

# Trend Analysis and Linearity Determination of Numerous Left Ventricular Strain Parameters in patients with Cardiovascular Risk Factors and Normal Four-Dimensional Ejection Fraction

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## Abstract

### Background:

4Dimensional XStrain speckle tracking echocardiography (4DXStrainSTE) is an ingenious technology which blends the STE information acquired from apical three-chamber (3CH), four-chamber (4CH) and two-chamber (2CH) views rendering an exhaustive delineation of multiple LV strain parameters (MLVSP) in a 3Dimensional domain.

### Methods:

We aimed to determine the Trend analysis and Linearity of MLVSP in patients with cardiovascular risk factors (CVRF) employing this tool. 500 adult Indian participants (18-60 years of both the sexes) were classified into: Healthy (Group A - n 152) and CVRF group (Group B - n 348). CVRF group was segregated into three categories (Risk category- 1, 2 & 3) based upon increment in risk factors. Nine strain parameters were estimated. The quintessential inclusion criteria for the participants were a 4Dimensional left ventricular ejection fraction (4D-LVEF) of > 50%.

### Results:

Trend analysis in CVRF group displayed significantly diminishing pattern of values of global longitudinal strain (GLS), global circumferential strain (GCS) at papillary muscle (pap) level and global circumferential strain rate (GCSR) at mitral valve (mv) level and linear reduction of GLS, GCS at pap level, GCSR at mv and pap level and global radial strain rate (GRSR) at mv level (p<0.05 to p<0.01).

### Conclusions:

To our knowledge this is the first research study to investigate the Trend analysis and Linearity in CVRF group on MLVSP utilizing 4DXStrainSTE.

**Key words:** 4dxstrain; speckle tracking echocardiography; strain imaging; 4d-lvef%; cardiovascular risk factors

## Introduction:

Contemporarily, determination of GLS by 2Dimensional STE is the most exhaustively researched all over the world [1]. American Society of Echocardiography advocated a GLS value of > - 20 + 2 % to be normal [2]. Three-dimension speckle tracking echocardiography necessitates a single LV apical acquirement, translating into lessened acquirement time alongwith an opportune moment to estimate the entire strain parameters [3]. Conversely,

because of inferior quality of temporal and spatial resolution, its tracing caliber is abnormally affected. A stitching artifact maybe created between sub-volumes, because of multiple beat acquisitions, resulting in imperfect analysis of speckle tracking [4, 5].

4DXStrainSTE is an ingenious and unique technology which amalgamates the Tomtec GMBH's 3Dimensional, 4Dimensional portrayal and BetuelTM computation competencies [6]. Consecutively, this distinctive software blends the STE information acquired from apical three chamber (3CH), four chamber (4CH) and two chamber (2CH) views and eventually rendering an exhaustive delineation of LV strain parameters in a 3D domain This tool depending on superior quality of 2D spatial and temporal resolution, rectifies the varying concerns of full volume 3D STE [7].

Single plane 3D echocardiography is affected by the fragmentation of the 3D STE. Nonetheless, the concomitant image resolution is of average variety compared to 2D imaging [8]. Demarcation of the endocardial and epicardial borders is impaired in 3D speckle tracking echocardiography. Conversely, XStrainTM 4D, devoid of these limitations represents a dependable, relatively cheap and easy to operate modality for estimating strain.

