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The impact of systemic hypertension-related heart remodeling on right ventricle mechanics: A two-dimensional echocardiographic speckle tracking study

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ABSTRACT

In spite of heart remodeling such as left ventricular hypertrophy (LVH) affects both left and right ventricles due to ventricular interdependence; still, a few studies had examined the outcomes of these effects on right ventricle (RV) and usually focusing on the left ventricle (LV). This study was aimed to evaluate the effect of systemic arterial hypertension (SAM) on RV mechanics using two-dimensional RV longitudinal strains. A case-control study was conducted during the period from July 2016 to April 2018 at Ibn Al-Bytar cardiac center Baghdad, Iraq. One hundred (61 males and 39 female) Patients with SAH were compared with one hundred (57 males and 43 female) healthy control subjects aged from (40-60) years. These groups were subjected to a detailed history, blood pressure measurement, ECG, anthropometry measurements, a list of investigations, and echocardiographic study. The results revealed that the thickness of interventricular septum at diastole (IVSd) was (11.13±1.46) mm in the hypertensive group and was (9.42±0.68) mm in the control group P-value < 0.001. Relative wall thickness (RWT)was (4.65 ±0.28) mm in the patient group and was (3.86 ± 0.34) mm in the control group and P value = 0.01. The mean right ventricular global longitudinal strain (RVGLS) was (- 20.12 ± 3.80) % in a patient group versus (- 25.90 ± 2.18) in the control group, the P value was 0. 001.IVSd significantly correlated with impaired RVGLS in multivariate logistic regression and P value was 0.001, and the odds ratio was 2.418. RV longitudinal strain is significantly impaired in hypertensive patients group and strongly correlates with heart remodeling

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INTRODUCTION

Systemic arterial hypertension (SAM) is common public health around the globe with high morbidity and mortality rate (Vancini-campanharo *et al.,* 2015). SAM along with its complications of cardiovascular remodeling are strongly accompanied with the increased risk of cardiovascular consequences, including coronary heart diseases, cardiac failure, cardiac arrhythmias, cerebrovascular accident (CVA), renal failure, and stroke (Yasuno *et al.,* 2009). Left ventricular hypertrophy (LVH) is the primary apparent heart remodeling in response to untreated hypertension. It is a homeostatic mechanism and physiological response against the workload of pressure overload on the

wall of the heart (Tadic *et al.,* 2015). Left ventricle (LV) geometry is measured by relative wall thickness (RWT) which is defined as two times left ventricular posterior wall thickness (LVPWd) divided by the left ventricular end diastolic (LVEDd), and it is a marker for adverse events in patients suffering from LV dysfunction (Page, 2016). The effect of SAM on left ventricular (LV) geometry and function have been widely studied in the last decades. In contrast, the effect of SAM on the right ventricle (RV) insufficiently studied. Recently, and because of ventricular interdependence, many studies have revealed that RV function is an important prognostic marker in different heart diseases (Leong *et al.,* 2013). Global Longitudinal strain (GLS) imaging by speckle tracking is a novel non-invasive echocardiographic method for assessment of global and regional myocardial function, so cardiac strain can be defined as the change of myocardial fiber length during stress at end-systole compared to its original length in a relaxed state at end-diastole (Leong *et al.,* 2013, Blessberger *et al.,* 2010).

GLS is not only has a good correlation between longitudinal strain and ventricular ejection fraction but in addition, GLS provides a quantitative myocardial deformation analysis of each ventricular segment, also allowing for early subclinical dysfunction detection in patients with a preserved systolic function by traditional echocardiographic measurements (Voigt *et al.,* 2015, Stefani *et al.,* 2016).

PATIENTS AND METHODS

A case-control study was carried out during the period from July (2016) to April (2018) at Ibn Al-Bytar Cardiac centre, Baghdad in cooperation with Department of Physiology, College of Medicine, University of Baghdad.

The total number of subjects enrolled in the study was 200 subjects of either sex (118 males and 82 female) divided into hypertensive patients' group (61 males and 39 female) and apparently healthy control group (57 males and 43 female), their age range from (40 – 60) year. These groups were subjected to a detailed history, blood pressure measurement, ECG, anthropometry measurements, a list of investigations, and echocardiographic study. All subjects informed to be included in this study, according to the Local Ethical Committee of the Ministry of Health, Iraq. All subjects with Ischemic heart diseases, heart failure, valvular and congenital heart diseases, cardiac arrhythmias, and acute or chronic renal or liver diseases were excluded from this study. Echocardiography was performed for all subjects using aVivid E9® system (GE Vingmed; Hortoen, Norway) with M5Sc Cardiac Sector 5 MHz transducer under observation of specialist echocardiographer. The examination position of all subjects during echocardiographic examination was left lateral decubitus position, to bring the heart forward to the chest wall and lateral to the sternum, as recommended by the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI) (Collier *et al.,* 2017, Lang et la., 2015). Three ECG leads wire connected to electrodes adhered to the patient chest wall, and 3 cardiac cycles images were obtained. The right ventricular focused apical 4 chambers view (RV- focused) was selected for measuring right ventricular longitudinal strains using two-dimensional speckle tracking. Left ventricular end diastolic (LVEDd) and systolic (LVEDs) dimension, Interventricular septum thickness at diastole (IVSd) thickness, and Left posterior ventricular wall (LVPWd) thickness were measured from 2-dimensionally guided M-mode recorded at a speed of 50–100 cm/s. Relative wall thickness (RWT) was calculated by the ratio of (LVPWd) 2 to LVIDd (Nadruz, 2015).

