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ORIGINAL ARTICLE

Global Left Ventricular Function Index as a Predictor of Subclinical Contractile Dysfunction in Patients with Concentric Left Ventricular Hypertrophy

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ABSTRACT

Background : Left ventricular (LV) ejection fraction (LVEF) is mostly used as a parameter of systolic function which is often assessed without considering changes in ventricular structure, geometry and hypertrophy. LV global function index (LVGFI) is a novel parameter that integrates LV structure with global function in the assessment of LV cardiac performance. Our study aimed to throw light on LVGFI as a diagnostic marker of early subclinical contractile dysfunction in patients with concentric Left ventricular hypertrophy.**Methods:** A case-control study involving 123 participants; they were divided into three groups, control (Group 1) 41 volunteers, LVH without systolic dysfunction (Group 2) 41 cases, and LVH with systolic dysfunction (Group 3)**.** Conventional systolic function assessment, LVGFI was expressed by the equation;(LV stroke volume / LV global volume) *100 and tissue doppler mitral annulus Sa wave, IVCT Isovolumetric contraction time.**Results:** (LVGFI), and Sa mitral annulus had the lowest mean value in G_3. LVGFI had a positive correlation with average Sa (r=0.755, p <0.001), EF (m-mode, r = 0.235, p=0.008) and EF (Simpson, r = 0.305, p=0.001)**.** Multivariate analysis showed that LVGFI had the best relationship with Sa average (p=0.001), EF Simpson (p= 0.002) and then hypertension(p=0.02*)**.** LVGFI had an area under the curve of 0.74, sensitivity of 85%, specificity of 80%, and cutoff of less than 22.4% for subclinical LV systolic dysfunction. **Conclusion:** LVGFI at a cut-off of less than 22.4% was useful in detecting subclinical LV systolic dysfunction in concentric LVH.**Keywords:** LVGFI; concentric hypertrophy; systolic function

INTRODUCTION

Heart failure is a common debilitating disease, linked to marked morbidity, mortality, and re-hospitalization, but the rising prevalence of heart failure underestimates the need to detect and manage patients with early left ventricular systolic dysfunction prior to the onset of symptoms [1]**.** Left ventricular hypertrophy (LVH) has been considered a compensatory mechanism that allows the heart to compensate in front of the increased workload, pathologic LVH may be due to several cardiac disease states. Pathologic LVH, although at first useful, but in the end may be associated with a reduction of the intrinsic contractile function of the myocardium [2]**.** Concentric hypertrophy typically develops when the left ventricle is subjected to continued and increased pressure overloads, such as cases of significant aortic stenosis or systemic hypertension [3]. Tissue Doppler imaging (TDI) is mostly used in routine echocardiographic assessment being simple, reproducible and available in nearly all echocardiographic machines whatever the image quality. Its role as a reliable parameter of ventricular systolic function has been established in several cases [3]. Consequently, left ventricular (LV) ejection fraction (LVEF) is mostly used as a parameter of ventricular systolic function that is mostly interpreted without considering alterations in ventricular structure, geometry, and hypertrophy. LV global function index (LVGFI) is a new parameter that incorporate LV structure with

global function in the assessment of LV cardiac performance. LVGFI has been investigated thoroughly as a prognostic parameter of cardiac events in several studies [4, 5, 6, 7]. Our study aimed to throw light on LVGFI as a diagnostic marker of early subclinical contractile dysfunction in concentric Left ventricular hypertrophy**.**

METHODS

This case-control study was conducted in the echocardiography unit at the cardiovascular department, Zagazig University Hospital from November 2021 to May 2023 on patients with concentric LVH secondary to hypertension or severe aortic stenosis. Hypertensive patients were defined as having BP more than or equal 140mmHg systolic or more than or equal 90 mmHg diastolic or on medical treatment for hypertension [8] and severe aortic stenosis patients documented by echocardiography study as by echo doppler [mean gradient ≥40 mmHg, peak gradient ≥ 60 mm Hg, peak velocity more than or equal 4.0 m/s, valve area ≤ 1cm^2 (or less than or equal 0.6 cm^2/m^2) [9], were included. Our population study was divided into control healthy volunteers with normal echocardiography, patients had LVH without subclinical systolic dysfunction with normal S_a wave velocity by TDI, and LVH with subclinical systolic dysfunction with abnormal S_a wave velocity by TDI. The cutoff value according to which we divided our cases was S_a wave velocity by TDI ≤6.8 was indicative of subclinical systolic dysfunction [10]. Left ventricular systolic dysfunction (EF< 50%)congenital heart diseases, ischemic heart diseases, and valvular disease (more than mild regurge were excluded from the current study.