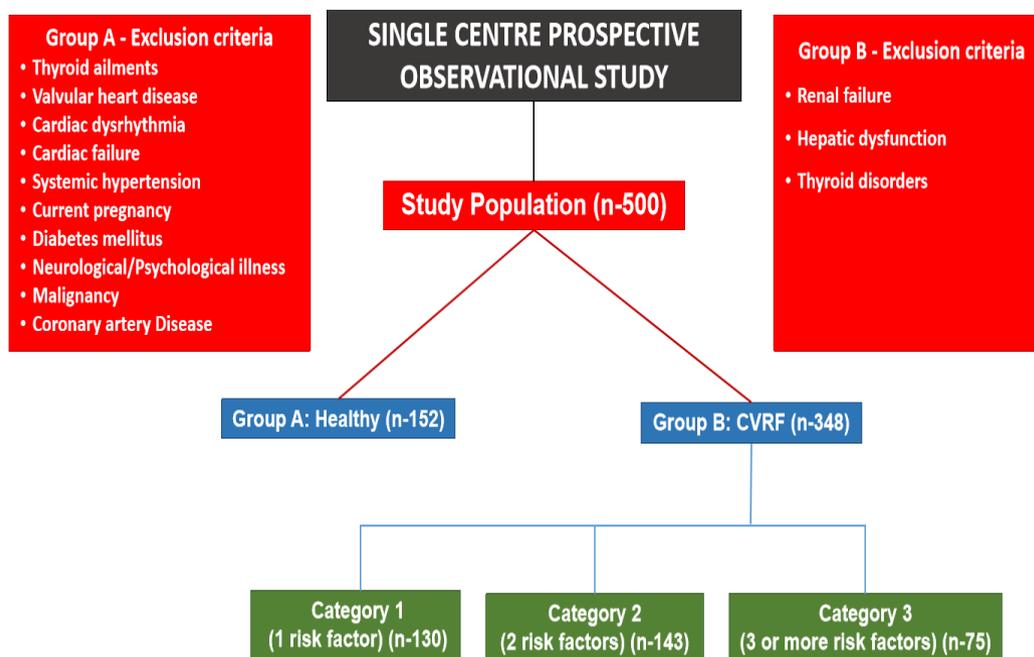
In the recent past multiple studies have demonstrated the influence of CVRF on GLS [9, 10]. It is noteworthy that majority of these studies were performed utilizing 2Dimensional STE. However, after exhaustive literature search, we could not encounter any study, where 4DXStrainSTE was employed for determination of Trend analysis and Linearity in MLVSP in the CVRF group. Hence, we embarked on this subject with the aim to thoroughly illustrate the above-mentioned theme by employing 4DXStainSTE.

**Method:**

**Study Design:** This is an original research, which was performed over a span of 28 months (September 2021 to December 2023) at Prakash Heart Station, Lucknow, UP, India. The approval for the research work was obtained from the Institutional ethics committee of Prakash Heart Station,(approval no. IEC/PDC/PHSD/2021:01,02).

**Study Population:**

This was a single center, observational, prospective research study in which the study population comprised of 500 adult Indian participant age 18-60 years of both sex. This research population was classified into two groups (Figure 1).



**Figure 1: Steps of classification of study design.**

**Group A - Healthy Group:**

152 healthy individuals aged 18-60 years of both sex, without any cardiovascular risk factors, having a normal resting ECG, 4DXStrainSTE with a 4D-LVEF  $\geq 50\%$  and treadmill stress test (TST) were enrolled.

**Group B -Cardiovascular Risk Factor Group**

Likewise, about 348 Indian adults of age 18-60 years of both sex with CVRF and in sinus rhythm and 4D-LVEF of  $\geq 50\%$  were registered.

**The quintessential criteria of this research was that the study participants had a 4D-LVEF of  $\geq 50\%$  derived from 4DXStrainSTE.**

Clinical evaluation and a thorough medical examination were executed by a cardiac physician. Detailed notes were prepared mentioning the presence of cardiovascular risk factors, if any.

**Cardiovascular Risk Factors**

- Cardiovascular Disease –
  - CAD: previous myocardial infarction, stable/unstable angina, history of acute coronary syndrome and previous percutaneous coronary intervention (PCI)
  - CVA (cerebrovascular accident)
  - PAD (peripheral arterial disease)
- Diabetes Mellitus
- Hypertension
- Dyslipidemia
- Obesity
- Smoking

Definition of risk factors was in accordance with the current recommendations [11-15].

**Echocardiography:**

All participants were subjected to a comprehensive assessment of their cardiac functions by conventional transthoracic 2Dimensional echocardiography and 4Dimensional STE. The detailed echocardiographic examination was conducted on the echocardiography system- MY LAB X7 4D XStrain of ESAOTE, ITALY with 1-5 MHZ transducer.

