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Value of 3D Speckle Tracking Echocardiography in Assessment of Left Ventricular Systolic Dysfunction in Hypertensive Patients

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ABSTRACT

Background: Hypertension is the most prevalent cardiovascular (CV) disorder, affecting 20–50% of the adult population in developed countries.

Objectives: The aim of this study is to test the capability of real-time three-dimensional speckle tracking echocardiography (RT3D STE) in characterizing early abnormalities of left ventricular LV systolic dysfunction in hypertensive patients with normal LV systolic function by standard 2D echocardiography.

Subjects & Methods: The study population included 150 consecutive hypertensive patients without complication and another age and sex matches 50 healthy controls. ECG, 2D and 4D echocardiography were performed for all cases.

Results: There was evidence of ECG voltage criteria of LVH in about 72% of hypertensive patients which absent in healthy controls. By comparing both group there were no statistically significant difference regarding EF%, AO, ESD, EDD, EDV.ESV, while there were statistically higher significant value in the patients group regarding RWT, LVPWD, IVSD and LV mass with (P<0.001) compared to controls where there were low statistically significant higher value in the patients group regarding LA dimension and volume (P<0.05).

Conclusion: 3D strain is an applicable technique; it can detect subtle or substantial changes of LV even with normal ejection fraction. The left ventricular strains (GAS, GLS and GRS) correlate negatively **Keywords:** hypertension, left ventricular systolic dysfunction, ECG, echocardiography

INTRODUCTION

Hypertension is the most prevalent cardiovascular (CV) disorder, affecting 20–50% of the adult population in developed countries. The prevalence of hypertension increases with age, rising steeply after the age of 50, and affecting more than 50% of this population [1].

The overall prevalence of hypertension in adults is around 30 - 45%. This high prevalence of hypertension is consistent across the world, irrespective of income status, i.e. in lower, middle, and higher income countries. Hypertension becomes progressively more common with advancing age, with a prevalence of >60% in people aged >60 years [2].

An innovative evaluation of left ventricular function has recently become available by 2D speckle tracking echocardiography (STE), a non-Doppler technique that allows to quantify myocardial deformation in the different spatial direction [3]. 3D Strain has the potential to become the reference method to assess myocardial function and detect early, subclinical myocardial involvement in many heart diseases [4]. 3D Strain derives several parameters, including longitudinal, circumferential, radial strain and global area strain [5].

AIM OF THE WORK

The aim of this study is to test the capability of real-time three-dimensional speckle tracking echocardiography (RT3D STE) in characterizing early abnormalities of left ventricular LV systolic dysfunction in hypertensive patients with normal LV systolic function by standard 2D echocardiography.

SUBJECTS AND METHODS

The study population included 150 patients with uncomplicated arterial hypertension coming for follow-up and to receive their monthly medications at the outpatient's clinics of Al-Hussein University Hospital and Islamic Cardiac Center, Al-Azhar University, Cairo, Egypt between January 2018 and March 2019. Also, 50 healthy controls recruited from normal asymptomatic personnel of the University staff and workers with examinations and investigations were considered to participate in this study.

Patients diagnosed as hypertensive with blood pressure ≥140/90 and sinus rhythm, according to the latest ESC guidelines [6]:

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.

Exclusion criteria:

- Significant arrhythmia.
- Decreased LVsystolic function.
- Significant valvular heart disease.
- Ischemic heart disease.
- Cardiomyopathies.
- Congenital heart disease.
- Pericardial disease.
- Poor Echogenicity
- Inability to give informed consent.

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Technical Design

All patients included in the study were subjected to the following:

- Thorough history taking.
- Complete clinical examination.
- Full general examination including cardiological, chest, and abdominal examination.

BP measuring: Blood pressure was measured according to the recommendation of European Society of Cardiology:

- Stop talking during the procedure.
- Avoid drinking coffee or smoking within 30 min of BP measurements.
- The patient does not need to use the toilet to be relaxed and comfortable during BP measurements.

Myocardial Performance Index using TDI.