Ethical standards:

Official permission was acquired by the local Institutional Review Board (IRB) (Zagazig University, Egypt) NO. (ZU-IRB # 9088-15-11-2021). Prior to including any of the participants in our study, we informed them about it and obtained their written consent.

Full history taking with special emphasis on demographic criteria including age, sex, risk factors, and detailed medical and cardiac history.

Two-dimensional (2D) Echocardiographic evaluation:

Using a 1.5-3.6 MHz phased array probe, transthoracic echocardiography was carried out using a GE Vivid E95 (GE Medical system). Based on recommendations from the American Society of Echocardiography and the European Association of Echocardiography, the following standard evaluations were carried out. [11]. left ventricular ejection fraction (LVEF) m-mode, Simpson's method, LV end-diastolic volume (EDV), LV end-systolic volume (ESV), LV stroke volume (SV) was assessed by the difference between LVEDV and LVESV, according to the Devereux formula, LV mass was defined as a left ventricular mass index of greater than 115 g/m2 in male patients and 95 g/m2 in female patients. The LV mass was indexed according to body surface area. Relative wall thickness (RWT) was assessed by the equation (2 × posterior wall thickness)/(LV internal diameter at end-diastole) with a value (RWT > 0.42) defining concentric hypertrophy. LVGFI was expressed by the equation;(LV stroke volume / LV global volume) *100. LV global volume was defined as the sum of the mean LV cavity volume [(LVEDV + LVESV)/2] and the myocardial volume. LV myocardial volume was calculated as LV myocardial mass divided by myocardial density, which is specified as1.05 g/mL22, SV is a calculated by the equation (EDV-ESV) [12].

$$LVGFI = \frac{\text{EDV} - \text{ESV}}{\frac{\text{EDV} + \text{ESV}}{2} + LV\ mass/1.05} X100\%$$

In order to measure the peak Sa velocities (cm/s), tissue Doppler imaging (TDI) was performed using a sample volume on the septal and lateral mitral annuli in the apical four chamber view, and Isovolumetric contraction time (IVCT).

STATISTICAL ANALYSIS

SPSS program version 18 was used to analyze the data. Every data point was noted as mean SD, Utilizing the ANOVA (F) test, statistical comparisons were made between the three groups. (P > 0.05) was not significant, and (P < 0.05) was significant. Post-hoc was used to compare every 2 groups separately. Frequency and percentage were used to describe categorical data, and the chi-square test or Fisher exact was used to compare them. To evaluate the relation between various study variables, Pearson correlation was used. Univariate logistic regression and then Multivariable linear regression showed the relationship between echocardiographic data, cardiovascular risk factors, and left ventricular global function index (LVGFI). ROC curve to investigate the performance of LVGFI in predicting subclinical contractile dysfunction The level of significance will be identified at P<0.05.

RESULTS

We enrolled 123 participants who were divided into control (Group1) 41 volunteers, LVH without systolic dysfunction (Group2) 41 cases, and LVH with systolic dysfunction (Group3). Demographic data and risk factors were presented in **Table 1.**

Echocardiographic data of the studied groups were presented in **Table 2** EF by m-mode, Simpson and LVMI had the lowest mean value in G_3. LVGFI in G_3 had the lowest mean value (G_3 19.07 ± 3.5 vs G_2 32.05 ± 3.4vs G_1 35.07 ± 5.2 p < 0.001).

