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Assessment of Left Ventricular Remodeling Index in Hypertensive Patients Using Two- and Three-Dimensional Transthoracic Echocardiography

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ABSTRACT

Background: Hypertensive heart disease (HHD) and coronary artery disease (CAD) generally develop left ventricular remodeling. Therefore, it is of great importance for how to assess HHD and CAD's left ventricular remodeling which can influence vital diagnosis, therapeutic decisions and prognosis. **Aim of the Work:** to assess left ventricular remodeling index in HTN patients compared to normal patients using 2D and 3D transthoracic echocardiography. **Patients and Methods:** This study included 120 subjects at Cardiology Department, Faculty of Medicine, Al-Azhar University during the period from October 2018 to June 2019. They were divided into two groups: Group A (Patient group): which included (100) hypertensive patient. Group B (Control group): which included (20) age and sex matched apparently healthy individuals. **Results:** There were no significant differences in age and sex inter-group. LVRI detected by RT3DE and 2DE showed significant differences inter-group (1.72±0.04 vs 1.94±0.07, 1.73±0.04 vs 2.17±0.05); and significant differences in patient (1.94±0.07 vs 2.17±0.05), but no significant differences in control group (1.72±0.04 vs 1.73±0.04). Correlation analysis indicated that there was a good positive correlation between LVRI detected by RT3DE and 2DE in control and patient groups (r=0.91, 0.79, all P<0.001).
Conclusion: LVRI derived from RT3DE can provide more superiority to LVRI derived from 2DE as an index for evaluating left ventricular remodelling.
Keywords: Left Ventricular Remodeling Index, Hypertension, Two- and Three-dimensional Transthoracic echocardiography.

INTRODUCTION

Hypertension is one of the major risk factors for coronary heart disease (CHD), myocardial infarction (MI), cerebrovascular accidents (CVA), chronic renal failure (CRF), and congestive heart failure (CHF). Essential hypertension is defined as an increase in BP ([BP] >140/90 mm Hg) of unknown cause that increases the risk for cardiovascular (CV) diseases such as cerebral, cardiac, large artery, and renal events. However, subclinical vascular target organ damage (TOD) occurs very early in the course of hypertension and can be identified with noninvasive testing. These subtle CV findings include left ventricular hypertrophy (LVH), diastolic dysfunction, microalbuminuria, abnormal vascular compliance, and abnormal cognitive dysfunction or vascular dementia [(1)].

As well known, hypertensive heart disease (HHD) generally develops left ventricular remodeling. Therefore, it is of great importance for how to assess HHD's left ventricular remodeling which can influence vital diagnosis, therapeutic decisions and prognosis [(2)].

Echocardiography, as a technique of assessment of left ventricular remodeling, has noninvasive, safe, convenient and repeatable advantages over other methods [(3)].

Recent advances in capability of new combination of ultrasound system, computer processing and commercial software, RT3DE resolved many of the limitations associated with the evaluation of left ventricular volume from 2DE images and significantly improved the accuracy of these measurements, and provided fast, accurate and available assessment of left ventricular volume, left ventricular mass without geometric assumptions, which resulted in higher levels of agreement and reproducibility with the CMR reference values [(4)].

AIM OF THE STUDY

The aim of this study is to assess left ventricular remodeling index in HTN patients compared to normal patients using 2D and 3D transthoracic echocardiography.

PATIENTS AND METHODS

This study included 120 subjects at Cardiology Department, Faculty of Medicine, Al-Azhar University during the period from October 2018 to June 2019. They were divided into two groups:

Group A (Patient group): which included (100) hypertensive patient.

Group B (Control group): which included (20) age and sex matched apparently healthy individuals.

Inclusion criteria:

Hypertensive patients diagnosed according to the hypertension diagnostic standard and left ventricular thickening [inter-ventricular septal thickness >11 mm] measured by two-dimensional echocardiography [(5)].

Exclusion criteria:

Serious arrhythmia, poor echocardiographic images, patients with cardiac intervention (PCI or CABG), patients with congenital heart disease, patients with conduction abnormalities, pacemaker and bundle branch block, patients with valvular disease, ischemic heart disease, congestive heart failure, EF < 50%, DM were

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excluded from the study.

Ethical approval and written informed consent:

An approval of the study was obtained from Al-Azhar University academic and ethical committee. Every patient signed an informed written consent for acceptance of the operation.