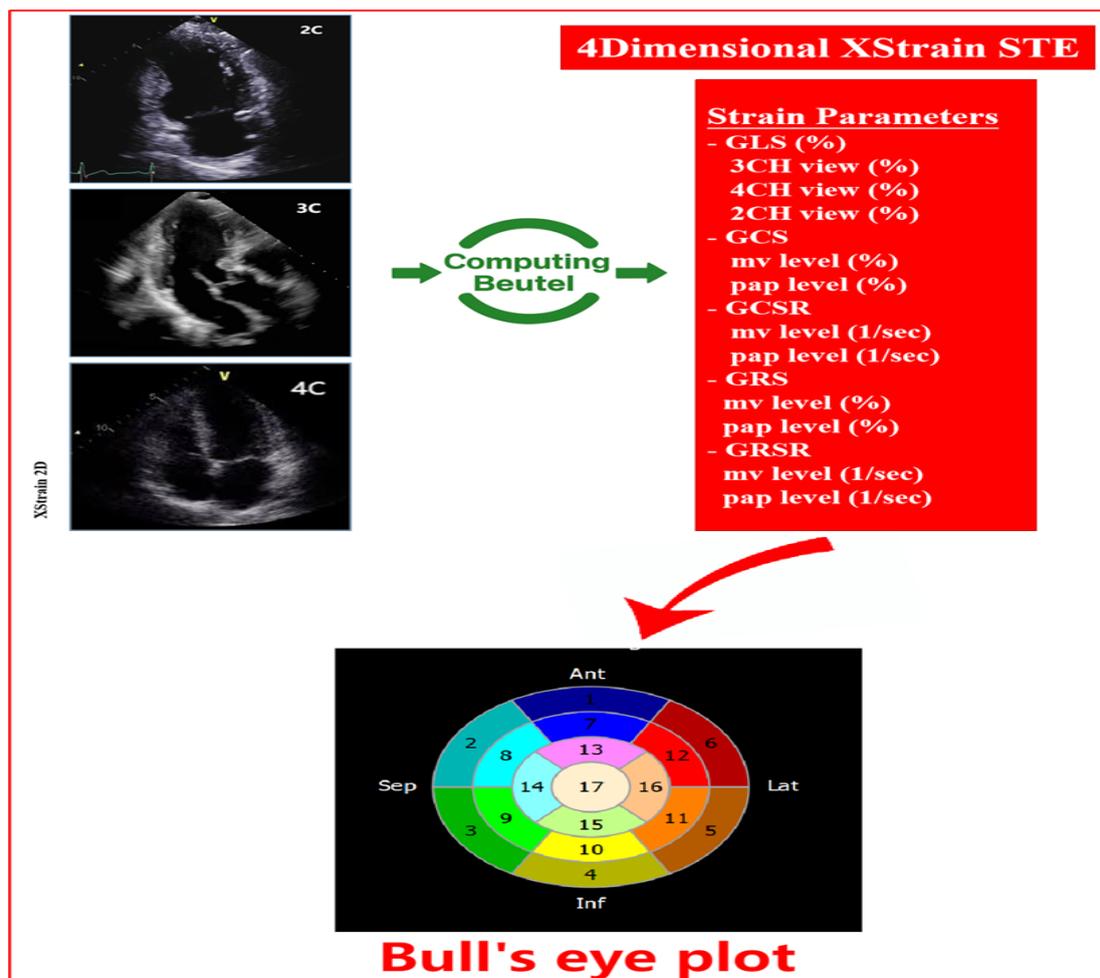
**Conventional echocardiography:**

Two-dimensional, M-mode, pulse wave doppler (PWD), and continuous wave doppler (CWD) was implemented to estimate the routine parameters of left ventricular (LV) volumes, LV systolic and diastolic functions, LV Mass, LV ejection fraction (LVEF %), cardiac output (CO), cardiac index (CI) early diastolic velocity (E), late diastolic velocity (A) and E/A ratio. Moreover, tissue doppler imaging (TDI) was accomplished and early diastolic myocardial relaxation velocity (E') and E/E' ratio was assessed.

**4Dimensional XStrain Echocardiography:**

**Image Acquisition**

Apical 4CH, 3CH, 2CH and short axis (SX) views at the level of mitral valve (mv) and papillary muscles (pap) were acquired (Figure 2). A minimum of three cardiac cycles were acquired of each one loop with a frame rate of 40-75 frame per second (FPS) and stored digitally on a hard disk for offline analysis.



**Figure 2:** Illustration of 4DXStrain speckle tracking echocardiography. GLS, Global Longitudinal Strain; GCS, Global Circumferential Strain; GRS, Global Radial Strain; GCSR, Global Circumferential Strain Rate; GRSR, Global Radial Strain Rate.

**Offline analysis of acquired images:**

Offline speckle tracking analysis was rendered employing XStrain-4D™ (Esaote), software package [16]. LV endocardial and epicardial borders were traced by 13 equidistant tracking points aligned automatically, navigated and supervised by border segmentation tool- AHS (Aided Heart Segmentation, Esaote) [16].

The paramount function of the Beutel Software - XStrain™ 4D is to blend the knowledge from 2D apical 3CH, 4CH and 2CH views and create a 3D/4D reconstruction to automatically furnish values of LV strain data [16]. A 17 segment model Bull's eye plot was generated displaying the values of LV strain.

