

AS=aortic strain, AD=aortic distensibility, ASI=aortic stiffness index, MV E=mitral valve E wave, MV A=mitral valve A wave, MV E/A=mitral valve E/A ratio, MV DT=mitral valve deceleration time, IVRT=isovolumetric relaxation time, MV S=mitral valve positive peak systolic velocity, MV E' =mitral valve negative early diastolic velocity, MV A'=mitral valve negative late diastolic velocity, MV E/E' =mitral valve E/E' ratio, MV E'/A' =mitral valve E'/A' ratio, LV=left ventricle, EF=ejection fraction, DD=diastolic dysfunction.

P > 0.05: NS, P < 0.05: S, P < 0.01: HS

Table 9: Multiple linear regression showing independent predictors of AS, AD and ASI regarding right side measurements (n=300)

Parameter	AS	AD	ASI
TV E (cm/sec)	0.299	0.275	0.090
TV A (cm/sec)	0.447	0.531	0.609
TV E/A	0.806	0.896	0.653
TV DT (msec)	0.135	0.134	0.908
TV S (cm/sec)	0.024	0.002	0.010
TV E'(cm/sec)	0.196	0.327	0.111
TV A'(cm/sec)	0.654	0.351	0.253
TV E/E'	0.020	0.020	0.000
TV E'/A'	0.833	0.785	0.821
TAPSE	0.027	0.034	0.043
RV DD Grade	0.010	0.004	0.003

AS=aortic strain, AD=aortic distensibility, ASI=aortic stiffness index, TV E=tricuspid valve E wave, TV A=tricuspid valve A wave, TV E/A=tricuspid valve E/A ratio, TV DT=tricuspid valve deceleration time, TV S=tricuspid valve positive peak systolic velocity, TV E' =tricuspid valve negative early diastolic velocity, TV A'=tricuspid valve negative late diastolic velocity, TV E/E' =tricuspid valve E/E' ratio, TV E'/A' =tricuspid valve E'/A' ratio, TAPSE=tricuspid annular plane systolic excursion, RV=right ventricle, DD=diastolic dysfunction

p > 0.05: NS, p < 0.05: S, p < 0.01: HS

DISCUSSION

Arteriosclerosis is the degenerative stiffness of arterial beds where arterial stiffness is among the first recognizable criteria of adverse functional and structural changes in the vessel wall while atherosclerosis is the occlusive consequence of plaque formation, inflammatory disease and lipid oxidation. Both conditions are present together and reflect a diffuse, progressive and age-connected process that takes place in all vascular beds.²³

Aortic stiffness and the geometric characteristics of the ventricle affect end systolic wall stress which is the most relevant factor in developing cardiac hypertrophy.²⁴⁻²⁶ Progressive deterioration that occurs in diastolic function which is followed by systolic function takes place due to increased systolic and diastolic myocardial stiffness occurring as a consequence of myocardial changes vanquishing end systolic stress.²⁷

Aortic stiffness is one of the indicators of vascular age and is increased after the fifth decade in normal individuals.^{28,29} Fracture and segmentation of elastin fibers with continuous stretch results in the transmission of the stretch to the less expandable collagenous fibers in the arterial wall which all leads to age related AS.³⁰ Circulatory function is strongly influenced by arterial-ventricular coupling.³¹ Heart failure is the end result of concentric left ventricular hypertrophy and remodeling which are consequences of AS which is considered chronic increased afterload.³²

Analyzation explained that the left ventricular diastolic dysfunction is a result of left ventricular myocardial structural changes which is due to increased afterload

occurring as a consequence of increased aortic stiffness. Impaired myocardial relaxation and/or increased ventricular stiffness results in diastolic dysfunction with high LV filling pressures.²⁶

Left ventricular function is supported by the elastic properties of the aorta. The aorta is a main modulator of the whole cardiovascular system that prevents rhythmic pulsatile flow to maintain a continuous flow in the capillary bed. In addition, the aorta is the main blood conduit for tissues. The aorta has a great impact on left ventricular function and coronary flow due to its elastic properties.³³

In this study, AS was related to MV A and MV E/A, AD was related to MV A and MV S. The situation was different for ASI where it was related to MV A, MV E/A, IVRT, EF and LV DD grade reflecting LV systolic and diastolic functions. The relation between aortic stiffness & left ventricular diastolic function was disclosed by many studies. A previous study found significant relation between AD, MV E/A and mitral inflow propagation velocity in newly diagnosed hypertensive patients.³ In another study, they found significant relation between, AD, MV E/A, MV IVRT and MV DT.³⁴

In this study, AS, AD and ASI were related to TV S, TAPSE, TV E/E' and RV DD grade indicating that aortic stiffness is related to systolic function of RV represented by TV S, TAPSE and RV diastolic function as reflected by TV E/E' and RV DD grade. As far as the search results obtained, no study observed the relation between right side measurements and aortic stiffness.

