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ROLE OF GLOBAL LONGITUDINAL STRAIN IN ASSESSMENT OF LEFT VENTRICULAR SYSTOLIC FUNCTION IN PATIENTS WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION

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ABSTRACT:

Background: a clinical illness brought on by structural along with functional abnormalities of the heart which induce a reduce in cardiac output in addition to an increase in cardiac filling pressure is Heart failure (HF). This study used global longitudinal strain (GLS) to determined systolic dysfunction in individuals with HF with preserved ejection fraction (HFpEF).

Methods: The 120 participants in this prospective research were split into three groups as follows: Group A consists of 50 individuals with overt HF, 40% of whom had HF with reserved ejection fraction (HFrEF) with a left ventricular ejection fraction (LVEF) below 40%. Group B consists of 50 individuals with signs or symptoms of HF, ejection fraction (EF) greater than 50%, left ventricular mass index (LVMI) of 115 g/m2 for men and 95 g/m2 for women, left atrial volume index (LAVI) of 34 mL/m2, as well as E/é, in accordance with criteria of European Society of Cardiology (ESC), with mean é lateral and septal wall of 9 cm/s (HFpEF). Group C (control group) comprised of 20 individuals with risk factors for HF who had moderate dyspnea or unusual chest pain and had LVEF > 50%, E/é below 8, and no structural abnormalities.

Results: A statistically substantial variation was existed among the three groups as regard Echo left ventricular end-systolic volume (LVESV), Echo left ventricular end-diastolic volume (LVEDV), A wave, Average Ee, Estimated Pulmonary arterial systolic pressure (PASP) and GLS. A high negative association was existed among GLS and Simpson EF in HFrEF, HFpEF groups. A moderate negative association was existed among GLS and Simpson EF in Control group.

Conclusions: In individuals with manifestations of HF and normal LVEF, GLS may be regarded as a crucial marker for the identification of left ventricular systolic dysfunction.

Keywords: Ejection Fraction, Left Ventricular Systolic Function, Global Longitudinal Strain, Heart Failure.

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INTRODUCTION:

Heart failure (HF) is a clinical illness brought on by structural along with functional abnormalities of the heart which induce a reduce in cardiac output in addition to an increase in cardiac filling pressure. The usual manifestations of this condition, such as exhaustion, breathlessness, and swelling of ankle, might be associated with signs, like pulmonary crackles, increased jugular venous pressure(JVP), and leg edoema **[1].**

The National Health and Nutrition Examination Survey (NHANES) produce data on the overall incidence of HF in the United States. According to estimates, 5.1 million Americans aged 20 and older suffer HF. In its 2016 recommendations, the ESC suggested that the following criteria be met in order to diagnose heart failure (HF) with preserved ejection fraction (HFpEF) [2].

The existence of signs or manifestations of HF; a 'preserved' ejection fraction [(EF) identified as LVEF = 50% or 40-49% for HF with mid-range ejection fraction (HFmrEF); a high level of natriuretic peptides (NPs) [N-terminal-proB type-natriuretic peptide (NT-proBNP) 125 pg/mL along with B type natriuretic peptide (BNP). 35 pg/mL]; and reliable proof of other cardiac structural and functioning abnormalities concerning HF. Echocardiography is very important in the identification of left ventricular (LV) diastolic failure among individuals with HFpEF due to its non-invasiveness and availability [3].

A variety of echocardiographic measures which may be utilised to assist establishing the identification of diastolic dysfunction were existed, although none of them are diagnostic. These include Doppler studies of the pulmonary vein inflow, mitral inflow pattern, and tissue Doppler. Multiple anomalies should be considered highly indicative of diastolic dysfunction, according to recommendations **[4]**.

When it comes to identifying decreased diastolic function in HFpEF individuals, Tissue Doppler Image (TDI) has shown to be more reliable compared with other indicators **[5].**

When evaluating LV systolic function, speckle tracking echocardiography (STE), which is better to myocardial velocities due to the measurement is angle independent and simple to determine, assesses the myocardial deformation (strain). The average of 18 cardiac segments derived from apical 3-chamber, 4-chamber, and 2-chamber views are used to determine GLS, which has a typical range of -18% to -21.5% [6].

