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Research Article

Significance of Left Ventricular Strain in Traditional Cardiac Risk Factor Population

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Abstract

Background: 4-Dimensional XStrain speckle tracking echocardiography (4DXStrainSTE) is an advanced cardiac imaging technique that synthesizes speckle tracking echocardiography (STE) data obtained from the apical three-chamber (3CH), four-chamber (4CH), and two-chamber (2CH) views, thereby enabling a comprehensive evaluation of multiple left ventricular strain parameters (MLVSP) within a three-dimensional framework.

Methods: This study aimed to evaluate the impact of cardiovascular risk factors (CVRFs) on MLVSP using 4DXStrainSTE. Nine strain parameters were analyzed: global circumferential strain (GCS), global circumferential strain rate (GCSR), global radial strain (GRS), and global radial strain rate (GRSR) at the mitral valve (mv) and papillary muscle (pap) levels, along with global longitudinal strain (GLS). A total of 500 Indian adults (aged 18–60 years; both sexes) were enrolled. Participants were categorized into four CVRF Risk Categories (1, 2, 3, and 4) according to the cumulative number of risk factors. The inclusion criterion was a 4-dimensional left ventricular ejection fraction (4D-LVEF) > 50%.

Results: The effect of CVRF on strain parameters was determined using trend and linearity analyses. Trend analysis across CVRF categories revealed a significant decline in GLS, GCS at the pap level, and GCSR at the mv level. Pearson's correlation demonstrated mild-to-moderate linear associations across MLVSP, and multivariate regression analysis identified significant associations of GLS and GCSR at the mv level with GLS across the risk categories.

Conclusion: To the best of our knowledge, this is the first study to provide a comprehensive evaluation of the impact of CVRFs on MLVSP in individuals with preserved ejection fraction.

Keywords: 4DXStrain, Speckle tracking echocardiography, 4D-LVEF%, Cardiovascular risk factors, Trend analysis.

Introduction

Currently, global longitudinal strain (GLS) assessment via two-dimensional speckle tracking echocardiography (2D STE) remains one of the most extensively investigated techniques worldwide [1]. The American Society of Echocardiography recommends a normal GLS value of > −20 ± 2% [2]. Three-dimensional speckle tracking echocardiography (3D STE) enables single-apical acquisition of the left ventricle, thereby reducing acquisition time and allowing a comprehensive evaluation of strain parameters [3]. However, its clinical application is constrained by suboptimal temporal and spatial resolution, which can impair tracking accuracy. In addition, multi-beat acquisitions may introduce stitching artifacts

between sub-volumes, further compromising speckle tracking analysis [4,5].

4DXStrainSTE is an innovative and advanced imaging modality that integrates Tomtec GMBH's 3D/4D imaging platform with Beutel™ computational technology [6]. It synthesizes STE data from apical 3CH, 4CH, and 2CH views to achieve a comprehensive three-dimensional reconstruction of left ventricular (LV) strain parameters. By capitalizing on the superior temporal and spatial resolution of 2D imaging, this technique effectively mitigates the inherent limitations of full-volume 3D STE [7]. While single-plane 3D echocardiography still suffers from lower resolution compared to 2D imaging [8], 4DXStrainSTE overcomes these constraints and offers an accessible, cost-efficient, and user-friendly solution for LV strain analysis.

Previous studies have documented the impact of cardiovascular risk factors (CVRFs) on GLS [9,10], though primarily using 2D STE. A thorough literature search revealed no prior studies that comprehensively evaluated the influence of CVRFs on multiple LV strain parameters (MLVSP) through rigorous statistical techniques-namely, trend analysis, Pearson's correlation, and multivariate regression for linearity assessment. This investigation was therefore designed to address this important methodological gap.

Method

Study Center

This original research was conducted over a 28-month period (September 2021 to December 2023) at Prakash Heart Station, Lucknow, Uttar Pradesh, India.