**Strain Parameters derived from XStrain 4DSTE**

**GLS (%)**

- 3CH view (%)
- 4CH view (%)
- 2CH view (%)

**GCS**

- mv level (%)
- pap level (%)

**GCSR**

- mv level (1/sec)
- pap level (1/sec)

**Global radial strain (GRS)**

- mv level (%)
- pap level (%)

**Global radial strain rate (GRSR)**

- mv level (1/sec)
- pap level (1/sec)

GLS and GCS are allocated negative value while GRS is nominated with positive values. Similarly, strain and strain rate are earmarked % and 1/sec, respectively.

**Statistical Analysis**

The enrolled study subjects were classified into Healthy group A and CVRF group B. Additionally, cardiovascular risk factor group was further categorized into:

- Category 1
- Category 2
- Category 3

depending on the presence of one risk factor, two risk factors or three or > three risk factors.

The statistical analysis was performed employing the standard software package - Microsoft excel<sup>(R)</sup> - Excel 2019, Microsoft corporation, Seattle, Washington, USA. Shapiro Wilk test was used to evaluate the normality of distribution for the continuous variables. The variables having normal distribution were displayed as mean ± standard deviation. The calculation of 95 % confidence interval of mean was also rendered.

Statistical significance of dissimilarity between various datasets was estimated by student's *t* test for independent groups. Multiple linear regression for determination of linearity or non linearity, Kruskal-wallis test for Trend analysis and displaying their graphs was achieved. The level of significance used was <0.05. A higher p value having a probability of <0.05 was designated significant. A p value of <0.01 was designated highly significant. Non-significant was having a value of p>0.05.

**Results:**

**Demographic data**

In Group A (Table 1), there were 152 healthy subjects (male 103, female 49) and the age of males and females was 29.5 ± 10.24 years and 34.16 ± 9.95 years, respectively, suggesting that females were having significantly higher age when compared to males (p<0.01). The weight, height, body mass index (BMI), blood pressure (BP) and heart rate (HR) in males was significantly greater in males as compared to females (p<0.01).

On scrutinizing the anthropometric data of Group B, there were 348 participants amongst which males were 204 and females were 144. The age of males was 49.85 ± 12.73 years and of females was 54.92 ± 12.58 years. The weight, height, BMI, and diastolic BP (DBP) of men was significantly greater than women (p<0.01). Conversely, systolic BP (SBP) and HR were higher in females (p<0.01).

**Conventional Echocardiography Data**

The conventional echocardiographic data was obtained by routine two dimensional echocardiographic.

In males of Group A (Table 1), the left atrium size, IVSd, LVID d, LVPW d, LVEDV, LV Mass d, CO, mitral E/A ratio, LV lateral wall TDI E ' and 2D-FS values were higher than females (p<0.01). Nevertheless, EPSS, lateral wall TDI E/E ' ratio and 2D-LVEF values were greater in females (p<0.01, p>0.05, p<0.05, respectively).

On appraisal of Group B conventional echocardiographic data there were 204 male subjects and 144 females subjects. EPSS, IVSd, LVIDd, LVPWd, LVEDV, LV Mass d, CO, TDI E ' and TDI E/E ' ratio values were greater in men in comparison to women (p<0.01, p<0.05). On the contrary, left atrium size, mitral E/A ratio, 2D-LVEF and 2D-FS values were greater in women (p<0.01).

Anthropometric Data								
Variable	Group A (N-152)				Group-B (N-348)			
	M (n-103)	F (n-49)	p		M (n-204)	F (n-144)	p	
	mn ± sd	mn ± sd	value	sign.	mn ± sd	mn ± sd	value	sign.
Age(years)	29.95 ± 10.24	34.16 ± 9.95	p<0.01	**	49.85 ± 12.73	54.92 ± 12.58	p<0.01	**
Weight(kg)	64.74 ± 11.28	57.51 ± 11.02	p<0.01	**	71.85 ± 11.41	63.33 ± 9.63	p<0.01	**
Height(cm)	164.68 ± 7.30	158.02 ± 7.60	p<0.01	**	167.12 ± 6.11	158.10 ± 6.26	p<0.01	**
BSA(M2)	3.42 ± 17.47	1.57 ± 0.17	p>0.05	NS	3.54 ± 16.67	2.72 ± 12.61	p>0.05	NS
BMI	23.85 ± 3.85	22.90 ± 3.29	p<0.01	**	25.37 ± 3.44	25.37 ± 3.80	p<0.01	**
SBP(mmHg)	118.39 ± 11.33	116.63 ± 11.76	p<0.01	**	132.30 ± 19.17	137.40 ± 19.76	p<0.01	**
DBP(mmHg)	77.14 ± 7.09	75.51 ± 7.30	p<0.01	**	82.05 ± 11.20	81.61 ± 10.98	p<0.01	**