Standard measures like EF and the E/A ratio are applicable everywhere but have certain restrictions. Clinicians may now get more detailed information on the strain on the ventricles and atria owing to STE. A wide range of medical conditions, including amyloidosis, rheumatoid arthritis, inflammatory disorders, and neoplasia, are now included in the therapeutic benefits of STE. The application of STE for people with HFpEF is the main topic of this review. [7].

The aim of this work was to use GLS to identify systolic dysfunction in people with heart failure and preserved ejection fraction (HFpEF).

PATIENTS AND METHODS:

This prospective work was carried out on 120 subjects with 100 of them are patients with HF, Validated congestive HF was taken into consideration if a pair of major or a single major and a pair minor criterion were present at the same time, as well as orthopnea, paroxysmal nocturnal dyspnea, rales, increased jugular venous pressure, 3rd heart sound (s3), pulmonary edoema, peripheral edoema, night cough, dyspnea when exerting oneself, hepatomegaly, loss of weight 4.5 kg within 5 days utilizing diuretics, pleural effusion ad heart rate (HR) more than 120/minute.

The work was done after approval from the Ethical Committee Al-Azhar (Assuit) University Hospitals. The patients provided signed permission after being fully briefed.

Exclusion criteria were individuals with no signs or manifestations of HF, end-stage liver or renal diseases, suboptimal echocardiographic window, persistent arrhythmia or frequent extra systoles.

Participants had been split in to 3 groups:

Group A: included 50 individuals with overt HF (met the Framingham requirements) with LVEF below 40% (HFrEF)

Group B: included 50 individuals with signs and or symptoms of HF (met the Framingham requirements) with EF greater than 50% and LVMI 115 g/m2 for males and 95 g/m2 for females or a LAVI 34 mL/m2 and/or E/é, based on criteria of ESC, and a mean é lateral and septal wall 9 cm/s (HFpEF). BNP measurements were not part of the criteria for diagnosis for this group since clinical practise didn't regularly test natriuretic peptides.

Group C, which was deemed the control group, consisted of 20 individuals with risk factors for HF whom presented with moderate dyspnea or atypical chest pain but no other specific signs or symptoms of HF. Echocardiography revealed intact LVEF greater than 50% with E/é below 8 with no structural abnormalities.

Everyone who participated underwent the following:

comprehensive taking of history, thorough clinical examination, including pulse rhythm and rate, vital signs (blood temperature, blood pressure, heart rate, and respiration rate),

indicators of (Cyanosis, Pallor, Jaundice, and enlargement of Lymph nodes), Head & neck, lower and upper limb, chest and heart examinations], cardiovascular examination, usual investigations, twelve-lead resting surface electrocardiogram (ECG).

Echocardiographic measures:

Measurements of LVEF, LA dimensions, and LV dimensions had been estimated with the participants in the left lateral posture based on the recommendation of American Echocardiographic Society (European Association of Cardiovascular Imaging/ American Society of Cardiology, 2016)

By assessing the LV volume in both diastole and systole from apical four- and two-chamber views, the conventional approach was used to estimate the LVEF.

Pulse waved Doppler inflow testing was used for evaluating deceleration time and peak early flow velocity (E), and the specimen quantity was positioned perpendicular to the mitral valve's tip.

A specimen with a volume of 1 cm has been placed at the septal and lateral annuli of the mitral valve, and the early diastolic peak E was determined there. The mitral annulus was quantified using tissue doppler imaging (TDI) from an apical four-chamber view. The average of the lateral and septal E has been employed to calculate the E é /eratio [8].

At a rate of frames 40 to 90 frames per second, 2-D tissue speckle tracking images were captured in long-axis views of the apical four-, three-, and two-chamber [9].

Utilizing Automated Functional Images (AFI) program from a vivid E9 GE Healthcare echocardiographic machine (GE Healthcare, USA), the same cardiologist analyzed the data.

In a single frame, an algorithm was used to follow the endocardium across the cardiac cycle. To make sure that all myocardial layers are included, the region of interest was carefully modified.

