

Evaluation of Left ventricular systolic function by Myocardial Deformation Imaging in Hypertensive patients with Preserved Left Ventricular Ejection Fraction

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Abstract

Background and Aims: Hypertension being one of the commonest non communicable diseases is major risk factor leading to premature death. With development of, the left ventricular strain imaging technique by echocardiography the consequences of hypertension may be identified and intervene earlier. The aim of study was to show abnormalities in cardiac function in the form of left ventricular strain imaging in hypertensive patients with preserved Ejection fraction.

Methods: This was a cross-sectional, comparative and observational study done in Shahid Gangalal National Heart Centre and National Academy of Medical Sciences, Bir Hospital Kathmandu which included hypertensive patients with baseline examination including a medical history, clinical examination and a standardized trans thoracic echocardiography and strain imaging examination and the findings were compared among age and sex frequency matched 82 healthy adults in 1 : 2 ratio. The independent paired t test was used for the comparative statistical analysis.

Results: We enrolled 240 patients in this study, 158 were hypertensive (mean age 48.5 ±6.1 years with 50.6 % female) and 82 healthy control (mean age 45.62 ±6.3 years with 51.2% female). There was no significant difference in conventional echocardiographic parameters between two groups except for left ventricular mass index and relative wall thickness that was highest in hypertensive group (p value of <0.001). The hypertensive population has lower mean global longitudinal strain (GLS) value of -18.6% ± 2.06 SD compared to the healthy control population with mean of -19.5% ± 1.1 SD (p value of <0.001).

Conclusion: Hypertensive patients with preserved left ventricular ejection fraction have subclinical left ventricular dysfunction revealed by GLS imaging technique.

Keywords: Global Longitudinal strain, Hypertensive patients, left ventricular ejection fraction

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Introduction

Hypertension is the commonest non communicable diseases which is major risk factor leading to premature death¹. Hypertension is defined as office SBP values ≥ 140 mmHg and/or diastolic BP (DBP) values ≥ 90 mmHg². Approximately 25% to 50% of affected individuals have evidence of left ventricular (LV) hypertrophy (LVH). Left ventricular hypertrophy in systemic hypertension is a risk factor for asymptomatic left ventricular (LV) dysfunction and congestive heart failure³. While conventional echocardiography can detect changes in LV diastolic dysfunction associated with LVH, global LV systolic function often remains preserved until late in the course of the disease, which can be missed in the early stages⁴. Therefore, subclinical changes in LV systolic function can be identified by quantifying myocardial strain. Two-dimensional speckle tracking is a novel echocardiographic technique for analysis of LV strains⁵.

Strain and Strain Rate Imaging (Deformation analysis) is analysis of ventricular mechanics or shape during the cardiac cycle. Strain is defined as the normalized change in length between two points. Negative strain implies shortening of a segment (contraction) and positive strain lengthening of a segment (relaxation). As such, normal contraction is defined by negative longitudinal systolic strain⁶. GLS value less than -18% was considered abnormal for detecting LV systolic dysfunction and a value above -20% with a standard deviation of $\pm 2\%$, is normal⁷. Strain analysis may detect subclinical cardiac changes in hypertensive and thus identify asymptomatic at higher risk of developing adverse changes⁸. Though global ejection fraction and fractional shortening are normal in hypertensive, the results showed that speckle tracking is able to detect sub-clinical myocardial dysfunction in hypertensive patients⁹.

There are only few studies found around globe about GLS imaging. GLS imaging help to find early LV systolic dysfunction

in asymptomatic hypertensive patients². Hypertensive patients may have evidence of left ventricular hypertrophy which is a risk factor for asymptomatic left ventricular (LV) dysfunction and congestive heart failure³. Development of congestive heart failure in hypertensive patients is worst condition. Therefore, identification of these adverse changes by GLS imaging is very important step.

The objective of this study is to assess subclinical LV systolic dysfunction in patients with systemic hypertension with preserved LV ejection fraction by GLS imaging for early detection of LV systolic dysfunction and identify those at increased risk of cardiovascular diseases in our population.

Methods

This study was a hospital based, single center cross-sectional comparative, observational study conducted in cardiology department of Shahid Ganganal National Heart Centre and National Academy of Medical Sciences, Bir Hospital Kathmandu from December 2020 to May 2020 for 6 months. Informed written consent was taken from each of the selected patient prior to enrolment in study. Formal permission for the study was taken from the institutional review board of the National Academy of Medical Sciences, Bir Hospital. Furthermore, noninvasive cardiac test such as heart rate, blood pressure, and a standardized transthoracic echocardiography and strain imaging examination was a part of the study protocol. We included 158 hypertensive patients by sample size calculation based on overall prevalence of 15.3% patients having subclinical left ventricular systolic dysfunction as assessed by global longitudinal myocardial strain in hypertensive group¹⁰. Sample size calculation was based on following equation. To compare the findings, we also included age and sex frequency matched normotensive adult population.