Resting 12 lead ECG:

Resting standard 12-leads surface electrocardiogram will be recorded for analysis of rate, rhythm, BBB and chamber enlargement with special attention to the ECG voltage criteria of LVH According to Sokolow-Lyon voltage criteria; SV1 + RV5 or RV6 ≥ 3.5 mV (35 mm) or R aVL ≥ 1.1 mV (11 mm) [7].

2D Echocardiographic study

Standard echo-Doppler examinations were performed using a 2.5 multi-frequency 1.7- 4 MHz transducer (GE Vivid 95 Ultrasound Machine).

3D Echocardiography

It was performed by using a 4D volumetric transducer of a Vivid E95 ultrasound machine (GE Healthcare) available in Islamic Cardiac Center- Al-Azhar University, Cairo-Egypt.

3D strain is a post-processing tool that tracks speckles in a 3D image from frame to frame in any of the three dimensions over time. By this software, the borders defined in the LV mass stage are propagated to end-systole, using the conservation of mass as a restriction, and used to define a region of interest (ROI) encompassing the LV myocardial wall. All areas inside the ROI (i.e. from the endocardium to the epicardium) are tracked. The quality of each match is automatically calculated and detected outliers are removed before obtaining weighted spatial averaging of the results. From the tracking results regional and global directional strains (longitudinal, circumferential, and radial) as well as the area strain can be generated and presented as strain curves and a color-coded 17-segment bull‘s eye plot [8].

Strain is defined as the deformation of an object, normalized to its original shape. It is the peak value that obtained at or before aortic valve closure, Curves of longitudinal strain, circumferential strain, and area strain are negative (sign —), whereas curves of radial strain are positive (sign +).

By using the Auto LVQ software, regional longitudinal, circumferential, and radial strain as well as area strain are generated and presented in both (regional and average) strain curves and color-coded 17-segment bull‘s eye plot. Color lines refer to regional strain; white dotted line is global (average) strain plot [8].

Data Analysis

Data were presented as mean ± standard deviation for quantitative variables & number and percentage for qualitative variables. Data were coded, entered and analyzed by SPSS computer package (version 20). Categorical data were compared using chi-square and calculated. Correlation coefficient (r) test was used. The significance level was considered at $P<0.05$.

Receiver operating characteristic (ROC curve) analysis was used to find out the overall predictivity of parameter in and to find out the best cut-off value with detection of sensitivity and specificity at this cut-off value.

The confidence interval was set to 95% and the margin of error accepted was set to 5%.

RESULTS
Data were collected, statistically analysed and tabulated as the following.

Table (1): Comparison between the two groups regarding demographic data& risk factors

Baseline	Cases (n=150)	Control (n=50)	$t/\chi^{2\#}$	p-value
Age (years) • Range • Mean ±SD	28 – 60 43.75 ± 7.24	28 – 60 42.64 ± 6.89	0.908	0.342
Sex • Male • Female	102 (68%) 48 (32%)	31 (62%) 19 (38%)	0.606	0.436
Weight [kg]	91.10 ± 11.21	76.41 ± 6.02	78.160	<0.001**
height [cm]	174.91 ± 5.68	175.41 ± 5.34	0.303	0.583
BMI [wt/(ht)^2]	29.70 ± 2.60	24.82 ± 1.39	160.404	<0.001**
HR (beat/min)	76.42 ± 8.47	75.96 ± 8.04	0.113	0.737
SBP (mmHg)	140.87 ± 6.80	118.00 ± 7.00	418.034	<0.001**
DBP (mmHg)	91.57 ± 7.44	70.00 ± 7.28	318.097	<0.001**
MBP (mmHg)	108.00 ± 6.51	86.00 ± 5.91	447.968	<0.001**
Smoking	72 (48%)	21 (42%)	0.543	0.461

This table shows statistically significant difference between the two groups according to SBP and DBP, MBP, Weight and BMI, other data were statistically insignificant.

Table (2): Comparison between the two groups in ECG voltage criteria of LVH

LVH Criteria	Cases (n=150)	Control (n=50)	χ^2	p-value
No	78 (52%)	50 (100%)	49.275	<0.001**
Yes	72 (48%)	0 (0%)		

There was evidence of ECG voltage criteria of LVH in about 52% from hypertensive patients (cases) which absent in healthy control group.