Ethical Approval

Ethical approval was granted by the Institutional Ethics Committee of Prakash Heart Station (Approval No. IEC/PDC/PHSD/2021:01,02). All participants provided written informed consent after receiving a detailed explanation of the study's aims. The research procedures were carried out in alignment with the International Conference on Harmonisation-Good Clinical Practice (ICH-GCP) standards and adhered to the ethical principles set forth in the Declaration of Helsinki.

Study Population

This was a single-center, observational, prospective study involving 500 Indian adults aged 18–60 years, of both sexes. Participants were classified into four CVRFs categories: category 1, 2, 3, and 4 (Figure 1).

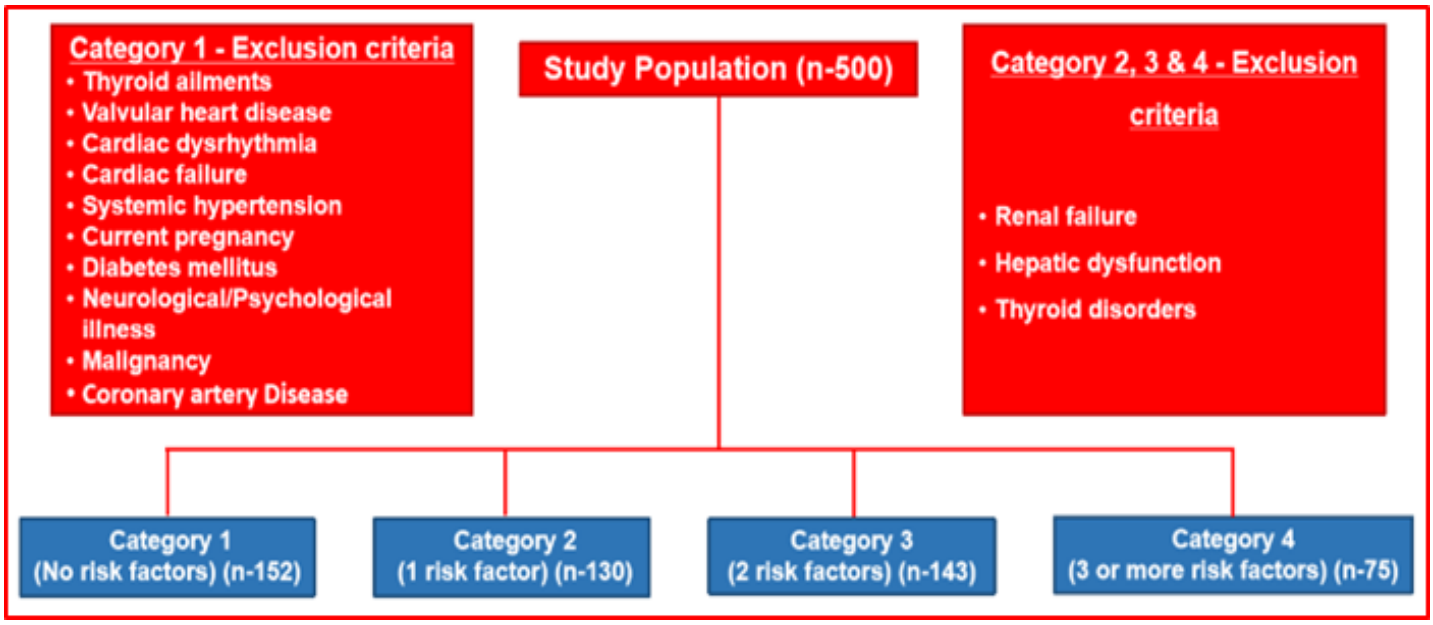

Figure1: Classification steps of the study design.

Category 1

This group included 152 healthy individuals (aged 18–60 years; both sexes) without any CVRFs, exhibiting normal resting electrocardiograms (ECG), 4DXStrainSTE findings with 4D-LVEF > 50%, and negative treadmill stress tests (TST).