Methods

The patients were subjected to the following:

Careful history taking: especially: age, sex, HTN, DM, Dyslipidemia. IHD, previous CABG or PCI, previous cerebrovascular stroke or peripheral vascular disease, general and local examination, resting surface 12 ECG leads, resting standard 12-leads electrocardiogram was recorded for analysis of rate, rhythm, BBB and chamber enlargement and ECG criteria of ischemic heart disease, two dimensional transthoracic echocardiography, a 2D (TTE) was performed to all patients, the standard views were obtained and the following parameters were assessed: LV internal dimensions and wall thickness by M-mode, LV end-diastolic and end-systolic volumes, LV EF by Biplane Simpson's method, LV mass (LV mass = 0.8[1.04 (STd + LVIDd + PWTd), - LVIDd] + 0.6 g), LV mass index (LV mass / BSA), LV remodeling index (left ventricular mass /EDV), three-dimensional echocardiograph, apical four chamber view over 3 consecutive cardiac cycles, left ventricular end-diastolic volume (EDV) and left ventricular end-diastolic epicardial volume (EDVepi) were automatically obtained, then left ventricular mass [1.05(EDVepi-EDV)], LVRI (left ventricular mass/ EDV) were calculated.

Analysis of the data:

Definition of normal LVRI, detection of changing in LVRI according to degrees of HTN and correlation between LVRI by (2D-TTE and 3D-TTE) in normal and HTN patients.

Statistical analysis:

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- Independent-samples t-test of significance was used when comparing between two means.
- Chi-square (x^2) test of significance was used in order to compare proportions between two qualitative parameters.
- The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value was considered significant as the following:
- Probability (P-value)
- P-value <0.05 was considered significant.
- P-value <0.001 was considered as highly significant.
- P-value >0.05 was considered insignificant.

RESULTS

Table (1): Comparison between patients and control according to demographic data

Demographic data	Patient *(n=100)*	Control *(n=20)*	P-value
Age (years)			
Mean ±SD	38.08±7.16	36.35±9.37	>0.05
Range	30-60	23-54	
Sex			
Female	46 (46%)	12 (60%)	>0.05
Male	54 (54%)	8 (40%)	
BMI [wt/(ht)^2]			
Mean ±SD	23.05±3.25	22.10±2.34	>0.05
Range	18-31	18-25	

There was no statistically significant difference between group A and group B as regard age, sex, and BMI.

A) Comparison between patients and control according to 2D echo data.

Table (2): Comparison between patients and control according to echo data at 2D.

ECHO 2D	Patient *(n=100)*	Control *(n=20)*	P-value
Aortic Dimensions			
Mean±SD	3.10±0.23	3.15±0.26	>0.05
Range	2.3-3.5	2.7-3.5	
Left atrial diameter			
Mean±SD	3.72±2.77	3.48±0.24	>0.05
Range	3-31	3-3.8	
Interventricular septum dimension			
Mean±SD	1.26±0.07	0.88±0.07	<0.001
Range	1.15-1.39	0.74-0.97	**
Posterior wall dimension			
Mean±SD	1.22±0.04	0.85±0.05	<0.001
Range	1.1-1.37	0.75-0.91	**
LV end-diastolic dimension			
Mean±SD	4.77±0.48	4.73±0.30	>0.05
Range	3.51-5.67	4.15-5.15	
LV end-systolic dimension			
Mean±SD	3.66±3.96	3.17±0.25	>0.05
Range	2.13-32.8	2.63-3.51	
LV ejection fraction			
Mean±SD	63.19±2.61	62.25±2.86	>0.05
Range	56-69	58-67	
LV end-diastolic volume			
Mean±SD	105.57±15.36	78.95±8.00	<0.001
Range	68-138	63-95	**
Left ventricle mass			
Mean±SD	228.96±34.13	136.96±16.95	<0.001
Range	147.04-310.92	104.20-171.77	**
LV remodeling index			
Mean±SD	2.17±0.05	1.73±0.04	<0.001
Range	2.09-2.25	1.67-1.79	**

This table shows statistically significant difference

between groups according to interventricular septum dimension, posterior wall dimension, LV end-diastolic volume, left ventricle mass and LV remodeling index.

B) Comparison between patients and control according to echo data at 3D.

This table shows statistically significant difference between groups according to LV end-diastolic volume, left ventricle mass and LV remodeling index.

Table (3): Comparison between patients and control according to 3D echo data.