The average of the three values of longitudinal strain that derived from the apical 2-, 3- , and 4-chamber views, it was interpreted as left ventricular GLS by the AFI program.

STATISTICAL ANALYSIS

Utilizing SPSS v26 (SPSS Inc., Chicago, IL, USA), statistical analysis was carried out. Mean and standard deviation (SD) had been utilized to display quantitative information. Frequency and percentages (%) were used to illustrate qualitative characteristics. Shapiro-Wilk's test has been applied to data with a normal distribution. The variation in the

quantitative parameters in two groups was determined using the independent t-test and the Mann-Whitney test. For contrasting two dependent groups of normally distributed parameters, the paired t-test was utilized. For qualitative parameters, the chi square and fisher exact tests are performed. The stepwise regression analysis was conducted to identify the probable risk factor for hypomagnesemia. Significant results were defined as two tailed P values < 0.05.

RESULTS:

Regarding Sex, no significant variation was existed among groups. while age showed statistically substantial variation among groups. As regard HTN, DM, CKD, CAD, there was a highly substantial variation among the three groups under the study. **Table 1.**

Table 1: Demographic characteristics and Risk factors among the study population

		HFrEF group (n =50)		HFpEF group (n = 50)		Control group (n = 20)		Test of Sig.	P
		n	%	n	%	n	%		
Sex	Male	25	50%	20	40%	11	55%	X2 = 3.346	0.067
	Female	25	50%	30	60%	9	45%		
		P1 = 0.039, P2 = 0.06, P3 = 0.084							
Age (years)		59.62 ± 6.46		57.2 ± 6.83		55.2 ± 4.87			
		P1 = 0.072, P2 = 0.176, P3 = 0.003							
Risk factors	HTN	25	50%	35	70%	6	30%	X2 = 9.539	0.002
		P1 = 0.006, P2 = 0.001, P3 = 0.008							
	DM	30	60%	35	70%	5	25%	X2 = 10.998	0.001
		P1 = 0.017, P2 = <0.001, P3 = 0.002							
	CKD	15	30%	25	50%	4	20%	X2 = 7.324	0.007
		P1 = 0.007, P2 = 0.006, P3 = 0.024							
	Smoker	25	50%	25	50%	6	30%	X2 = 4.044	0.044
		P1 = 0.054, P2 = 0.036, P3 = 0.036							
	CAD	45	90%	30	60%	3	15%	X2 = 30.296	<0.001
		P1 = <0.001 , P2 = <0.001 , P3 = <0.001							

Data are presented as mean ± SD or frequency (%). DM: diabetes mellitus, CKD: Chronic kidney diseases, HTN: Hypertension.

Regarding NYHA, a highly substantial variation was exited among the three groups under the study. **Table 2.**

Table 2: NYHA classification among the study population

	HFrEF group (n =50)		HFpEF group (n = 50)		Control group (n = 20)		Test of Sig.	P
	n	%	n	%	n	%		
NYHA classification							X2 = 96.059	<0.001
0	0	0%	0	0%	20	100%		
I	28	56%	35	70%	0	0%		
II	15	30%	15	30%	0	0%		
III	6	12%	0	0%	0	0%		
VI	1	2%	0	0%	0	0%		
	P1 = <0.001 , P2 = <0.001 , P3 = <0.001							

Data are presented as frequency (%). NYHA: the New York Heart Association

A highly statistically substantial variation was existed among the three groups regarding LVESD, LVEDD, EF, Echo LVEDV, Echo LVESV and Simpson EF. **Table 3**

Table 3: LVEDD, LVESD, EF, Echo LVEDV, Echo LVESV, Simpson EF among the study population