Table (3): Comparison between cases and control groups according to conventional M=Mode Echocardiographic criteria

2D Echo	Cases (n=150)	Control (n=50)	t-test	p-value
LVEDD(cm)	4.86 ± 0.45	4.75 ± 0.62	1.904	0.169
LVESD(cm)	2.85 ± 0.44	2.94 ± 0.25	1.968	0.162
RWT	0.46 ± 0.05	0.33 ± 0.05	238.401	<0.001**
LV mass index (g/m^2)	116.27 ± 15.36	98.54 ± 10.41	57.650	<0.001**
LVEDV (ml)	112.12 ± 23.27	107.49 ± 37.62	1.061	0.304
LVESV (ml)	32.04 ± 11.71	33.71 ± 6.46	0.922	0.338
LVEF%	69.84 ± 13.22	65.89 ± 11.14	3.601	0.059
LVPWD(cm)	1.11 ± 0.13	0.78 ± 0.09	275.450	<0.001**
IVSD(cm)	1.33 ± 0.13	0.80 ± 0.08	729.321	<0.001**
LAD(cm)	3.54 ± 0.45	3.07 ± 0.36	46.656	<0.001**
LAV(ml)	37.32 ± 4.58	30.92 ± 2.38	89.554	<0.001**
AOD (cm)	2.94 ± 0.36	3.00 ± 0.39	1.051	0.306

This table shows statistically significant increase mean of cases group compared to control group according to RWT, LV mass index, LVPWD, IVSD, LAD and LAV.
By comparing both groups there were no statistically significant difference as regarding LVEDD, LVESD, LVEDV, LVESV, LVEF, EF%, AOD. While there were statistically significant higher value in Hypertensive group (cases) as regarding RWT, LV mass index, LVPWD, IVSD, LAD and LAV with (P-value<0.001).

Table (4): Comparison between cases and control according to Echo-Doppler criteria

Diastolic dysfunction	**Cases (n=150)**	**Control (n=50)**	**t-test**	**p-value**
Mitral E	81.90 ± 23.56	106.58 ± 9.18	52.062	<0.001**
mitral A	79.70 ± 10.12	80.07 ± 11.86	0.047	0.829
Mitral E/A ratio	1.05 ± 0.35	1.35 ± 0.18	34.489	<0.001**
Em	8.97 ± 2.74	13.55 ± 1.51	126.346	<0.001**
E/Em Ratio	9.33 ± 1.59	7.97 ± 1.12	31.452	<0.001**

The echo Doppler criteria of study population was listed in this table and shows that there were highly statistically significance with lower value in hypertensive group (cases) as regarding mean of Mitral E , Mitral E/A ratio and Em (P-value<0.001 and higher value in hypertensive group (cases) as regarding of E/Em ratio.(P-value<0.001) when compared with control group.in addition there was no significant statistical difference between two groups as regarding of Mitral A .

Table (5): Comparison between cases and control groups according to 3D global strain.

4D Global Strain	**Cases *(n=150)***	**Control *(n=50)***	**t-test**	**p-value**
GLS	-17.11 ± 1.33	-19.78 ± 1.49	142.312	<0.001**
GCS	-16.67 ± 1.85	-16.48 ± 1.30	0.468	0.495
GAS	-26.00 ± 2.07	-32.04 ± 1.65	351.823	<0.001**
GRS	45.01 ± 6.29	53.38 ± 2.75	83.058	<0.001**

GLS (global longitudinal strain), GCS (global circumferential strain), GRS (global radial strain), GAS (global area strain).