ECHO 3D	Patient *(n=100)*	Control *(n=20)*	P-value
LV end-diastolic volume			
Mean± SD	111.20±16.52	80.52±8.08	<0.001**
Range	76.72-145.62	63.16-98.07	
Left ventricle mass			
Mean± SD	215.80± 31.68	138.74± 16.33	<0.001**
Range	146.54-285.98	104.85-174.58	
LV remodeling index			
Mean± SD	1.94±0.07	1.72±0.04	<0.001**
Range	1.81-2.07	1.66-1.78	

C) Comparison between Echo 2D and 3D according to left ventricle mass (g) in each group.

Table (4): Comparison between Echo 2D and 3D according to left ventricle mass (g) in each group.

Left ventricle mass (g)	Patient *(n=100)*	Control *(n=20)*
Echo 2D		
Mean±SD	228.96±34.13	136.96±16.95
Range	147.04-310.92	104.20-171.77
Echo 3D		
Mean±SD	215.80±31.68	138.74±16.33
Range	146.54-285.98	104.85-174.58
p-value	<0.001**	>0.05

This table shows statistically significant difference between Echo 2D and 3D according to left ventricle mass in patients' group.

Comparison between 2D and 3D Echo according to LV remodeling index in each group.

Table (5): Comparison between 2D and 3D Echo according to LV remodeling index in each group

LV remodeling index (g/ml)	Patient *(n=100)*	Control *(n=20)*
ECHO 2D		
Mean±SD	2.17±0.05	1.73±0.04
Range	2.09-2.25	1.67-1.79
ECHO 3D		
Mean±SD	1.94±0.07	1.72±0.04
Range	1.81-2.07	1.66-1.78
p-value	<0.001**	>0.05

This table shows statistically significant difference between echo 2D and 3D according to LV remodeling index in patients' group.

D) Correlation between 2D and 3D echo according to LV remodeling index, using Pearson Correlation Coefficient in each group.

Table (6): Correlation between 2D and 3D echo according to LV remodeling index.

Echo Data		Patient	Control
LV remodeling index (g/ml)	*r-value*	0.798	0.916
	P-value	<0.001**	<0.001**

This table shows positive correlation and significant between 2D and 3D Echo according to LV remodeling index.

DISCUSSION

Hypertension induces a compensatory thickening of the ventricular wall in an attempt to normalize wall stress, which results in concentric LVH, which in turn decreases LV compliance and LV diastolic filling, causing heart failure. Diastolic dysfunction develops in hypertensive patients even in the absence of LVH. Impaired isovolumic relaxation leads to decreased velocity of early diastolic filling [(6)].

In HHD, left ventricular cardiomyocyte produced hypertrophy, hyperplasia and cardiomyocyte lengthening when a pressure load leaded to growth in cardiomyocyte thickness and a volume load produced cardiomyocyte lengthening. As a result, left ventricle developed concentric hypertrophy or eccentric hypertrophy, and left ventricular shape changed into ellipse or sphericity, which caused left ventricular mass increased more than left ventricular volume [(7)].

Left ventricular (LV) remodeling may be defined as a modification in shape, size, and function of the left ventricle due to physiological or pathological conditions. For example, an adaptation to increased hemodynamic overload induced by chronic and intensive exercise was extensively described and reported as ''athlete's heart''. In contrast, pathological changes can be seen in different primary and secondary disorders of the ventricles due to ischemic cardiomyopathy, hypertension, valvular heart disease, and hypertrophic and dilated cardiomyopathy. For many years, morphological and volumetric assessment of the left ventricle was based on 2D echocardiography. However, this approach has some limitations, principally due to the use of geometric assumptions for deriving volumetric parameters, a high interobserver variability and a probe positioning bias. The ideal imaging technique for the assessment of serial ventricular volumes should be widely available, accurate and reproducible. Real-time three-dimensional (3D) echocardiography can meet these criteria [(8)].

Echocardiography, as a technique of assessment of left ventricular remodeling, has noninvasive, safe, convenient and repeatable advantages over other methods. RT3DE is showing left ventricular cubic shape, mass, volume achieved by using a matrix array

probe and multi-directional beam steering, and is especially appealing because it can potentially allow nearly online quantification of left ventricular volume and mass without the need for tedious reconstruction [3].

In our study we found that no statistically significant difference between the two groups as regard age, sex and body mass index.

This study showed that there was statistically significant difference between patients and control according to interventricular septum dimension, posterior wall dimension, LV end-diastolic volume, left ventricle mass and LV remodeling index by 2D echocardiography. This was in agreement with Lang *et al.* [9].

In this study we found statistically significant difference between patients and control according to LV end-diastolic volume, left ventricle mass and LV remodeling index by RT3DE. This was in agreement with Lang *et al.* [9].