Tissue doppler data of the studied groups were presented in **Table 3** Sa (lateral, medial and average mitral annulus) in G_3 had the lowest mean value but IVCT (lateral, medial and average mitral annulus) in G3 had the highest mean value. Pearson correlation showed that LVGFI had a negative correlation with average IVCT (r= -0.519, p<0.001), LVMI (r = -0.7, p<0.001), and RWT(r = -0.2, p = 0.006), but LVGFI had a positive correlation with average Sa (r=0.755,p <0.001), EF (m-mode, r = 0.235, p=0.008) and EF (Biplane Simpson, r = 0.305, p=0.001) **(Figure 1)**. Multivariate analysis showed that LVGFI had the best relationship with Sa average (p=0.001) and LVMI (p=0.001) followed by EF Simpson(p= 0.002) and then hypertension(p=0.02*)(**Table 4).**LVGFI was a good predictor for subclinical LV systolic dysfunction at a cut off less than 22.4% had a sensitivity of 85% and specificity of 80%, and an area under the curve of 0.74**(Table 5&Figure 2)**

Table (1): Demographic data and risk factors of the studied groups.

	Group 1 Control (N=41)	Group 2 LVH without systolic dysfunction (N=41)	Group 3 LVH with systolic dysfunction (N=41)	F/X^2	P value	Post -hoc
Age	38.1 ± 13.02 (21-60)	49.2 ± 6.02 (36-66)	55.16 ± 9.3 (33-72)	31.6	P <0.001	P1<0.001 P2<0.001 P3=0.01
Gender Male Female	26 (63.4%) 15 (36.6%)	30 (73.2%) 11 (26.8%)	30 (73.2%) 11 (26.8%)	X^2=1.2	0.53	
Smoking	21 (51.2%)	28 (68.3%)	32 (78.0%)	X^2=21.05	<0.001	
Diabetes mellitus	3 (7.3%)	14 (34.1%)	12 (29.3%)	X^2=9.2	0.009	
Hypertension	0 (0%)	34 (82.9%)	40 (97.6%)	Fischer exact	<0.001	
Severe AS	0 (0%)	7 (17.1%)	1 (2.4%)		0.003	

AS: aortic stenosis.
LVH: left ventricular hypertrophy
P1 G1 Control vs. G2 LVH without systolic dysfunction
P2 G1 Control vs. G3LVH with systolic dysfunction
P3 G2 LVH without systolic dysfunction vs.G3 LVH with systolic dysfunction

Table (2): Echocardiographic data of the studied groups

	Group 1 Control (N=41)	Group 2 LVH without systolic dysfunction (N=41)	Group 3 LVH with systolic dysfunction (N=41)	F	P value
EF(m-mode)	66.15 ± 3.8 (61-77)	68.5 ± 5.12 (60-86)	65.07 ± 7.05 (56-86)	3.2	P1=0.22 P2=0.68 P3=0.03 0.04
EF(biplane simpson)	66.6 ± 4.8 (58-78)	69.1 ± 5.5 (58-79)	64.8 ± 6.7 (54-80)	5.5	P1=0.14 P2=0.33 P3=0.003 0.004
LV mass	118.9 ± 30.4 (38.7-188)	175.8 ± 37.4 (99.3-253.3)	252.8 ± 48.3 (165.4-378.7)	121	P1<0.001 P2<0.001 P3<0.001 <0.001
LVMI	64.4 ± 16.4 (22.3-103.4)	106.9 ± 12.9 (95.14-149.5)	135.5 ± 23.9 (95.29-192.34)	159.2	P1<0.001 P2<0.001 P3<0.001 <0.001
RWT	0.35 ± 0.04 (0.24-0.43)	0.67 ± 0.12 (0.44-1.06)	0.61 ± 0.12 (0.43-0.94)	117.1	P1<0.001 P2<0.001 P3=0.02 <0.001
LVGFI	35.07 ± 5.2 (28-51)	32.05 ± 3.4 (28-46)	19.07 ± 3.5 (11-24)	175	P1=0.003 P2<0.001 P3<0.001 <0.001

EF:ejection fraction.
LV:left ventricle.
LVMI: left ventricle mass index.
RWT: relative wall thickness.
LVGFI: left ventricle global function index
P1 G1 Control vs. G2 LVH without systolic dysfunction
P2 G1 Control vs. G3LVH with systolic dysfunction
P3 G2 LVH without systolic dysfunction vs.G3 LVH with systolic dysfunction