	HFrEF group (n =50)	HFpEF group (n = 50)	Control group (n = 20)	Test of Sig.	P
LVEDD	61.54 ± 2.95	52.76 ± 3.65	46.95 ± 4.35	F = 149.1	<0.001
	P1 = <0.001 , P2 = <0.001 , P3 = <0.001				
LVESD	49.3 ± 2.87	38.8 ± 3.19	34.35 ± 3.12	F = 232.293	<0.001
	P1 = <0.001 , P2 = <0.001 , P3 = <0.001				
EF	0.38 ± 0.06	0.54 ± 0.03	0.62 ± 0.07	F = 224.31	<0.001
	P1 = <0.001 , P2 = <0.001 , P3 = <0.001				
Echo LVEDV	158.88 ± 9.58	112.72 ± 15.5	146.75 ± 23.09	F = 122.48	<0.001
	P1 = <0.001 , P2 = <0.001 , P3 = 0.033				
Echo LVESV	99.84 ± 11.1	52.5 ± 8.68	65.05 ± 10.25	F = 289.643	<0.001
	P1 = <0.001 , P2 = <0.001 , P3 = <0.001				
Simpson EF	0.39 ± 0.06	0.54 ± 0.02	0.8 ± 0.04	F = 564.105	<0.001
	P1 = <0.001 , P2 = <0.001 , P3 = <0.001				

Data are presented as mean ± SD. LVESD: Left ventricle end-systolic dimension. EF: ejection fraction. LVEDD: left ventricular end-diastolic.

Regarding Mitral regurge, there was a highly substantial variation among the three studied groups. **Table 4**

Table 4: Mitral regurge grade among the study population

	HFrEF group (n =50)		HFpEF group (n = 50)		Control group (n = 20)		Test of Sig.	p
	n	%	n	%	n	%		
Mitral regurge							**X2 = 66.025**	**<0.001**
Grade I	**5**	**10%**	**15**	**30%**	**0**	**0%**		
Grade II	**25**	**50%**	**15**	**30%**	**0**	**0%**		
Grade III	**20**	**40%**	**5**	**10%**	**0**	**0%**		
No	**0**	**0%**	**15**	**30%**	**20**	**100%**		
	P1 = <0.001 , P2 = <0.001 , P3 = <0.001							

Data are presented as frequency (%). A statistically substantial variation was existed among the three groups as regard E, A wave, EA ratio, Lateral e, Septal e, Average Ee, Estimated PASP and GLS

No statistically substantial variation was existed among the three groups as regard E Deceleration time. **Table 5**

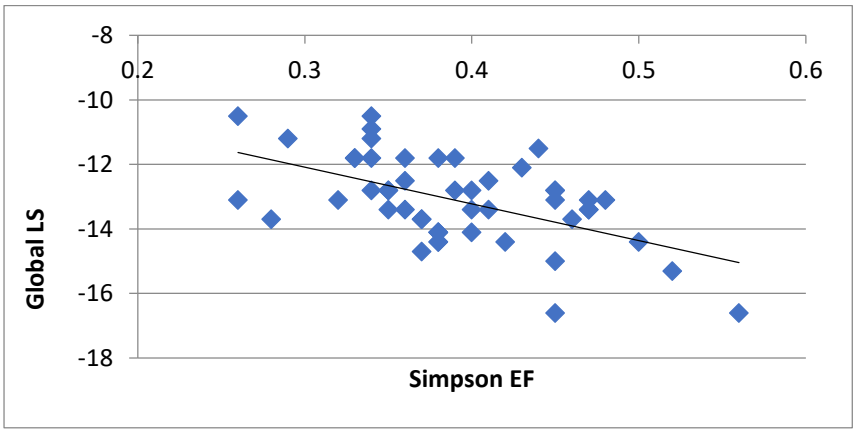
Table 5: E wave, E Deceleration, A wave, EA ratio, Lateral e, Septal e, Average Ee, Estimated PASP, GLS among the study population