Table (6): Correlation between GLS with all parameters, using Pearson Correlation Coefficient in cases group

Parameters	**GLS**		**GCS**		**GAS**		**GRS**	
	r	**P**	**r**	**P**	**r**	**P**	**r**	**P**
SBP (mmHg)	0.403	<0.001	0.015	0.859	0.311	<0.001	-0.288	0.001
DBP (mmHg)	0.596	<0.001	-0.013	0.874	0.535	<0.001	-0.401	0.001
MBP(mmHg)	0.140	0.087	-0.098	0.235	0.313	<0.001	-0.260	0.001
BMI [wt/(ht)^2]	-0.156	0.056	-0.032	0.697	0.275	<0.001	-0.153	0.062
RWT	0.314	<0.001	-0.102	0.215	0.230	0.005	-0.207	0.011
LV mass index	0.492	<0.001	-0.063	0.440	0.297	<0.001	-0.207	0.011
LVPWD(cm)	0.188	0.021	-0.094	0.250	0.166	0.042	-0.118	0.149
IVSD(cm)	0.122	0.137	0.029	0.722	0.204	0.012	-0.107	0.192
LAD (cm)	0.165	0.044	0.008	0.923	0.381	<0.001	-0.298	0.001
Mitral E	0.018	0.826	-0.129	0.115	0.514	<0.001	-0.325	0.001
Mitral E/A ratio	0.010	0.901	-0.102	0.214	0.466	<0.001	-0.277	0.001
Em	0.469	<0.001	0.001	0.987	0.285	<0.001	-0.297	0.001
E/Em Ratio	0.334	<0.001	-0.031	0.710	0.394	<0.001	-0.216	0.008

Significant negative correlation between GLS with SBP, DPB, RWT, LV mass index, Em and E/Em ratio (P-value < 0.001) and MBP, BMI, LVPWD and LAD.
No statistically significant correlation between GCS with all parameters.
Negative correlation and significant between GAS with all parameters.
Negative correlation and significant between GRS with SBP, DBP, MBP, BMI, RWT, LV mass, LAD, Mitral E,Mitral E/Em ratio, Em and E/Em Ratio.

Table (7) Receiver operating characteristic (ROC) curve between hypertensive group and control group as regard global strain

4D global strain	Cut-off	Sensitivity	Specificity	PPV	NPV	Accuracy
GAS	≤-30	93.3	90	96.6	81.8	92.5
GLS	≤-19	83.3	78	91.9	60.9	82
GRS	>51	78	66	87.4	50.8	75.5
GCS	≤-17	68.7	56	82.4	37.3	65.5

The cut off differentiate normal from hypertensive group as regarding
-GAS is -30 with sensitivity 93.3, specificity 90.0 and accuracy 93.5
-GLS is -19 with sensitivity 83.3, specificity 78.0 and accuracy 82.0
-GRS is 51 with sensitivity 87.0, specificity 66.0 and accuracy 75.5
-GCS is -19 with sensitivity 68.0, specificity 66.0 and accuracy 65.5