Table (3): Tissue Doppler imaging data of the studied groups

	Group 1 control (N=41)	Group 2 LVH without systolic dysfunction (N=41)	Group 3 LVH with systolic dysfunction (N=41)	F	P value
Sa (lateral mitral annulus)	10.7 ± 1.31 (9-13)	10.1 ± 1.35 (8-13)	5.8 ± 0.83 (4-7)	209.1	P1=0.06 P2<0.001 P3<0.001 <0.001
Sa (medial mitral annulus)	8.8 ± 0.94 (7-11)	8.6 ± 1.01 (7-11)	4.5 ± 0.68 (3-6)	318.8	P1=0.55 P2<0.001 P3<0.001 <0.001
Sa (average)	9.8 ±1.07 (8-12)	9.3 ± 1.1 (7.5-12)	5.18 ± 0.7 (3.5-6)	303.6	P1=0.04 P2<0.001 P3<0.001 <0.001
IVCT (lateral mitral annulus)	45.4 ± 4.5 (36-52)	85.6 ± 13.5 (56-110)	95.06 ± 10.7 (72-106)	269.3	P1=0.7 P2=0.0009 P3=0.001 <0.001
IVCT (medial mitral annulus)	42.2 ± 4.08 (34-49)	78.5 ± 11.4 (54-102)	87.6 ± 11.9 (61-102)	246.8	P1<0.001 P2<0.001 P3<0.001 <0.001
IVCT(average)	43.8 ± 4.1 (35-49.5)	82.05 ± 12.3 (55-106)	91.35 ±11.1 (68-104)	267.6	P1<0.001 P2<0.001 P3<0.001 <0.001

Sa: Systolic myocardial velocity.
IVCT: Isovolumetric contraction time.
P1 G1 Control vs. G2 LVH without systolic dysfunction.
P2 G1 Control vs. G3LVH with systolic dysfunction.
P3 G2 LVH without systolic dysfunction vs.G3 LVH with systolic dysfunction

Table (4): Univariate and multivariate linear regression showing the relationship of hypertension, severe AS, Echocardiographic parameters and LVGFI

Model	Univariate Beta Coefficients	Univariate *P value*	Multivariate Beta Coefficients	Multivariate *P value*
Hypertension	1.2	**0.009**	0.08	**0.02**
Severe AS	0.53	0.08	0.02	0.41
S Average	2.4	**<0.001**	0.407	**0.001**
IVCT Average	0.08	0.43	0.039	0.651
LVMI	-0.76	**<0.001**	-0.511	**0.001**
RWT	0.21	**0.01**	0.070	0.314
EF M Mode	0.04	0.802	0.003	0.965
EF Simposon	0.28	**0.026**	0.233	**0.002**

AS:aortic stenosis.
EF:ejection fraction.
IVCT: isovolumetric contraction time.
LVMI: Left ventricular mass index.
RWT:relative wall thickness.

Table (5):ROC of LVGFI to predict subclinical LV systolic dysfunction.

Area	Cut off	Sensitivity	Specificity	Asymptotic Sig.[b]	95% Confidence Interval	
					Lower Bound	Upper Bound
0.74	22.4	85%	80%	<0.0001	0.99	1.000