	HFrEF group (n =50)	HFpEF group (n = 50)	Control group (n = 20)	Test of Sig.	P
E wave	126.82 ± 27.69	80.7 ± 36.78	125.8 ± 45.71	F = 24.968	<0.001
	P1 = <0.001 , P2 = <0.001 , P3 = 0.926				
E Deceleration time	187.96 ± 17.76	189.14 ± 12.32	178.85 ± 45.04	F = 1.526	0.222
	P1 = 0.7 , P2 = 0.326 , P3 = 0.39				
A wave	84.82 ± 8.1	73.8 ± 22.1	86.6 ± 21.86	F = 6.334	0.002
	P1 = 0.002 , P2 = 0.034 , P3 = 0.726				
EA ratio	1.5 ± 0.3	1.11 ± 0.46	1.44 ± 0.31	F = 14.495	<0.001
	P1 = <0.001 , P2 = 0.001 , P3 = 0.463				
Lateral e	6.47 ± 1.33	5.67 ± 0.88	5.97 ± 1.51	F = 5.652	0.005
	P1 = 0.001 , P2 = 0.408 , P3 = 0.208				
Septal e	5.79 ± 1.19	5.02 ± 0.67	5.35 ± 1.35	F = 6.924	0.001
	P1 = <0.001 , P2 = 0.318 , P3 = 0.205				
Average Ee	15.99 ± 3.28	14.05 ± 0.5	5.35 ± 1.33	F = 168.252	<0.001
	P1 = <0.001 , P2 = <0.001 , P3 = <0.001				
Estimated PASP	41.08 ± 4.21	44.88 ± 3.97	21.3 ± 1.59	F = 284.14	<0.001
	P1 = <0.001 , P2 = <0.001 , P3 = <0.001				
GLS	-13.12 ± 1.35	-15.15 ± 0.68	-19.7 ± 0.38	F = 317.028	<0.001
	P1 = <0.001 , P2 = <0.001 , P3 = <0.001				

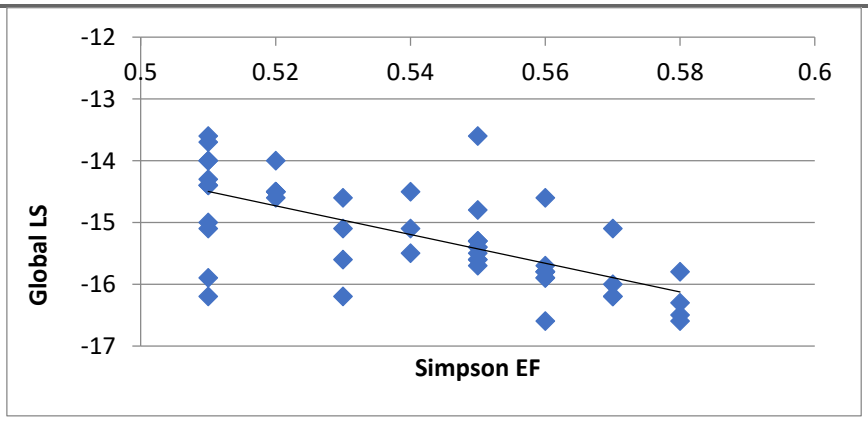
Data are presented as mean ± SD. GLS: Global longitudinal strain

A high negative association was existed among GLS and Simpson EF in HFrEF, HFpEF group. A moderate negative association was existed among GLS and Simpson EF in Control group.