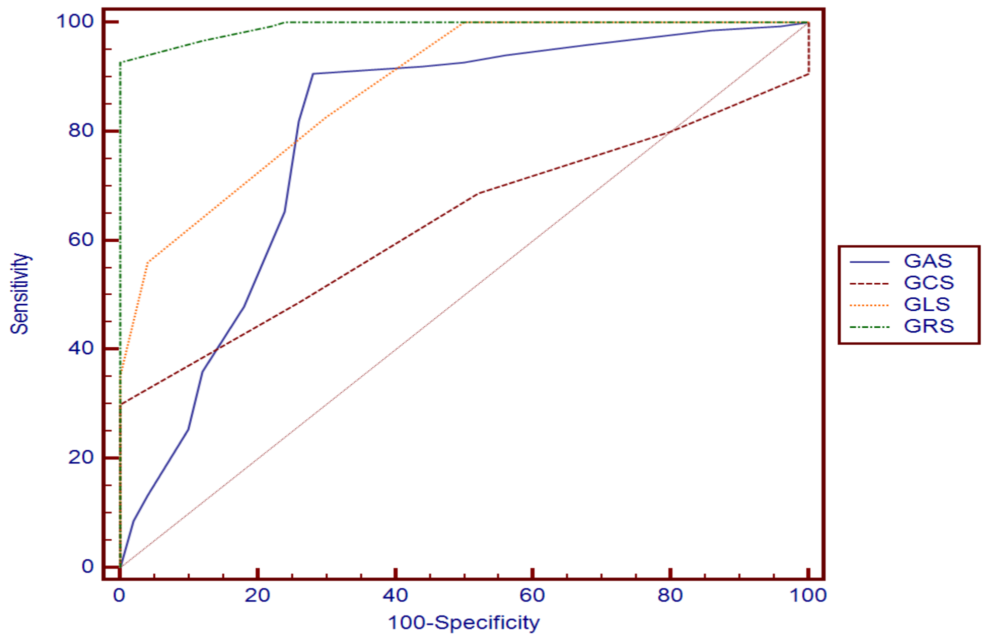

Fig. (1) Receiver operating characteristic (ROC) curves of GAS, GCS, GLS and GRS

DISCUSSION

In the present study there were no significant statistical difference between both groups regarding demographic data (sex & age), smoking, height and HR. While there were highly statistically significant higher values in group 1 (cases) as regarding weight, BMI, SBP, DBP, MBP, (P<0.001) when compared with control group. ECG voltage criteria of LVH were present in 48% of hypertensive patients. The results were compatible with those of **Kansal *et al.*** (9) who documented that the current electrocardiographic criteria for the diagnosis of LVH fail to diagnose 30-40% cases of increased LVM.

Devereux *et al.* (10) found that in validation studies, the sensitivity of echocardiography to detect LVH has been reasonably high (85-100%), whereas that of ECG has ranged from as high as 50% in severely diseased populations to as low as 6-17% in recent studies by Cornell and Framingham (11).

In the present study there were non-significant difference between both groups regarding LVESV, LVEDV and EF% but IVSD and LVPWT were significantly higher in hypertensive group when compared with control group. Meanwhile the present study clarified that LV mass and RWT in hypertensive patients were significantly exceeded that of control group. We have demonstrated that hypertensive patients in the present work have LV hypertrophy while control group have normal LV geometry.

Regarding to the RWT (Relative Wall Thickness) category of study population there were an evidence of increased RWT in 74.7% of the hypertensive patients which is absent in healthy control group.

Regarding the LVMI grade of study population there were an evidence of increased LVMI in 56% of hypertensive patients which is absent in healthy control group.

Regarding the LVH grade of study population there were an evidence of LVH in hypertensive group which is absent in healthy control group. The Hypertensive group subdivided according to RWT and LVMI into 4 grades 9.3% were normal, 36.7 were concentric remodeling, 35.3% were concentric hypertrophy and 18.7% were eccentric hypertrophy.

There was concordance between our study and the study done by **Galderisi *et al.*** (12) who found that the hypertensive patients had higher LV mass and RWT when compared with healthy control group and no difference between both groups as regard LVESV, LVEDV and LVEF%.

Przewlocka-Kosmala *et al.* (13) stated that LVMI, interventricular septum thickness (IVS) and LV posterior wall thickness (PWT) were significantly higher in hypertensive patients with LVH than in the controls. These findings agreed with the present study.

Możdżan *et al.* (14) found that hypertensive patients compared with controls presented larger dimensions of both ventricles, thicker left ventricular walls, and higher LV mass and mass index. These findings occurred independently of sex, age, BMI and diurnal BP levels, which coincided with the present study. The difference in LV dimensions (i.e. LVEDD and LVESD) may be attributed to long standing hypertension or the large number of patients who have eccentric LV geometry in Monika study.

As regard left atrium (LA) dimension and volume, the present study showed that LA dimension and volume in hypertensive patients were significantly larger than control group. The study results are compatible with those of **Tedesco *et al.*** (15) who found that left atrial enlargement was present in 36% of patients with and in 21% of patients without LVH.

This study is compatible with the study of **Xian-Chu *et al.*** [16] who studied two thousand patients with hypertension and 500 normotensive ones. There were significant differences in LA dimension between the two groups with higher value in hypertensive patients.

Our study showed that there were highly statistically significant lower value as regarding transmitral E/A velocity ratio and velocity of mitral annulus (Em) (P<0.001) and higher value as regarding of tissue Doppler E/Em ratio.(P<0.001) in hypertensive group when compared with control group. Our results are compatible with study done by **Galderisi *et al.*** [12] who found that E/A ratio was lower in hypertensive patients and tissue Doppler E/Em ratio was higher in hypertensive patients when compared with control group.