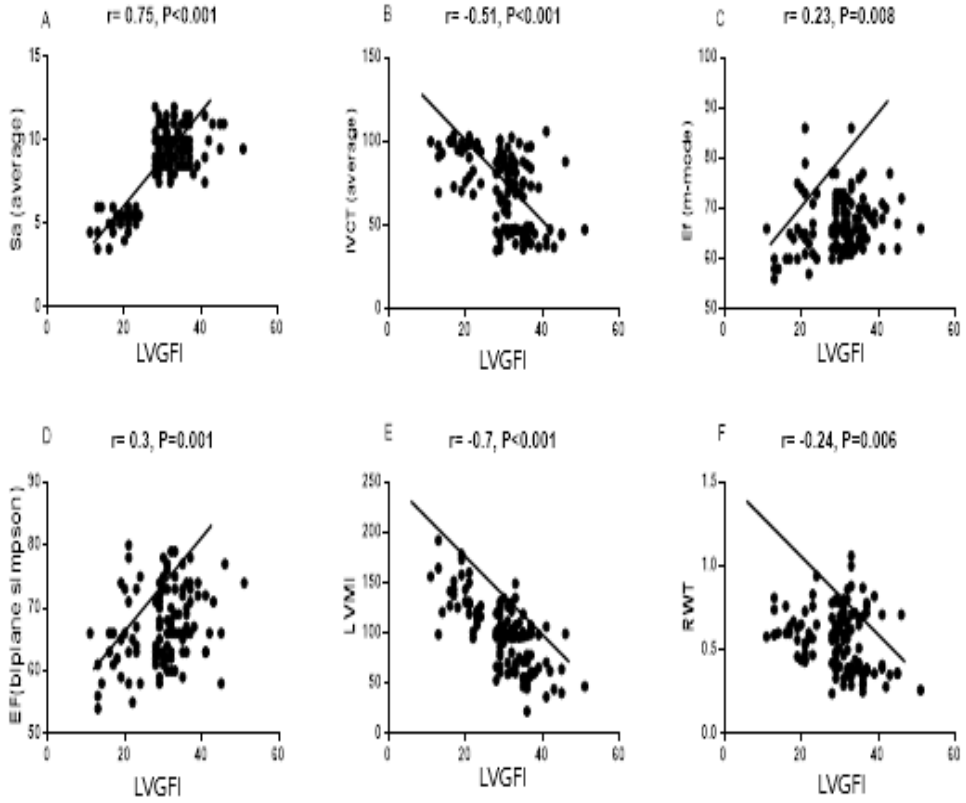

Figure (1): Correlations between LVGFI and other parameters.

EF: ejection fraction.
Sa: systolic myocardial motion .
LVMI: left ventricle mass index.
RWT: relative wall thickness.
LVGFI: left ventricle global function index.

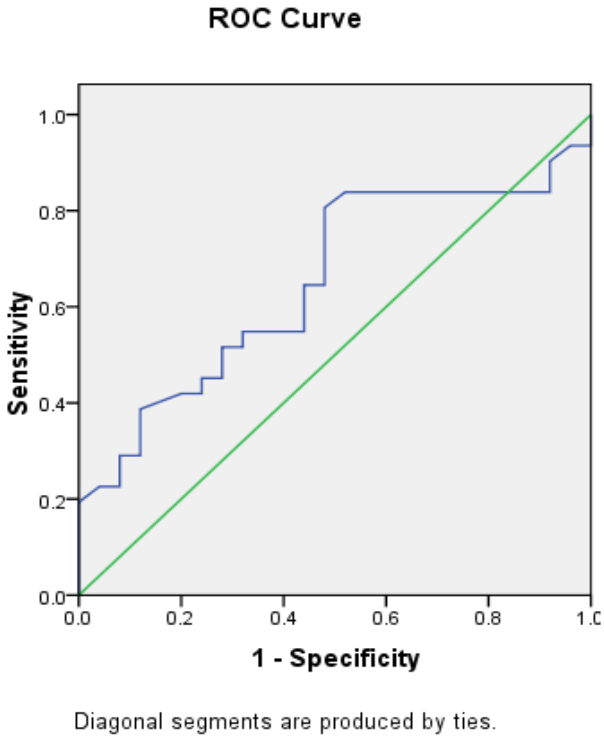

Figure (2): Roc curve of LVGFI to predict subclinical LV systolic dysfunction.