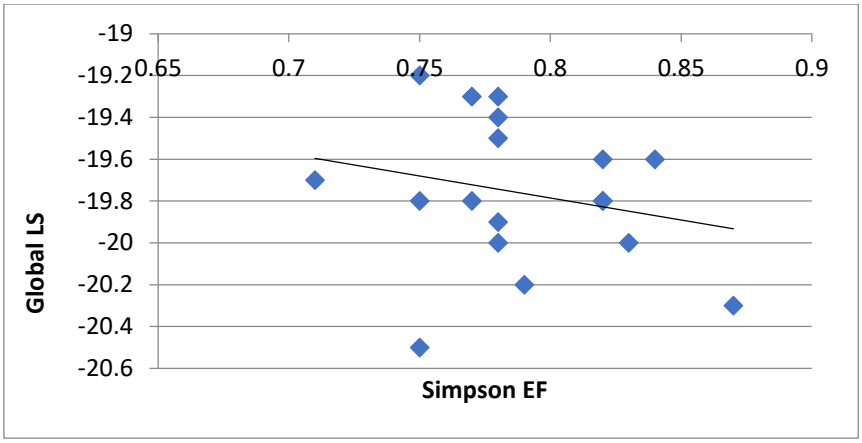
Figure 1



A



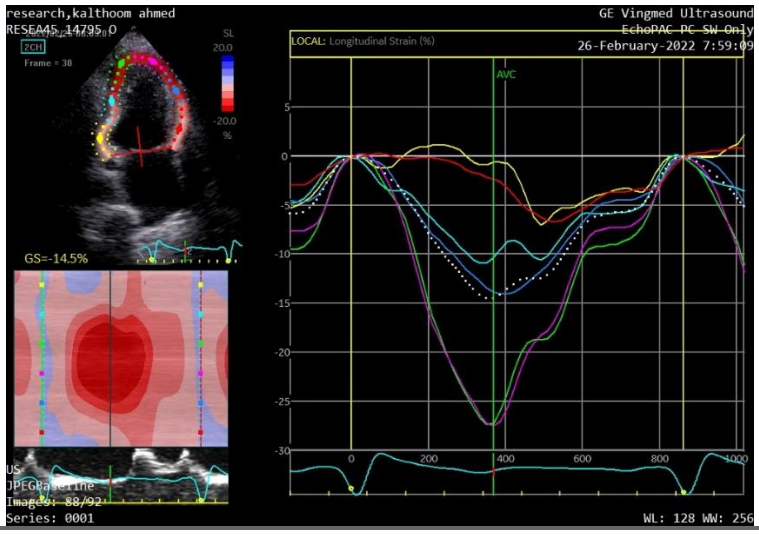
B



C

Figure 1: Scatter plot graph showing correlation between Global LS and Simpson EF in (A)HFrEF group, (B) HFpEF group, (C) Control group.

Case: Female patient 53 years old DM not HTN known IHD complaining of shortness of breath on exersion, dyspnea on lying flat, her 2D echo show preserved LV systolic function EF= 54% and diastolic dysfunction grade II. STE was done and show impairment of LV systolic function GS=-14 which suggest subclinical impairment of LV systolic function. **Figure 2**