HR(bpm)	77.83 ± 14.26	81.27 ± 16.34	p<0.01	**	75.60 ± 14.28	77.41 ± 15.56	p<0.01	**
Conventional Echocardiography Data								
Variable	Group A (N-152)				Group-B (N-348)			
	M (n-103)	F (n-49)	p		M (n-204)	F (n-144)	p	
	mn ± sd	mn ± sd	value	sign.	mn ± sd	mn ± sd	value	sign.
EPSS(mm)	0.71 ± 0.63	0.73 ± 0.48	p<0.01	**	0.61 ± 0.31	0.60 ± 0.46	p<0.01	**
LA (cm)	2.86 ± 0.55	2.79 ± 0.50	p<0.01	**	3.35 ± 0.67	3.42 ± 1.81	p<0.01	**
IVS d (cm)	0.78 ± 0.18	0.72 ± 0.18	p<0.01	**	0.99 ± 0.21	0.95 ± 0.21	p<0.01	**
LVID d (cm)	4.80 ± 0.41	4.41 ± 0.74	p<0.01	**	4.71 ± 0.57	4.53 ± 0.60	p<0.01	**
LVPW d (cm)	0.80 ± 0.14	0.72 ± 0.16	p<0.01	**	0.95 ± 0.23	0.90 ± 0.17	p<0.01	**
LVEDV(ml)	108.88 ± 25.49	92.21 ± 24.59	p<0.01	**	105.56 ± 25.84	96.44 ± 29.42	p<0.01	**
LV Mass d (gm)	128.46 ± 36.16	102.84 ± 30.99	p<0.01	**	158.93 ± 44.79	139.24 ± 38.15	p<0.01	**
CO (L/min)	5.29 ± 1.44	4.94 ± 1.72	p<0.01	**	5.16 ± 1.57	4.88 ± 1.55	p<0.01	**
E/A ratio	1.58 ± 0.60	1.40 ± 0.52	p<0.01	**	1.08 ± 0.41	1.09 ± 0.89	p<0.01	**
TDI E'	11.61 ± 5.96	9.86 ± 6.72	p<0.01	**	9.68 ± 2.55	9.06 ± 2.84	p<0.01	**
TDI E/E' ratio	0.16 ± 0.24	0.28 ± 0.40	p>0.05	NS	0.26 ± 0.81	0.19 ± 0.23	p<0.05	*
2D-EF(%)	62.62 ± 7.04	65.82 ± 7.61	p<0.01	**	65.25 ± 7.40	66.93 ± 8.18	p<0.01	**
2D-FS (%)	10.07 ± 17.09	9.15 ± 14.99	p<0.01	**	36.10 ± 5.61	37.44 ± 6.40	p<0.01	**

sd, standard deviation; sign, significance; M, male; F, female; mn, mean; HR, heart rate; n, number; SBP, systolic BP; DBP, diastolic BP; EPSS, E point septal separation; CO, cardiac output; 2D, two dimensional; EF, ejection fractional; FS, fractional shortening; sign, significance.

**Table 1: Anthropometric Data & Conventional Echocardiography Data**

**Comparison of 4Dimensional XStrain speckle tracking data of Group A and Group B**

**LV Strain Data**

On comparing the LV Strain data between Group A and B (Table 2), the levels of GLS and GCS at pap level were significantly lower in Group A (p<0.01). The levels of GCS at mv level, GRS at mv and pap level and GCSR at mv and pap level in Group B were lower than Group A, even though, the values did not reach significance (p>0.05). On the contrary insignificant higher levels of GRSR at mv and pap level were present in Group B (p>0.05).

Variables	Groups		p	
	Group A (n=152)	Group B (n=348)	value	sign.
	mn ± sd	mn ± sd		
GLS(%)	-19.03 ± 3.14	-17.33 ± 3.16	0.00000005	**
GCS				
at mv level (%)	-15.91 ± 6.06	-15.34 ± 7.22	0.40	p>0.05
at pap level (%)	-23.27 ± 6.81	-21.38 ± 8.25	0.01	**
GRS				
at mv level (%)	21.88 ± 10.25	22.34 ± 11.19	0.67	p>0.05
at pap level (%)	25.67 ± 11.32	25.49 ± 10.89	0.87	p>0.05
GCSR				