The RV which weights approximately one-sixth of the LV

mass, carries out 25% of the LV stroke work to pump blood in pulmonary circulation that poses 10% of the resistance of the systemic circulation as a result of its big cross-sectional area.¹¹

Both ventricles are anatomically and functionally interdependent, force is transferred between the two ventricles irrespective of humoral, neural and hemodynamic control. As a consequence, LV contraction modifies nearly 20-40% of the beat to beat RV systolic volume and pressure outflow.³⁵ The prognostic role of RV systolic dysfunction in numerous pathological cases has long been established. Many studies concentrating on tricuspid annular displacement showed convincing results.^{36,37}

Right ventricular diastolic dysfunction pathophysiology is a very complicated process more than just measuring the thickness of the myocardium. A great number of acute and chronic diseases, including pressure and volume overload pathologies have been connected with RV DD. Myocardial ischemia, congenital heart diseases, primary pulmonary disease, systemic conditions and LV dysfunction (due to ventricular interdependence).^{38,39} Diseases inherent to the LV influence the RV size and function. LV dysfunction occurring as a consequence of myocardial infarction and heart failure elevate the risk for RV dysfunction and dilation.^{40,41} RV dysfunction is among the absolute prognostic factors of the consequences of myocardial infarction, even if manifest RV infarction did not occur.^{42,43}

LIMITATIONS

No invasive procedure was used in the study to assess aortic elasticity, pulse pressure and ventricular diastolic function. Although, they are considered the gold standard for assessment but many studies reported that M-mode echocardiography was a reliable method for aortic elasticity assessment and has excellent relation with the data obtained from the invasive methods.^{33, 44} Also, right ventricular diastolic function can be accurately assessed by echo-Doppler.⁴⁵

CONCLUSION

Impaired aortic elasticity had a significant effect on the RV and LV systolic and diastolic functions. The right ventricular systolic function as assessed by TAPSE and TV S together RV diastolic function represented by E/E' are independent predictors of aortic parameters reflecting the aortic stiffness. The relation between the aorta and the right side, needs further study.

REFERENCES

1. Laurent S, Boutouyrie P, Asmar R, Gautier I, Laloux B, Guize L, et al. Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. *Hypertension* 2001;37(5):1236-41.
2. Arnett DK, Evans GW, Riley WA. Arterial stiffness a new cardiovascular risk factor. *Am J Epidemiol* 1994;140(8):669-82.
3. Eren M, Gorgulu, Uslu N, Celik S, Dagdeviren B, Tezel T, et al. Relation between aortic stiffness and left ventricular diastolic function in patients with hypertension, diabetes, or both. *Heart* 2004;90(1):37-43.
4. Ikonomidis I, Lekakis J, Stamatelopoulos K, Markomihelakis N, Kakkamanis PG, Mavrikakis M, et al. Aortic elastic properties and left ventricular diastolic function in patients with Adamantiades-Behcet's disease. *J Am Coll Cardiol* 2004;43(6):1075-81.
5. Pitsavos C, Toutouzas K, Dernellis J, Skoumas J, Skoumbourdis E, Stefanadis C, et al. Aortic stiffness in young patients with heterozygous familial hypercholesterolemia. *Am Heart J* 1988;135(4):604-8.
6. Stefanadis C, Dernellis J, Vlachopoulos C, Tsioufis C, Tsiamis E, Toutouzas K, et al. Aortic function in arterial hypertension determined by pressure-diameter relation effect of diltiazem. *Circulation* 1997;96(6):1853-8.
7. Aslan AN, Ayhan H, Cicek OF, Akçay M, Durmaz T, Keles T, et al. Relationship between aortic stiffness and the left ventricular function in patients with prediabetes. *Intern Med* 2014;53(14):1477-84.
8. Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *J Am Soc Echocardiogr* 2009;22(2):107-33.
9. Redfield MM, Jacobsen SJ, Burnett JC Jr, Mahoney DW, Bailey KR, Rodeheffer RJ. Burden of systolic and diastolic ventricular dysfunction in the community: appreciating the scope of the heart failure epidemic. *JAMA* 2003;289(2):194-202.
10. Karaye KM, Bonny A. Right ventricular dysfunction in systemic hypertension: a call to action. *Int J Cardiol* 2016;206:51-3.
11. Haddad F, Doyle R, Murphy DJ, Hunt SA. Right ventricular function in cardiovascular disease, part II: pathophysiology, clinical importance, and management of right ventricular failure. *Circulation* 2008;117:1717-31.
12. Ghio S, Gavazzi A, Campana C, Inserra C, Klersy C, Sebastiani R, et al. Independent and additive prognostic value of right ventricular systolic function and pulmonary artery pressure in patients with chronic heart failure. *J Am Coll Cardiol* 2001;37(1):183-8.