This study showed that there was no significant difference, and had good relationship between LVRI detected by RT3DE and 2DE in control group, which indicated that the two techniques of measurement of LVRI were feasible when left ventricular morphology was normal. In HHD patient develop concentric left ventricular hypertrophy and left ventricular shape changed into ellipse or sphericity and so we found statistically significant difference between patients and control according to left ventricle mass and LV remodeling index and correlation analysis indicated that there was a good positive correlation between LVRI detected by RT3DE and 2DE in control and patient groups.

This was in agreement with Chen *et al.* [7] who studied 60 selected subjects. In HHD group, there were 18 cases of hypertension diagnosed according to the hypertension diagnostic standard and left ventricular thickening [inter-ventricular septal thickness ≥11 mm measured by two-dimensional echocardiography containing (11 males and 7 females with mean age of 52.2±12.6 years), 9 cases of concentric hypertrophy and 9 cases of eccentric hypertrophy. In CAD group, there were 20 cases of CAD verified by coronary artery angiography without left ventricular thickening, containing (13 males and 7 females with mean age of 54.3±13.2 years). There were 5 cases of angina, 6 cases of acute myocardium infarction, 9 cases of old myocardium infarction (4 cases of aneurysm). In normal control (NC) group of 22 healthy volunteers, there were (14 males and 8 females with mean age of 48.4±11.2 years). The results showed that LVRI measurements detected by RT3DE and 2DE showed significant differences inter-groups ($P<0.01$). There was no significant difference in NC group ($P>0.05$), but significant difference in HHD and CAD intra-group ($P<0.05$). There was good positive correlations between LVRI detected by RT3DE and 2DE in NC and HHD groups ($r=0.69$, $P<0.01$; $r=0.68$, $P<0.01$), but no significant correlation in CAD group ($r=0.30$, $P>0.05$). It was concluded that LVRI derived from RT3DE as a new index for evaluating left ventricular remodeling can provide more superiority to LVRI derived from 2DE.

Avegliano *et al.*, [10] also found that three-dimensional echocardiography is an accurate method for the quantification of LVM in patients with different subtypes of HCM that is in better agreement with CMR reference values than M-mode measurements in a study included 48 patients containing (35 males and 13 females with mean age of 57.4 ± 13.7 years) with HCM who had a complete transthoracic examination and CMR performed within 7 days. LVM was calculated by M-mode and RT3DE and compared to CMR that served as gold standard. With these results: Left ventricular mass calculated by RT3DE was (195 ± 41 g) and (187 ±49 g) by CMR. The correlation between the two methods was moderate, with a Lin index of 0.63 and good linear correlation ($r = 0.63$, $P < 0.0001$). The correlation was high when RT3DE was of high or adequate image quality. The correlation between LVM by M-mode and CMR was poor.

Caiani *et al.* [11] who studied 21 patients (13 males and 8 females with mean age of 48 ± 16 years); seven patients with suspected coronary artery disease, seven with dilated cardiomyopathy, two after a myocardial infarction, three with aortic disease, one with a right atrial mass, and one with mitral valve regurgitation. They found that RT3DE measurement was feasible in 19 of 21 patients and resulted in higher correlation with MR ($r = 0.96$) than did 2DE ($r = 0.79$). RT3DE measurements also had a significantly smaller bias (22.1 g) and tighter limits of agreement (2SD = ¡23 g) with MR than did the 2DE values (bias (2SD) 234.9 (50) g). Additionally, interobserver variability of RT3DE (12.5%) was significantly lower than that of 2DE (24.1%). Conclusions: Direct three-dimensional model independent LV mass measurement from RT3DE images is feasible in the clinical setting and provides fast and accurate assessment of LV mass, superior to the two-dimensional analysis techniques.

Chang *et al.* [12] who studied 69 patients with hypertrophic cardiomyopathy (HCM) (58 males and 11 females with mean age of 58.2 ± 10.9 years) with adequate two-dimensional (2D) and three-dimensional echocardiographic image quality underwent cardiac magnetic resonance (CMR) imaging and echocardiography on the same day. Real-time three-dimensional echocardiographic images were acquired, and CMR-determined LV mass was considered the reference standard. Left ventricular mass was derived using the formula of the American Society of Echocardiography (M-mode mass), the 2D-based truncated ellipsoid method (2D mass), and the RT3DE technique (RT3DE mass).