at mv level (1/sec)	-2.17 ± 0.69	-2.05 ± 1.79	0.43	p>0.05
at pap level (1/sec)	-2.22 ± 1.75	-2.01 ± 0.76	0.06	p>0.05
<b>GRSR</b>				
at mv level (1/sec)	3.14 ± 0.97	3.29 ± 2.57	0.49	p>0.05
at pap level (1/sec)	2.72 ± 0.96	2.75 ± 1.26	0.78	p>0.05

mn, mean; sd, standard deviation; sign, significance; GLS, global longitudinal strain; GCS, global circumferential strain; GRS, global radial strain; GCSR, global circumferential strain rate; GRSR, global radial strain rate; mv, mitral valve; pap, papillary muscle

**Table 2: Comparison of LV strain parameters in Group A & Group B**

**Trend analysis of MLVSP:**

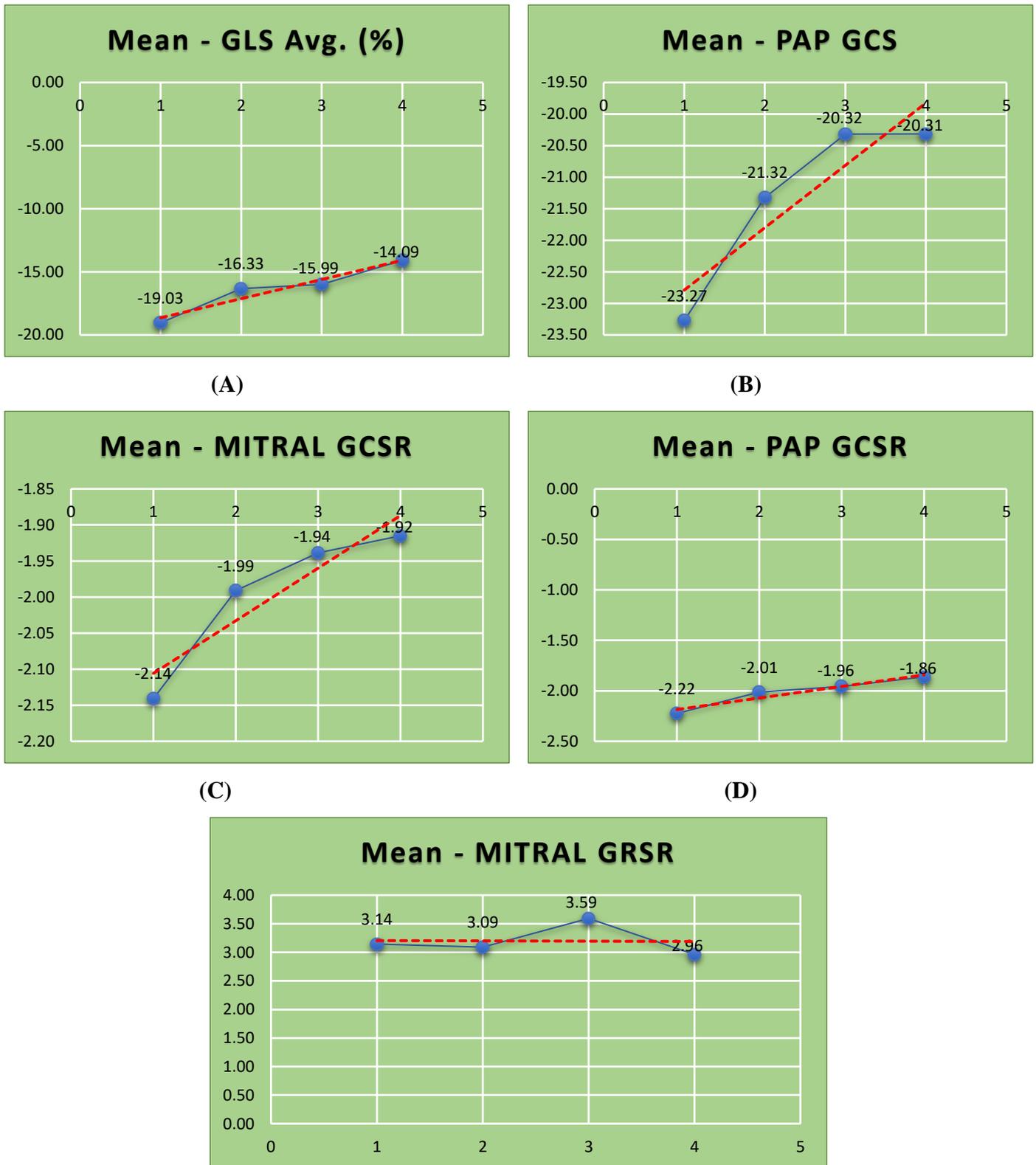
On determination of Trend analysis of MLVSP with increasing risk categories (Table 3, 4, Figure 3), there was significantly diminishing pattern of values of GLS, GCS at pap level and GCSR at mv level with increasing risk categories (p<0.01, p<0.01, p<0.05, respectively). Rest of the strain parameters demonstrated fluctuating pattern (p>0.05).