13. Aziz EF, Kukin M, Javed F, Musat D, Nader A, Pratap B, et al. Right ventricular dysfunction is a strong predictor of developing atrial fibrillation in acutely decompensated heart failure patients, ACAP-HF data analysis. *J Card Fail* 2010;16:827-34.
14. Warnes CA. Adult congenital heart disease importance of the right ventricle. *J Am Coll Cardiol* 2009;54(21):1903-10.
15. Zoghbi WA, Habib GB, Quinones MA. Doppler assessment of right ventricular filling in a normal population. *Circulation* 1990;82(4):1316-24.
16. Kaul S, Tei C, Hopkins JM, Shah PM. Assessment of right ventricular function using two dimensional echocardiography. *Am Heart J* 1984;107(3):526-31.
17. Stratos C, Stefanadis C, Kallikazaros I, Boudoulas H, Toutouzas P. Ascending aorta distensibility abnormalities in hypertensive patients and response to nifedipine administration. *Am J Med* 1992;93(5):505-12.
18. Lacombe F, Dart A, Dewar E, Jennings G, Cameron J, Laufer E, et al. Arterial elastic properties in man: a comparison of echo-Doppler indices of aortic stiffness. *Eur Heart J* 1992;13(8):1040-5.
19. Stefanadis C, Wooley CF, Bush CA, Kolibash AJ, Boudoulas H. Aortic distensibility in post stenotic aortic dilatation: the effect of co-existing coronary artery disease. *J Cardiol* 1988;18(1):189-95.
20. Ikonomiidis I, Lekakis J, Stamatelopoulos K, Markomihelakis N, Kaklamanis PG, Mavrikakis M. Aortic elastic properties and left ventricular diastolic function in patients with Adamantiades- Behcet's disease. *J Am Coll Cardiol* 2004;43(6):1075-81.
21. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the European Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology and the Canadian Society of Echocardiography. *J Am Soc Echocardiogr* 2010;23(7):685-713.
22. Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN, et al. Recommendations for blood pressure measurement in humans and experimental animals: Part 1: blood pressure measurements in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. *Hypertension* 2005;45(1):142-61.
23. Izzo JL Jr. Arterial stiffness and the systolic hypertension syndrome. *Curr Opin Cardiol* 2004; 19: 341-52.
24. Bouthier JD, De Luca N, Safar ME, Simon AC. Cardiac hypertrophy and arterial distensibility in essential hypertension. *Am Heart J* 1985;109(6):1345-52.
25. Nichols WW, O'Rourke MF, Avolio AP, Yaginuma T, Murgu JP, Pepine CJ, et al. Effects of age on ventricular vascular coupling. *Am J Cardiol* 1985;55(9):1179-84.
26. Grossman W, Jones D, McLaurin LP. Wall stress and patterns of hypertrophy in the human left ventricle. *J Clin Invest* 1975;56(1):56-64.
27. Weber KT. Cardiac interstitium in health and disease: the fibrillar collagen network. *J Am Coll Cardiol* 1989;13(7):1637-52.
28. van der Heijden-Spek JJ, Staessen JA, Fagard RH, Hoeks AP, Boudier HA, van Bortel LM. Effect of age on brachial artery wall properties differs from the aorta and is gender dependent: a population study. *Hypertension* 2000;35(2):637-42.
29. Redheuil A, Yu WC, Wu CO, Mousseaux E, de Cesare A, Yan R, et al. Reduced ascending aortic strain and distensibility: earliest manifestations of vascular aging in humans. *Hypertension* 2010;55(2):319-26.
30. Benetos A, Waeber B, Izzo J, Mitchell G, Resnick L, Asmar R, et al. Influence of age, risk factors, and cardiovascular and renal disease on arterial stiffness: clinical applications. *Am J Hypertens* 2002;15(12):1101-8.
31. Kass DA. Ventricular arterial stiffening: integrating the pathophysiology. *Hypertension* 2005;46(1):185-93.
32. Chen CH, Nakayama M, Nevo E, Fetis BJ, Maughan WL, Kass DA. Coupled systolic ventricular and vascular stiffening with age: implications for pressure regulation and cardiac reserve in the elderly. *J Am Coll Cardiol* 1998;32(5):1221-7.
33. Stefanadis C, Stratos C, Boudoulas H, Kourouklis C, Toutouzas P. Distensibility of the ascending aorta: comparison of invasive and non-invasive techniques in healthy men and in men with coronary artery disease. *Eur Heart J* 1990;11(11):990-6.
34. Ikonomidis I, Protogerou A, Kotsis V. Arterial stiffness and aortic distensibility are associated with left ventricular diastolic dysfunction in newly diagnosed hypertensive patients. *Eur J Echocardiogr* 2002;3(suppl I):S102.
35. Santamore WP, Dell'Italia LJ. Ventricular interdependence: significant left ventricular contributions to right ventricular systolic function, *Prog*