Intraclass correlation analysis showed a close relationship between RT3DE and CMR LV mass ($r =$

0.86, P <.0001). However, LV mass by the M-mode or 2D technique showed a smaller intraclass correlation coefficient compared with CMR-determined mass (r = 0.48, P =.01, and r = 0.71, P <.001, respectively). Bland-Altman analysis showed reasonable limits of agreement between LV mass by RT3DE imaging and by CMR, with a smaller positive bias (19.5 g [9.1%]) compared with that by the M-mode and 2D methods (_35.1 g [_20.2%] and 30.6 g [17.6%], respectively). Conclusions: RT3DE measurement of LV mass using the single-beat capture technique is practical and more accurate than 2D or M-mode LV mass in patients with hypertrophic cardiomyopathy.

Jenkins *et al.* **(13)** studied 50 patients with previous infarction and varying degrees of LV function (44 males and 9 females with mean age of 61 ± 11 years) at baseline and after 1-year follow-up. Images were obtained during breath-hold and measurements of LV volumes and ejection fraction were made offline. Over follow-up, end-diastolic volume decreased from (192± 53 to 187 ± 60 ml) (P <0.01), end-systolic volume decreased from (104 ± 51 to 95 ± 53 ml) (P <0.01), and ejection fraction increased from (48 ± 12% to 51 ± 12%) (P <0.01). MRI showed that LV mass shrank from (183 ± 39 to 182 ± 37 g) (P <0.01). The correlation between change in RT3DE and change in MRI was greater than the correlations of 2DE with MRI for measurement of end-diastolic volume (r = 0.47 vs 0.02, P <0.01), end-systolic volume (r = 0.44 vs 0.17, P <0.01), and ejection fraction (r = 0.58 vs 0.03, P <0.01). The change in end diastolic volume between baseline and follow-up with RT3DE (-4 - 20, P <0.01) was similar to that with MRI but was unrecognized by 2DE (4 - 19, P 0.09). There was good test–retest and inter- and intra-observer correlation within RT3DE for volumes, ejection fraction, and mass and they concluded that if sequential measurement of LV volumes is used to guide management decisions, 3DE appears preferable to 2DE.

A total of 205 patients were studied in 2 protocols: (1) RT3DE and CMR imaging was performed on the same day in 55 subjects; (2) in an additional 150 subjects (117 males and 33 females with mean age of 60 ± 14 years), RT3DE, 2D, and M-mode images were acquired. In both protocols, RT3DE endocardial and epicardial surfaces were semi automatically identified at end diastole to calculate LVM. CMR, 2D, and M-mode–derived LVM were obtained using standard techniques. A significant correlation (r = 0.95) was noted between RT3DE and CMR-derived LVM with a small bias of -2 g. M-mode–derived LVM measurements (175-64 g) were significantly larger than RT3DE LVM (123 -39 g, bias: 52 g) with moderate correlation (r - 0.76). No significant differences in LVM were noted between 2D (125 - 42 g) and RT3DE values (bias: 1.2 g) with good correlation (r - 0.91, P -0.001). However, the best correlation was noted between RT3DE and RT3DE-guided biplane LVM values (r - 0.95, P -0.001, bias: -4.6 g). Intra observer, interobserver variability, and test–retest variability of the RT3DE measurements were 9%, 12%, and 6%, respectively. Conclusion: RT3DE imaging using the 3D surface detection algorithm allows accurate and reproducible measurements of LVM. RT3DE-guided biplane technique can be used as an accurate time-saving alternative in clinical practice.

Yap *et al.*, **(14)** who studied 18 adult patients with congenital aortic stenosis, LV mass was measured using CMR and echocardiography (M-mode, two-dimensional echocardiography (2DE), and RT3DE). RT3DE data were analyzed using a biplane and multiplane method. No geometric assumptions were necessary using the multiplane RT3DE method. With regard to biplane or multiplane RT3DE, no tendency of over- or underestimation of LV mass was observed. Pearson's correlation coefficients for RT3DE versus CMR were 0.84 and 0.90 for the biplane and multiplane method, respectively. In addition, the accuracy of both RT3DE methods were comparable (Fisher's R-to-Z transformation: Z ¼ 0.69, P ¼ NS). Finally, off-line analysis using biplane RT3DE was significantly faster than multiplane RT3DE (3.8+1.2 vs. 7.8+1.7 minutes, P, 0.001).

CONCLUSIONS

LVRI derived from RT3DE can provide more superiority to LVRI derived from 2DE as an index for evaluating left ventricular remodelling.

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