Variables	Group A (n=152) mn ± sd	Group B			p	
		Category 1 (n 130) mn ± sd	Category 2 (n 143) mn ± sd	Category 3 (n 75) mn ± sd	value	sign.
<b>GLS(%)</b>	-19.03 ± 3.14	-16.33 ± 2.17	-15.99 ± 3.53	-14.09 ± 1.58	0.0000000 000000000 000000000 00000002	**
<b>GCS</b>						
at mv level (%)	-15.91 ± 6.06	-14.95 ± 6.96	-15.37 ± 7.98	-15.62 ± 5.94	0.70	p>0.05
at pap level (%)	-23.27 ± 6.81	-21.32 ± 8.05	-20.32 ± 8.32	-20.31 ± 7.81	0.005	**
<b>GRS</b>						
at mv level (%)	21.88 ± 10.25	23.16 ± 11.81	21.77 ± 10.73	21.94 ± 10.82	0.70	p>0.05
at pap level (%)	25.67 ± 11.32	25.05 ± 10.84	24.46 ± 10.93	24.91 ± 10.31	0.82	p>0.05
<b>GCSR</b>						
at mv level (1/sec)	-2.14 ± 0.79	-1.99 ± 0.65	-1.94 ± 0.69	-1.92 ± 0.62	0.04	*
at pap level (1/sec)	-2.22 ± 1.75	-2.01 ± 0.89	-1.96 ± 0.64	-1.86 ± 0.65	0.09	p>0.05
<b>GRSR</b>						
at mv level (1/sec)	3.14 ± 0.97	3.09 ± 1.19	3.59 ± 3.77	2.96 ± 0.93	0.13	p>0.05
at pap level (1/sec)	2.72 ± 0.96	2.70 ± 1.23	2.81 ± 1.41	2.75 ± 1.33	0.87	p>0.05

sd, standard deviation; sign, significance; \*, significant; \*\*, highly significant; GLS, global longitudinal strain; GCS, global circumferential strain; GRS, global radial strain; GCSR, global circumferential strain rate; GRSR, global radial strain rate; mv, mitral valve; pap, papillary muscle

**Table 3: Trend of LV strain parameters in different cardiovascular risk factor categories**





**Figure 4:** Linear relationship graph depicting trend with increasing category of CVRF; (A), GLS; (B), GCS at pap level; (C), GCSR at mv level; (D), GCSR at pap level and (E), GRSR at mv level. (E)

**Discussion:**

2D STE is consistently utilized all over the world, owing to the fact that it has the incredible capability to non-invasively evaluate the LV systolic functions and also to analyse LV strain, volumetric and rotational (twist, torsion, rotation) mechanics [16, 17]. However, 2D, 3D and 4D STE is afflicted by several inherent limitations [17]. In the recent past an advanced version of XStrain™ 4D has been employed for superior appraisal of contractile properties of LV [17].

Nevertheless, this advanced technique has not been thoroughly utilized in clinical practice and its outstanding evaluation of deformation, rotational and volumetric mechanics remains underutilized, currently.

#### 4Dimensional / Realtime 3Dimensional / 3Dimensional versus 2Dimensional Echocardiography

Earlier research publications have illustrated the supremacy and accuracy in quantification of LVEF% and LV strain employing realtime three-dimensional (RT3DE) or 4Dimensional echocardiography in comparison to 2Dimensional echocardiography [18-20]. Superiority of these techniques is due to the 2D-LVEF % derivation being based on geometric assumptions [21].

More importantly, a couple of authors [22, 23] have made noteworthy observations that LVEF % and LV volumes were significantly higher by 2D echocardiography in comparison to RT3DE/4Dimensional echocardiography. We have conducted our research study applying 4DXStrainSTE, which estimates 4DLVEF % and LV volumes in a 3D/4D domain. Earlier studies of Takahashi et al [9] and STAAB cohort study [24] studied the impact of CVRF on LV strain engaging 2Dimensional echocardiography. Perhaps, there was limitations in the accuracy of their projected strain values due to utilization of 2D echo system.