RESULTS

Age, height, body surface area (BSA) and heart rate were similar in both groups. Body mass index (BMI), body weight, systolic (SBP) and diastolic blood pressures (DBP) were significantly higher in the patient group. General characteristics of patient and control groups are listed in Table 1.

Table 2 demonstrates M-Mode echocardiographic left linear ventricular parameters IVSd, PWDd, and RWT were increased inpatient group (11.13mm, 10.96 mm, and 0.52 mm vs 9.42 mm, 9.22 mm, and 2.8 mm in controls, $P < 0.05$ for all). Regarding LV ejection fraction and LV internal dimensions were no significant differences between both groups.

Table 3 demonstrates Global right ventricular strain using two-dimensional speckle tracking echocardiography in the two studied groups. The mean 2D-RVGLS was (- 20.12 ± 3.80) % in hypertensive patients versus (- 25.90 ± 2.18) in normal subjects, the P value was 0.001, and there was a significant difference between the two groups.

Figure 1 and show the statistically negative significant correlation between IVSd and RVGLS, so when the value of IVSd increases the value of RVGLS decreases. Table 4 demonstrates univariate and multivariate logistic regression analysis for prediction of impaired RVGLS between the studied subjects, the cut value between impaired and normal RVGLS was -20 % in univariate analysis, only the parameters of significant correlation were enrolled in multivariate logistic regression from them only IVSd, RWT, LVEDd were

Table 1: Comparison between hypertensive and normotensive groups regarding demographic data

Parameters	Patients (N=100) Mean ± SD	Control (N=100) Mean ± SD	P value
Age (year)	50.65±4.22	48.38± 3.44	0.236
Weight (kg)	83.01±11.62	77.03±10.48	0.002
Height (cm)	172.94±4.65	1.69±9.56	0.723
BMI (kg/m^2) *	29.51±3.140	26.89±3.08	0.001
BSA(m^2) **	1.96±0.19	1.92±0.17	0.138
Heart rate(beats/min)	76±9	71±6	0.067
SBP (mmHg) ***	139.70±11.15	121.50±8.52	0.001
DBP(mmHg)****	84.00±4.13	70.95±5.11	0.001

* Body mass index; ** Body surface area; *** Systolic Pressure; ****Diastolic Blood Pressure; P-Value < 0.05 sig

Table 2: Comparison between hypertensive and normotensive group regarding M-Mode echo-cardiographic left ventricular linear parameters

Parameter	Patients (N=100) Mean ± SD	Control (N=100) Mean ± SD	P value
IVSd(mm)	11.13±1.46	9.42±0.68	< 0.001
LVEDd (mm)	45.54±3.29	46.70±3.36	0.215
LVEDs (mm)	31.38±2.53	30.92±2.372	0.185
LVPWd (mm)	10.96±1.07	9.22±0.62	0.001
RWT (mm)	0.52±0.13	0.39±0.9	0.001
LVEF (%)*	63.55±2.40	65.88±2.78	0.125

* Left ventricular ejection fraction; P-Value < 0.05 sig

Table 3: Comparison between hypertensive and normotensive group regarding two-dimensional right ventricular speckle tracking strains

Parameters	Patients (N=100) Mean ± SD	Control (N=100) Mean ± SD	P value
2D - RVGLS % *	- 20.12 ± 3.80	- 25.90 ± 2.18	0.001

* Two-dimensional right ventricular global longitudinal strain P-Value < 0.05 sig

significantly correlated with impaired RVGLS P-value < 0.05. The odds ratio of multivariate logistic regression revealed that IVSd was the strongest factor affect RVGLS in this study (figure 1), the odds ratio for IVSd, RWT, LVEDd were respectively 2.418, 1.978, and 1.262.

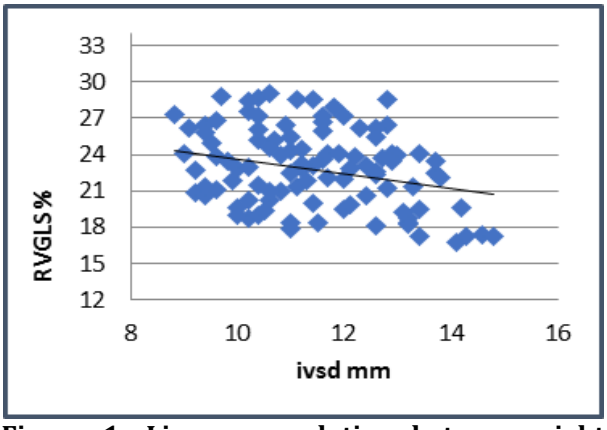

Figure 1: Linear correlation between right ventricular global longitudinal strain and diastolic interventricular septum thickness in hypertensive group