The Sample size is calculated by the formula

$$n_0 = r / (1+r) \cdot (z_{a/2} + z_{b/2})^2 \cdot PQ / e^2$$

Where

$$z_a = 1.96 \text{ (at 95\% confidence level)}$$

$$z_b = 0.84 \text{ (at 80\% power of test)}$$

$$r \text{ (Ratio)} = 1/2$$

$$P = 15.3\% \text{ (0.153) prevalence of subclinical left ventricular systolic dysfunction as assessed by global longitudinal myocardial strain}$$

$$e = (0.05) \text{ 5\% of maximum tolerable error}$$

$$Q = 100 - P(1 - 0.153)$$

Study procedure: Baseline examination including a medical history, clinical examination including height, weight and body mass index were calculated. Furthermore, noninvasive cardiac test such as heart rate, blood pressure, and a standardized transthoracic echocardiography and strain imaging examination were studied. The study subjects comprise of selected patients that have fulfilled the inclusion criteria The inclusion criteria were adults age ≥ 18 years with systemic hypertension (defined as Systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg or Antihypertensive treatment with a documented history of hypertension) and have an echocardiography evidence of normal LV systolic function. The exclusion criteria were Patients with coronary artery disease, cardiomyopathy, valvular heart disease, arrhythmia and conditions that affect LA size and function. We also included control group in 1: 2 case ratio with total of 82 normotensive adults which were visitors and hospital staff with age and sex frequency matched group to compare our findings.

Details of echocardiography findings were noted. Transthoracic echocardiography was performed with a commercially available imaging system with PHILLIP Affiniti 50c Echocardiography machine using a 2.5 MHz phased array transducer. Cardiac dimension and cardiac function were measured according to the recommendations of the American Society of Echocardiography¹¹. Global longitudinal strain (GLS) was calculated by the mean

longitudinal strain of the six walls (basal, mid and apical segments) in apical view. The software automatically displayed tracing to include the entire myocardial width, and was later adjusted manually for optimal delineating. GLS value above -20% with a standard deviation of $\sim \pm 2\%$, is likely to be normal and less than -18% was considered abnormal for detecting LV systolic dysfunction as given by the American Society of Echocardiography¹². After 2 weeks on stored offline images of 25 random study population the intra-observer reproducibility was determined by an author's own analysis and inter-observer reproducibility was done by the analyses of two other echocardiographers for strain imaging.

Statistical analysis: All the data were entered into spreadsheet of Microsoft Excel and by using SPSS version 20 software, the statistical analysis was done. Dichotomous variable with normal distribution presented as mean \pm SD and categorical variables were analyzed as percentage. After processing of all available information, statistical analysis of their significance was done. Dichotomous variable was compared using Chi-Square test as appropriate and independent paired t test for means of continuous variable. Odds ratio was calculated to see association between variables. Coefficient of variation analysis were performed for intra- and inter-observer reproducibility of strain imaging. For the purpose of this study a 95% confidence interval was accepted and a p value < 0.05 was taken as significant.

Results

The study population consisted of 240 subjects, including 158 patients of systemic hypertension (48.5 ± 6 years, 78 male) and 80 age- and sex-matched healthy controls (45.6 ± 6.3 years, 40 male). Clinical and demographic data of patients with systemic hypertension and controls are listed in Table 1. There was a significant higher systolic and diastolic blood pressure in patients with systemic hypertension than the control group ($P < 0.001$).

Table 1: Demographic and Baseline characteristics of study population

	Control (82)	Hypertensive Group (158)	p-value
Age(years)			
≤ 40	17 (51.5%)	16 (48.5%)	0.096
41 – 50	48 (34%)	93 (66%)	
51 – 60	15 (25.9%)	43 (74.1%)	
61+	2 (25%)	6 (75%)	
Mean Age	45.62 \pm 6.3	48.57 \pm 6.19	
Sex			
F	42(34.4%)	80(65.6%)	0.931
M	40(33.9%)	78(66.1%)	
BMI			
Normal	23(32.9%)	47(67.1%)	0.762
over weight	26(32.1%)	55(67.90%)	
Obese	33(37.1%)	56(62.9%)	
Risk Factors			
Smoking	15 (23.8%)	48(76.2%)	0.044
DM	14(25.9%)	40(74.1%)	0.147
Dyslipidemia	6(18.2%)	27(81.8%)	0.037
Family H/o HTN	6(20.7%)	23(79.3%)	0.103
Alcohol	14(37.8%)	23(62.2%)	0.609

Conventional echocardiography: Conventional echocardiographic data of patients with systemic hypertension and controls are listed in Table 2, which revealed significantly higher Posterior wall thickness and Relative wall thickness in hypertensive patient (P< 0.001). Also, the Left ventricular mass index was significantly higher in the hypertensive group. There was no significant difference in the global LV ejection fraction (LVEF) between the two groups.