The present study showed that GLS, GRS and GAS of LV were lower (to the positive side) in hypertensive patients when were compared with control group while global circumferential strain was lower in hypertensive patients but not reaching statistical significance.

It has been found from the present study that there were negative significant correlations of:

- BMI with GLS, GRS and GAS.
- SBP, DBP, MBP with GLS, GRS and GAS.
- RWT with GLS, GRS and GAS.
- LVM with GLS, GRS and GAS.
- E/Em with GLS and GAS.

Of all available strain parameter, left ventricular global longitudinal strain certainly had the major importance and the largest clinical utility. Recent study done by **Saito *et al.***[17] showed that LV global longitudinal strain represent a good predictor of cardiovascular and total morbidity and mortality in hypertensive population as the major adverse cardiac events were associated with higher prevalence of concentric hypertrophy and impaired GLS.

Our results were concordant with study done by **Kim *et al.*** [18] who assess LV function with layer-specific strain in patients with hypertension by 2D echocardiography and showed that longitudinal strain of hypertensive patients were significantly lower than longitudinal strain of normotensive controls in all three layers of left ventricle.

The decrease of left ventricular longitudinal strain despite normal ejection fraction in hypertensive patients may be explained by increased serum tissue inhibitor of metalloproteinase-1 (TIMP-1), which suggests that the change in collagen turnover and the myocardial fibrotic process which was present and correlated with impaired longitudinal strain (ε) and increased LV torsion in patients who are hypertensive with normal ejection fraction, may affect the early contractile dysfunction of LV which was proven by **Kang *et al.*** [19].

The LV myocardial layer consists of a characteristic myocardial fiber orientation in which the longitudinal fibers in the subendocardial layer gradually change to a circumferential direction in the mid-wall layer and revert to longitudinal in the sub-epicardial layer [20].

A study done by **Ishizu *et al.*** [21] on salt sensitive rats, a well-validated model of heart failure with preserved EF attributable to hypertension versus a control group. They found that longitudinal wall deformation was affected mainly by the subendocardial fibrosis and collagen-subtype alternation present in the subendocardial layer.

Furthermore, radial strain was affected by the myocardial to epicardial layer fibrosis that extended from the sub endocardium. Therefore, trans-murality of collagen deposition might be associated with longitudinal strain early, and with radial strain late, in the disease course. The impairment in LV contractility has been thought to occur mainly because of cardiac myocyte injury, and a definitive cause–effect relation between fibrosis and systolic function has not been established. Recently, several reports have assumed that abnormalities in the extracellular matrix impair organ contractile function even if myocyte contractility is preserved [22].

In several clinical investigations, longitudinal systolic dysfunction was associated with adverse clinical outcome [23].

Regarding impairment of 3D STE (3 Dimensional Speckle tracking Echocardiography) in hypertensive patients with normal EF(Ejection fraction), a recent study has been published in nature stated that: LV function assessed by SR was reduced in HTN with concentric and eccentric hypertrophy compared with normotensive controls, despite no reduction in LV EF and SW (Stroke work). Furthermore, LV relaxation assessed by radial SR was reduced even in hypertensive patients with normal geometry. Endocardial function was decreased in association with HTN-induced changes in LV geometry. The assessment of LV SR by novel 3D-STE method may be useful to detect early and subclinical LV layer dysfunction in patients with HTN [17].

In the study by **Galderisi *et al.*** [12] there was evidence of reduction of GAS in hypertensive patients which were compatible with finding of the present work. GAS was corresponds to the percentage change of the myocardium from its original dimensions [8].

GAS correlates very well with both EF and wall motion score index, area strain was introduced as a novel automatic index for quantitative echocardiographic evaluation of global and regional LV function. During LV contraction, the endocardial surface area decreases in size because of longitudinal and circumferential shortening, and radial myocardial thickening. Area strain reflects this change in the endocardial surface area and quantifies it by giving the percentage change in area from its original dimensions [24].

CONCLUSION

3D strain is an applicable technique; it can detect subtle or substantial changes of LV even with normal ejection fraction. The left ventricular strains (GAS, GLS and GRS) correlate negatively with BMI, LVMI, RWT, E/Em ratio.

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