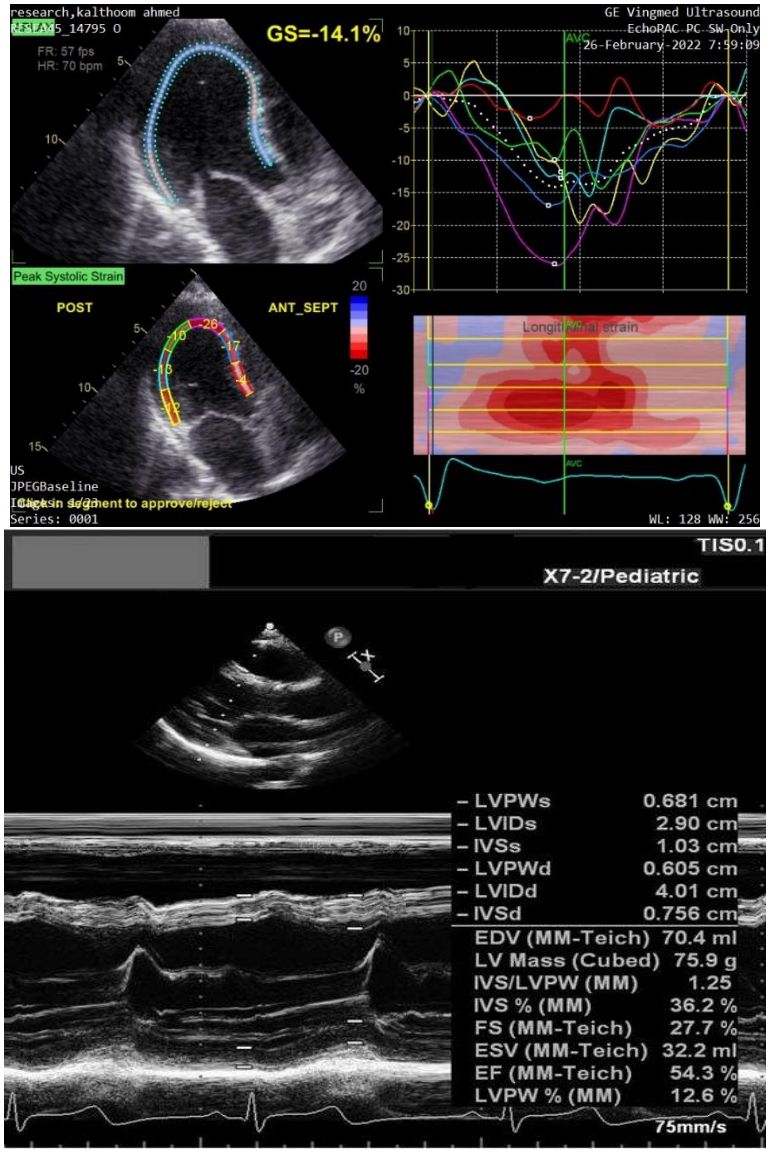


Figure 2: 2D and Speckle tracking echocardiography

DISCUSSION

A clinical illness brought on by a structural or functioning defect in the heart that lowers or raises the filling pressure in the heart is HF [6].

Concerning DM, coronary artery disease (CAD), hypertension (HTN), chronic kidney diseases (CKD), and the New York Heart Association (NYHA), a substantial variation was existed among the three analyzed groups in the present research.

According to Edelmann et al.'s research [10], which supports our results, there is an extremely substantial distinction among HFrEF and HFpEF in terms of NYHA class; individuals with HFpEF had a reduced classification of NYHA and a higher score of SF-36 PF. Except for obesity and hypertension, that were more common in HFpEF, additional conditions were considerably more common in HFrEF.

LVESD, LVEDD, and EF demonstrated a highly

statistically substantial variation among the three groups in the current investigation. S. Liu et al.'s results [11], which are consistent with our own, showed that the LVEF was considerably decresed in the HFrEF group comparing with the other groups, but that no statistically substantial variation was existed among the LVEF in the groups of healthy controls, asymptomatic LVDD individuals, and the HFpEF group.

Individuals with LVDD and HFpEF had substantially higher values for IVSD, LVEDD, PWD, and LAD than did healthy controls. Individuals with HFpEF had considerably lower LV GLS, LSrS, and LSrE values than did healthy controls and asymptomatic LVDD individuals, who had even lower values than HFrEF individuals. However, when asymptomatic LVDD patients were contrasted to healthy controls, no alteration was existed in GLS and LSrS readings.

The Echo LVEDV was a very statistically substantial variation among the three groups in the investigation at hand. According to Liu et al., [11] individuals with asymptomatic HFpEF, LVDD, and HFrEF had considerably higher LVEDP echo and E/e' values, but the mitral annular velocity e' was much lower than it was in the control group.

Between the three analyzed groups, there was a significantly substantial distinction in the present study's analysis of Mitral regurge.

The EA ratio, Estimated PASP, Average Ee, A wave, Lateral, and Septal e had a substantial variation across the groups in the present research when it came to echo findings. no statistically substantial distinction was existed among the groups in E Deceleration Time.

Patients with HFpEF showed a reduce in LV radial and longitudinal strain, according to Wang et al [9]The control groups have been younger compared with the HFpEF patients and didn't possess any factors of risk like diabetes mellitus, ischemic heart disease (IHD), or HTN that might have reduced the value of GLS among the groups, despite the fact that there is a substantial variation in GLS among individuals with normal control and HFpEF groups. It was not possible for Wang et al. [9] to determine whether the decline in GLS was brought on by HF, age, or another concurrent risk factor.

Belghitia et al. [12] discovered that while there was an important variation in the GLS value among the normal control and HFpEF groups, there was no change in LVEF among these groups.

A statistically substantial correlation was existed among the EF groups and all examined echocardiographic measures in the research by Subki et al. [13]. Patients with EF40% were shown to have larger LVs, LVd, left atrium volumes, and dimensions of the aortic root. Conversely, EF40% was connected to decreased FS.

After examining the various echocardiographic findings associated with the various forms of HF, it was shown that individuals with HFpEF often had greater FS, whereas those with HFrEF frequently had greater LVs, LVd, left atrial volume, and dimensions of the aortic root. LVd, FS and Diastolic dysfunction were the only substantial correlations of the EF on logistic regression analysis in the Subki et al. [13] investigation. Regarding left-ventricular dysfunction and wall alterations, there was no discernible difference between HFrEF and HFmrEF, and ventricular dysfunction was noticeably higher frequent in HFpEF individuals.