#### Impact of Cardiovascular risk factors on LV strain parameters:

CVRF are frequently encountered in the elderly population, and if they are not addressed promptly then may cause cardiovascular disease (CVD) [25]. Consequently, the impact of multiple CVRF may lead to subclinical myocardial dysfunction [26]. An aberration in GLS in individuals with preserved LVEF has been previously documented [27] and it has been shown that risk factors could be a marker of early LV dysfunction [9]. Importantly, several studies have reported that the cardiovascular mortality increases with the presence of multiple CVRF [28, 29]. Interestingly, only few studies have been published in the recent past which have aimed to study the influence of CVRF on strain parameters in adults by 2D STE [24, 9].

In a retrospective report of Takahashi et al [9] and STAAB cohort study [24] primarily GLS was the only strain parameter estimated by 2Dimensional speckle tracking echocardiography (2DSTE) systems. In the current research LV strain analysis was achieved by 4DXStrainSTE, the superiority of which has been already established [7, 30]. Our study revealed significantly lower values of GLS and GCS at pap level in CVRF group in comparison to Healthy group ( $p<0.01$ ). The values of GCS at mv level, GRS at mv and pap level and GRSR at mv and pap level were also lower, even though, these values did not reach the level significance ( $p<0.05$ ).

Furthermore, we assessed the Trend Analysis, which displayed significantly diminishing pattern of values of GLS, GCS at pap level and GCSR at mv level with increasing risk categories ( $p<0.01$ ,  $p<0.01$ ,  $p<0.05$ , respectively). Rest of the strain parameters demonstrated fluctuating pattern ( $p>0.05$ ). Additionally, Linearity estimation exhibited linearity reduction of values of GLS, GCS at pap level, GCSR at mv and pap level and GRSR at mv level with increasing risk category ( $p<0.01$ ,  $p<0.01$ ,  $p>0.05$ ,  $p>0.05$ ,  $p<0.05$ , respectively). Trend analysis & linearity determination has never been attempted earlier.

#### Conclusion:

In the current research we have demonstrated extensive normative data on LV strain parameters in healthy Indian adults and patients with CVRF, utilizing 4DXStrainSTE. On determining the consequences of overall CVRF on LV strain the study showed lower values of GLS and GCS at pap level, ( $p<0.01$ ). The levels of GCS at mv level, GRS at mv and pap level and GCSR at mv and pap level in CVRF group were lower than Healthy Group, even though, the values did not reach significance ( $p>0.05$ ). On the contrary insignificant higher levels of GRSR at mv and pap level were present in CVRF group ( $p>0.05$ ).

Moreover, trend analysis of LV strain parameters with increasing risk category revealed significantly diminishing pattern of values of GLS, GCS at pap level and GCSR at mv level with increasing risk categories ( $p<0.01$ ,  $p<0.01$ ,  $p<0.05$ , respectively). Rest of the strain parameters demonstrated fluctuating pattern ( $p>0.05$ ). Furthermore, there was linear reduction of mean GLS, mean GCS at pap level, mean GCSR at mitral and pap level and mean GRSR at mv level with increasing risk categories ( $p<0.01$ ,  $p<0.01$ ,  $p>0.05$ ,  $p>0.05$ ,  $p<0.05$ , respectively). Contrarily, the values of GCS at mv level, GRS at mv and pap level and GRSR at mv and pap level exhibited non-linearity ( $p>0.05$ ).

To our knowledge this is singular research in the world in which 4DXStrainSTE was employed for comprehensively portraying the Trend analysis and Linearity of multifold LVSP in patients with CVRF. Additionally, the consequences on LV strain parameters on CVRF risk group was correlated with healthy group. The novel technology of XStrain 4D STE is relatively cheap and immensely valuable in generating new understanding of the intricate ventricular motion and is highly beneficial in determining the values of GLS and other multifold LV strain parameters.

#### Limitation of the present research

- This study was single center research in healthy Indian adult subjects and therefore, the normal reference values of this study cannot be considered to be similar to the other ethnic groups: Africans, Europeans, Americans etc.
- The ultrasound machine utilized has an important relevance for the assessment of numerous parameters of LV strain. The values obtained by one system may differ from the other echocardiography unit because of dissimilar software algorithm employed for tracing the endocardium [31].
- Another worrisome limitation is the non-standardization of GLS values spanning throughout different vendors, because of which the strain values will be altered [32, 33].
- Furthermore, the study was not validated against MRI, which is considered to be the gold standard for strain measurements.

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