- Cardiovasc Dis 1998;40(4):289-308.
36. Samad BA, Alam M, Jensen-Urstad K. Prognostic impact of right ventricular involvement as assessed by tricuspid annular motion in patients with acute myocardial infarction. *Am J Cardiol* 2002;90(7):778-81.
 37. Vinereanu D, Khokhar A, Fraser AG. Reproducibility of pulsed wave tissue Doppler echocardiography. *J Am Soc Echocardiogr* 1999;12(6):492-9.
 38. Berman GO, Reichek N, Brownson D, Douglas PS. Effects of sample volume location, imaging view, heart rate and age on tricuspid velocimetry in normal subjects. *Am J Cardiol* 1990;65(15):1026-30.
 39. Weber KT, Janicki JS, Shroff S, Fishman AP. Contractile mechanics and interaction of the right and left ventricles. *Am J Cardiol* 1981;47(3):686-95.
 40. Berger PB, Ruocco NA Jr, Ryan TJ, Jacobs AK, Zaret BL, Wackers , et al. The TIMI Research Group. Frequency and significance of right ventricular dysfunction during inferior wall left ventricular myocardial infarction treated with thrombolytic therapy (results from the Thrombolysis In Myocardial Infarction [TIMI] II trial). *Am J Cardiol* 1993;71(13):1148-52.
 41. Di Salvo TG, Mathier M, Semigran MJ, Dec GW. Preserved right ventricular ejection fraction predicts exercise capacity and survival in advanced heart failure. *J Am Coll Cardiol* 1995;25(5):1143-53.
 42. Zornoff LA, Skali H, Pfeffer MA, St John Sutton M, Rouleau JL, Lamas GA, et al. Right ventricular dysfunction and risk of heart failure and mortality after myocardial infarction. *J Am Coll Cardiol* 2002;39(9):1450-5.
 43. Anavekar NS, Skali H, Bourgoun M, , Kober L, Maggioni AP, et al. Usefulness of right ventricular fractional area change to predict death, heart failure, and stroke following myocardial infarction (from +the VALIANT ECHO study). *Am J Cardiol* 2008;101(5):607-12.
 44. Stefanadis C, Dernellis J, Tsiamis E, Stratos C, Diamantopoulos L, Michaelides A, et al. Aortic stiffness as a risk factor for recurrent acute coronary events in patients with ischaemic heart disease. *Eur Heart J* 2000;21(5):390-6.
 45. Pye MP, Pringle SD, Cobbe SM. Reference values and reproducibility of Doppler echocardiography in the assessment of the tricuspid valve and right ventricular diastolic function in normal subjects. *Am J Cardiol* 1991;67(4):269-73.