LVEF was considerably decreased in the HFrEF group contrasted to other groups, according to Liu et al. [11], but it wasn't statistically substantial in asymptomatic LVDD patient, the normal control, and HFpEF groups. Individuals with LVDD and HFpEF had substantially higher LVEDD, PWD, IVSD, and LAD values than healthy controls. Additionally, individuals with asymptomatic HFpEF, HFrEF, and LVDD had considerably higher values of LVEDP echo and E/e' than the control group, but e' of the velocity of mitral annuli was much lower. Despite the fact that the variations in values of LVEDP echo and E/e' did not achieve statistical importance, Patients with HFpEF tended to have bigger ones comparing with those with asymptomatic LVDD, and the E/e' and LVEDPecho were both considerably greater in the HFpEF group in comparison to each of the other 3 groups. Also, according to Liu et al [11], Patients with HFpEF had considerably lower values of

LV global LS, LSrE and LSrS than did healthy controls and asymptomatic LVDD individuals, who had even lower values in HFrEF individuals. However, when asymptomatic LVDD individuals were contrasted to healthy controls, no alteration was existed in GLS and LSrS readings. Ts-SD and Te-SD were both considerably longer in the HFrEF and HFpEF groups compared to the control group, although Ts-SD was fewer in the HFpEF group.

PH in HFrEF has long been researched in advanced phases (individuals who are waiting for a heart transplantation or a left ventricular assist device (LVAD)). Considering the significant epidemiologic burden and the absence of efficient care, the involvement of PH in HFpEF is under close study, and a detailed understanding of possible pathways is required. Vachiéry and others **[14]**

Research by Guazzi et al. **[15]** found that Participants with HFrEF or HFpEF as well as healthy control individuals had their LA strain and LA pump functioning (strain rate) evaluated while resting, throughout exercise, as well as throughout the recovery period. With a sharp rise in the PASP/tricuspid annular plane systolic excursion relationship for reduced LA strain, either HFpEF or HFrEF had a noticeably suppressed response, indicating the function of the LA in the RV to pulmonary circulation (Pc) uncoupling.

Intriguingly, a very statistically substantial variation (p=<.001) was existed in GLS across the three groups in the present investigation.

Although normal LVEF, the assessment of GLS values in Groups 2 (HFpEF) and 3 (control) indicated substantial GLS impairments in Group 2 compared to control Group 3, according to Bshiebish et al.'s [6] report. Despite normal LVEF, there was a substantial variance concerning GLS value among Group 2 (HFpEF) and Group 1 (HFrEF), but the reduction was severe in Group 1. The LVEF was the same in the HFpEF group and the control group, but a noticeable variation was existed in the value of GLS, which was greater in the control group. Patients with HFpEF showed a reduce in LV radial and longitudinal strain, according to Wang et al. The control group was young compared to the HFpEF group and had no warning signs like diabetes mellitus, IHD, or HTN which could have reduced the value of GLS between the groups, despite the fact that A substantial variation was existed in GLS among individuals with normal control and HFpEF groups. It was unable to determine whether the decline in GLS was brought on by HF, age, or another concurrent risk factor.

A decrease in the left ventricle's GLS value is seen in all patients with HFpEF. As a result of It seems that deterioration of LV systolic functioning in people with HFpEF may be detected by AFI whether or not ischemia is present due to the longitudinal fibre of the subendocardial layer remaining in an orientation which renders these individuals further vulnerable to hypertrophy of the ventricular wall, ischemia, and any abnormalities in contractions and relaxation. [6].

Limitations: The research subjects did not have their BNP or pro-BNP levels measured; instead, the diagnosis was made using the clinical history, clinical exam, ECG, and echocardiogram. The ESC recommendations advise patients to have their circulating NP levels checked; in the event that this is not possible, an echocardiogram should be done on the patient.

CONCLUSIONS:

In individuals with symptoms of HF and normal GLS, LVEF may be thought of as a crucial marker for the left ventricular systolic dysfunction detection.

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