DISCUSSION

The most commonly used parameter of LV function in routine echocardiographic assessment, the LV ejection fraction (LVEF), does not consider the relationship between LV mass and LV dimensions which might explain its limited sensitivity and specificity in different cardiovascular (CV) diseases [4]. Recently cardiac magnetic resonance (CMR) LVGFI is an accurate measure of LV cardiac performance that incorporate ventricular structure into ventricular functional assessment [5].LVGFI has been previously investigated in several studies as a prognostic marker of adverse cardiac events [4, 5, 6, 7], so to the best of our knowledge; our study is the first one to assess LVGFI as a diagnostic parameter of subclinical systolic function in concentric hypertrophy due to hypertension and severe AS. Our result showed that EF by m-mode and biplane Simpson had significantly the lowest mean value in G_3 (LVH with systolic dysfunction). In agreement with our results, Mizuguchi et al [13] found that The LV ejection fraction was lower in the LVH with systolic dysfunction group than in the control group. In disagreement with our study, Shehata et al [14] stated that there was non-significant difference regarding EF in the hypertension group and control group, this may be related to that in the hypertension group not all patients have concentric LVH. LV mass and LVMI had significantly the lowest mean value in G_3. In agreement with this, Baral et al [15] conducted a study on left ventricular global strain in hypertensive patients with normal ejection fraction and found that the cases group had a substantially greater Left Ventricular Mass & Left ventricular mass index. RWT had significantly the highest mean value in G_3 (table 2), this result was in agreement with Baral et al [15] and also Ayoub et al [16] LVGFI had significantly the lowest mean value in G_3 in comparison to 1st and 2ndgroups. Mewton et al [4] conducted a study to assess LVFI predictive value for cardiovascular events and found that LVGFI was lower in heart failure group in comparison to no events group. Nwabuo et al [5] assessed the prognostic role of LVGFI in comparison to LVEF and found that the LVGFI was higher in no events group in comparison to the events group. Doganay et al [6] evaluate the prognostic value of the LVGFI in acute coronary syndrome and found that lower LVGFI was independent predictor of adverse cardiac events. Desai et al [7] conducted a study in adult hypertrophic cardiomyopathy (HCM) with normal LVEF (55%) and found that with patients with LVGFI less than 37% had a primary event versus those with LVGFI more than 37% [8%**].** Sa velocity either septal, lateral, and average had the

lowest mean value in G_3 in agreement with our study Gab Allah et al[17] found that Sa velocity decreased in hypertensive cases than the control. In disagreement with our study, Ayoub et al [16] found no difference between his group studies as regard Sa wave; this discrepancy with our study may be due to different group design according to global longitudinal strain (GLS) and his study included hypertensive patients only. IVCT (lateral, medial and average mitral annulus) had significantly the highest mean value in G_3 this was in agreement with Biering-Sørensen et al [18]. In the current study, we found that by multivariate regression LVGFI had the best relationship with Sa average and LVMI followed by EF Simpson and hypertension Nwabuo et al [5] found an association between LVGFI and risk factors; higher BMI, higher diastolic blood, current smokers, male sex, and black race were associated with worse LVGFI. In our study, LVGFI was a good predictor for subclinical LV systolic dysfunction at a cut off less than 22.4% had a sensitivity of 85% and specificity of 80% and an area under the curve of 0.74. Desai et al [7] found that LVGFI cutoff less than 37% was related to increased risk of cardiac events in hypertrophic cardiomyopathy (HCM) with preserved LVEF (≥55%).

CONCLUSIONS

LVGFI with a sensitivity of 85% & specificity of 80% appears to be beneficial in the identification of subclinical LV systolic impairment in concentric LVH whatever the cause was hypertension or severe AS, despite preserved LVEF. This suggests that early discovery and treatment of these patients could be beneficial in preventing symptomatic heart failure.

RECOMMENDATIONS

LVGFI can be used in addition to conventional echocardiographic parameters in the routine assessment of concentric hypertrophy due to hypertension & severe AS to detect subclinical systolic impairment. Further studies are recommended to compare the accuracy of LVGFI in detection subclinical assessment in comparison to other modalities such as speckle tracking echocardiography. Further studies with large sample sizes are recommended.

Limitations

The relatively small sample size. Some causes of subclinical LV systolic dysfunction e.g., silent ischemic heart diseases or diabetic patients weren't excluded. Subclinical systolic dysfunction was defined in relation to tissue doppler results only. Assessment was done by single operator so inter-observer variability was not assessed.

Conflict of interest

The authors state that they have no competing interest.

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