Table 2: Echocardiography parameters found in patients

	Control (82)		Hypertensive Group (158)		p-value
	Mean	SD	Mean	SD	
ECHO-LV mass (gm)	130.80	12.59	134.89	18.50	0.074
ECHO- LV Index (gm/m2)	76.53	6.45	79.28	9.16	0.016
ECHO-Septal Wall Thickness(cm)	0.83	0.11	0.88	0.16	0.009
ECHO-LVEDD(cm)	4.58	0.27	4.44	0.36	0.003
ECHO-PWT(cm)	0.82	0.12	0.88	0.17	0.005
ECHO-LViSD(cm)	2.68	0.24	2.57	0.28	0.003
ECHO-EDV(ml)	101.59	15.21	94.62	18.21	0.003
ECHO-ESV(ml)	28.38	5.97	25.88	6.56	0.004
ECHO-SV(ml)	72.05	13.93	68.11	15.70	0.057
ECHO-FS (%)	40.88	5.40	41.49	5.58	0.423
ECHO-EF (%)	71.28	6.04	72.10	6.28	0.329
ECHO-RWT	0.36	0.07	0.40	0.11	0.001

2D speckle tracking: In comparison with normal controls, GLS was significantly attenuated in patients with systemic hypertension (-19.5.75 ± 1.1 in the control group vs. -18.6 ± 2.06 in the hypertensive group) as shown in Table 3. We found that 54 of 158 patients (34.2%) in the hypertensive group had subclinical LV systolic dysfunction defined as GLS less negative than -18 %, but only 1 of 82 controls (1.2%) had subclinical LV dysfunction as listed in Table 4.

Table 3: Mean GLS between two groups.

	GLS			
	Number	Mean	Std. Deviation	p-value
Control Group	82	19.5451	1.10209	<0.001
Hypertensive Group	158	18.6392	2.06961	

Table 4: Comparison of GLS between two groups.

	GLS			
	Reduced GLS	Normal GLS	p-value	Odds(95%CI)
Control	1(1.2)	81(98.8)	<0.001	1
Hypertensive Group	54(34.2)	104(65.8)		42.06(5.70-310.54)

There was no significant difference between hypertensive patients with normal GLS and hypertensive patients with reduced GLS (subclinical LV systolic dysfunction) in terms of age and sex distribution or duration of hypertension. BMI was significantly higher among patients with reduced GLS than those with normal GLS (P <0.003) as listed in Table 5. Relative wall thickness (RWT), posterior wall thickness (PWT), left ventricular mass index (LVMI), and septal wall thickness (SWT) were statistically significant higher among hypertensive patients with reduced GLS than those with normal GLS. However fractional shortening (FS) and Global ejection fraction was normal in both groups as listed in Table 6.

Table 5: Risk Factors found in two GLS Groups

		GLS			
		Reduced GLS	Normal GLS	p-value	Odds (95%CI)
Age (years)	<= 40	4 (12.1)	29 (87.9)	0.129	0.28 (0.09-0.92)
	41 - 50	30(21.3)	111(78.7)		0.55 (0.28-1.10)
	51 - 60	19(32.8)	39(67.2)		1
	61+	2(25)	6 (75)		0.68 (0.13-3.71)
Sex	F	25 (20.5)	97 (79.5)	0.363	0.06 (0.01-0.26)
	M	30 (25.4)	88 (74.6)		1
DM	N	41(22)	145(78)	0.550	0.81 (0.40-1.63)
	Y	14(25.9)	40(74.1)		1
Dyslipidemia	N	44 (21.3)	163(78.7)	0.125	0.54 (0.24-1.20)
	Y	11(33.3)	22(66.7)		1
BMI	normal	6(8.6)	64(91.4)	0.003	1
	over weight	25(30.9)	56(69.1)		4.57 (1.74-11.98)
	Obese	24(27)	65(73)		4.64 (1.77-12.17)