DISCUSSION

In the present study, hypertensive patient group had a significantly higher interventricular septum, left ventricular posterior wall thickness and relative wall thickness over the control group. The fact of left ventricular hypertrophy in hypertensive patient had been well established (Cuspidi *et al.,* 2012). This result of left ventricular hypertrophy was in agreement with the result of Cuspidi and his coworker in their review paper, so they made analysis for 30 studies and demonstrated one of the largest databases on echocardiographic LVH prevalence in the hypertensive population of 37 700 patients from different studies. The main finding of their work was that 36 - 41% of both treated and untreated hypertensive patients had alterations in cardiac structure (Cuspidi *et al.,* 2012). The more likely explanation for developing LVH in hypertensive patients is because hypertension increases the hemodynamic load on the LV, which make LV remodels in an attempt to compensate wall stress and regulate myocardial oxygen consumption (Stanton., 2016). Diez and Frohlich demonstrate that the mechanisms responsible for progression to hypertrophy include not only a response to increased hemodynamic load from elevated blood pressure but also the effects of neurohormones such as catecholamines, renin-angiotensin system, endothelins, cytokines, and certain growth factors by increasing cardiomyocyte size, enhancing myocardial fibrosis, and increasing interstitial and perivascular collagen

Table 4: Univariate and Multivariate strategic relapse examination for worldwide right ventricular strain between the considered subjects

Parameters	Univariate logistic regression			Multivariate logistic re ɜression		
	OR *	95%CI **	P value	OR	95%CI	P value
IVSD (mm)	4.348	4.252– 15.408	0.001	2.418	0.308– 17.038	0.001
Relative wall thickness	4.012	3.222– 12.023	0.005	1.978	0.328– 17.044	0.03
LVEDd (mm)	2.973	1.107 – 2.33	0.011	1.262	0.868 – 2.138	0.235
BSA	2.667	0.817 – 8.708	0.104	-	-	-
BMI	2.640	0.785 – 8.874	0.117	-	-	-
LVEDs (mm)	1.178	0.952 – 1.005	0.104	-	-	-
LVEF (%)	1.003	0.925 – 1.087	0.950	-	-	-

* Odds ratio; ** 95% confidence interval; P-Value < 0.05 sig

deposition (Page, 2016, Díez and Frohlich, 2015). The clear prognostic importance of RV function in various diseases has encouraged investigations about new echocardiographic methods for accurate diagnosis of RV function (Smolarek *et al.,* 2017). Two-dimensional speckle tracking echocardiography is a novel technique of cardiac imaging for measuring cardiac motion quantification depends on the frame to frame tracking of ultrasonic speckles in grey scale 2D images. 2D STE overcomes most of the limitations present in conventional echocardiography and tissue Doppler imaging because it is angle and load independent, thus allowing accurate quantification of regional and global myocardial function (Stefani *et al.,* 2016).

In this study, global longitudinal RV strains were significantly decreased in the hypertensive patient group compared to the normotensive control group. The present study agreed with formerly studies supposing that longitudinal RV strain is damaged in patients with hypertensive disease (Braik *et al.,* 2014, Lu *et al.,* 2015). The present investigation revealed a marked dysfunction of systolic RV, in spite of the lack of clinical symptoms of systolic impairment as evaluated by extra conventional parameters of systolic performance such as ejection fraction. These observations reinforce the fact that speckle tracking technology is more sensitive and traditional echocardiographic efficient measurements of RV systolic function and are additionally supported by results of a "cardiovascular magnetic resonance imaging which is an essential parameter for RV measurement" (D'Andrea *et al.,* 2010). Our results are in agreement with previous studies that revealed subclinical systolic dysfunction by measuring 2D speckle tracking longitudinal strain compared with other conventional echocardiographic parameters (D'Andrea *et al.,* 2010, Hense *et al.,* 2014, Younan, 2015). This finding can be explained by many facts:

Longitudinal strain establishing by "two-dimensional intra tissue velocities rather than 1-dimensional transducer-tissue velocities" which obtained by traditional echo methods (Collier *et al.,* 2017, Al-Hajjiah *et al.,* 2018),

Longitudinal strain "allows for discrimination between normal, active myocardial segmental deformation versus passive displacement of a dysfunctional myocardial segment due to adjacent segment tethering and global cardiac motion and this is particularly useful in non-thinned segments like cardiac hypertrophy" (Kurt *et al.,* 2014, Al-Hajjiah and Almkhadree, 2018).

Longitudinal strain measure tissue deformation according to "Lagrangian strain which compares deformation to original length" while conventional methods measures deformations between time points (Voigt *et al.,* 2015), and the longitudinal strain is not angle and load dependent versus tissue Doppler method which is angle and load dependent (Smiseth *et al.,* 2016).

CONCLUSION

SAM and its consequences of heart remodeling are considered the cornerstone of target end organ damage; it is accompanied by RVGLS impairment with combined systolic and diastolic RV dysfunction. RV longitudinal strain is "superior to more conventional functional parameters of RV systolic function."

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