Table 6: Echocardiography parameters found in two GLS Groups

	Reduced GLS (n=55)		Normal GLS (n=185)		p-value
	Mean	SD	Mean	SD	
ECHO-LV mass(gm)	144.55	19.68	130.20	14.34	<0.001
ECHO- LV Index(gm/m ²)	83.43	10.17	76.83	7.19	<0.001
ECHO-SWT(cm)	0.97	0.17	0.83	0.12	<0.001
ECHO-LVEDD(cm)	4.29	0.38	4.55	0.30	<0.001
ECHO-PWT(cm)	0.96	0.18	0.83	0.13	<0.001
ECHO-LViSD(cm)	2.51	0.34	2.64	0.24	0.002
ECHO-EDV (ml)	87.28	18.98	99.89	16.02	<0.001
ECHO-ESV (ml)	24.63	7.78	27.36	5.90	0.006
ECHO-SV (ml)	62.11	13.54	71.64	15.01	<0.001
ECHO-FS (%)	41.05	5.09	41.35	5.64	0.722
ECHO-EF (%)	71.79	5.91	71.83	6.30	0.970
ECHO-RWT	0.46	0.12	0.36	0.08	<0.001
BSA (m ²)	1.73	0.06	1.69	0.08	0.005

Intra-observer and inter-observer coefficients of variation were < 10% in strain imaging echocardiography.

Discussion

In systemic hypertension the development of left ventricular hypertrophy (LVH) is an established risk factor for the development of asymptomatic left ventricular (LV) dysfunction and congestive heart failure.³ while conventional echocardiography can detect changes in LV diastolic dysfunction, global LV systolic function often remains preserved until late, making subtle changes in LV contractile function difficult to interpret in the early stages. In hypertensive subjects with normal LVEF, GLS reduction is observed independent of LV hypertrophy and diastolic dysfunction and it confers elevated cardiovascular risk¹³.

The above study demonstrated that 2D speckle tracking is able to detect sub-clinical myocardial dysfunction in hypertensive patients with normal global ejection fraction.

In our study we found that, GLS was significantly reduced in patients with systemic hypertension compared with normal controls. We also found that 34.2% of hypertensive patients had subclinical systolic LV dysfunction defined as 2D derived GLS less negative than -18%. The findings are in concordance with the study done by Imbalzano et al, who showed that 2D-STE showed an impairment of systolic longitudinal strain in all hypertensive patients including those without LVH¹⁴. Hypertension and LVH are important risk factors for developing chronic congestive heart failure and the mortality risk is still significantly increased over control patients¹⁵.

The finding of LV systolic longitudinal contraction by 2D speckle tracking suggest new approach in myocardial function in hypertension. This will help to identify patients at high risk who would benefit from treatment. In our study, LVMI was higher in hypertensive patients with subclinical LV systolic dysfunction (reduced GLS) than hypertensive patients with normal GLS, however the finding was not statistically significant. This finding was similar to finding of a

study done by Saghir et al who revealed that hypertensive individuals with LVH had significantly decreased systolic longitudinal strain and strain rate values compared with control subjects¹⁶.

In our study, we found that hypertensive patients had higher BMI and higher LVMI than normal subjects. This finding was in consistent with the study done by Lavie et al who reported that HTN occurs in nearly 50% of obese patients and more so in class III obesity (35 < BMI < 40)¹⁷. However in our study we did not find any significant association of reduced GLS with cardiovascular risk and BMI. It was in contrast with the study finding of Schillaci et al who showed that there is a relationship between increased LV mass and cardiovascular risk in primary hypertension, even in the absence of hypertensive mediated organ damage¹⁸. Similarly the result of this study was in contrast with the study done by A.M. Ayoub et al, who reported that with regard to the effect of BMI on GLS, increasing BMI showed a greater likelihood of developing subclinical LV dysfunction¹⁹.

We excluded patients older than 60 years on myocardial contractility function and hence affecting GLS to avoid aging effect in this study. Aging effect was seen in the study done by Fernandes et al where he showed that patients with subclinical atherosclerosis presented with greater carotid intima media thickness has associated alternations of myocardial strain parameters²⁰. We also found that 1.2% of healthy individuals had subclinical LV dysfunction, and we attribute this to smoking,²¹ or atherosclerosis.

Limitation

The study was hospital based and general population was not included. It is limited by small sample size. Also, radial and circumferential strain have not been discussed. The operator was not double blinded about hypertensive patients and control subjects. However, this study is preliminary and provides a base for future larger studies. Hence larger randomized population would more likely reflect the true pictures.

Conclusion

Detecting subclinical LV dysfunction in systemic hypertension by GLS imaging technique is an important tool which is not noticed by conventional echocardiography. Therefore it is better to use these technique in systemic hypertension patients for early detection of subclinical LV dysfunction. We concluded that 2D-STE detected subclinical LV systolic dysfunction in 34.2% of our patients with systemic hypertension (patients with GLS less negative than -18%), despite preserved LVEF and independent LV structural changes. This suggests that detecting subclinical LV dysfunction in systemic hypertension by GLS imaging technique is an important tool for early management of hypertensive individuals for prevention of future events.

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Conflict of interest:

None

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