Category 2, 3 & 4

This cohort comprised 348 adults (aged 18–60 years; both sexes) with one or more CVRFs, all in sinus rhythm and exhibiting a 4D-LVEF > 50%. Inclusion criteria stipulated that all participants maintain a 4D-LVEF ≥ 50%, as quantified by 4DXStrainSTE. Comprehensive clinical and medical assessments were conducted by a cardiac physician, with meticulous documentation of the CVRF profile for each participant.

Cardiovascular Risk Factors

- Cardiovascular disease:

(i) CAD: history of myocardial infarction, stable/unstable an-

gina, acute coronary syndrome, or percutaneous coronary intervention (PCI)
(ii) CVA (cerebrovascular accident)
(iii) PAD (peripheral arterial disease)
- Diabetes mellitus
- Hypertension
- Dyslipidemia
- Obesity
- Smoking

Definitions of all risk factors adhered to current guidelines [11–15].

Echocardiography

All participants underwent comprehensive cardiac evaluation using conventional two-dimensional (2D) transthoracic echocardiography and 4DXStrainSTE. Examinations were conducted on the MY LAB X7 4D XStrain system (ESAOTE, Italy) equipped with a 1–5 MHz transducer. All acquisitions were performed by the experienced study authors, with measurements obtained in accordance with the American Society of Echocardiography guidelines [16].

Conventional Echocardiography

Two-dimensional, M-mode, pulse-wave Doppler (PWD), continuous-wave Doppler (CWD), and tissue Doppler imaging (TDI) modalities were employed to evaluate standard cardiac parameters, including left ventricular (LV) volumes, systolic and diastolic function, LV mass, left ventricular ejection fraction (LVEF%), cardiac output (CO), cardiac index (CI), early diastolic (E) and late diastolic (A) velocities, E/A ratio, early myocardial relaxation velocity (E′), and the E/E′ ratio.

4-Dimensional X-Strain Echocardiography

Image Acquisition

Apical 4CH, 3CH, 2CH, and short-axis (SX) views at the mitral valve (mv) and papillary muscle (pap) levels were obtained (Figure 2). Each cine loop comprised at least three cardiac cycles, recorded at 40-75 frames per second (FPS) and stored digitally for offline analysis.

High-quality image acquisition was prioritized. Optimal ECG tracing was ensured by adjusting electrode placement on the chest and selecting the lead from the PHYSIO menu of the echocardiography system that yielded the smoothest waveform with well-defined R/Q waves and minimal noise. Traces exhibiting prominent P or T waves were avoided to prevent gating interference during 4DXStrainSTE acquisition. Participants were instructed to hold their breath at end-expiration to minimize translational and respiratory artifacts. The LV was positioned to fill the majority of the imaging sector, avoiding foreshortening. Particular care was taken to exclude papillary muscle bulges when tracing the endocardium.

High-quality short-axis views at the mv, pap, and LV apex levels were acquired to facilitate accurate computation of circumferential strain, circumferential strain rate, radial strain, and radial strain rate [17]. Clear delineation of cardiac borders was confirmed throughout the cardiac cycle.

Offline Analysis of Acquired Images

Speckle tracking analysis was performed offline using XStrain-4D™ (Esaote) software [18]. The LV endocardial and epicardial borders were automatically delineated from 13 equidistant tracking points, supported by the Aided Heart Segmentation (AHS) tool [18].

The Beutel computational platform, integrated into XStrain™ 4D, synthesizes STE data from apical 2D 3CH, 4CH, and 2CH views to reconstruct a 3D/4D LV model, enabling automated derivation of LV strain parameters [18]. A standardized 17-segment Bull's-eye plot was generated for visualization.

Strain Parameters Derived from XStrain 4DSTE

Nine strain parameters (Figure 3) were evaluated as outlined below:

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

GCS
mv level (%)
pap level (%)

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

GRS
mv level (%)
pap level (%)

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

GLS and GCS are expressed as negative values, whereas GRS is represented as positive values. Similarly, strain and strain rate are denoted in % and 1/sec, respectively.

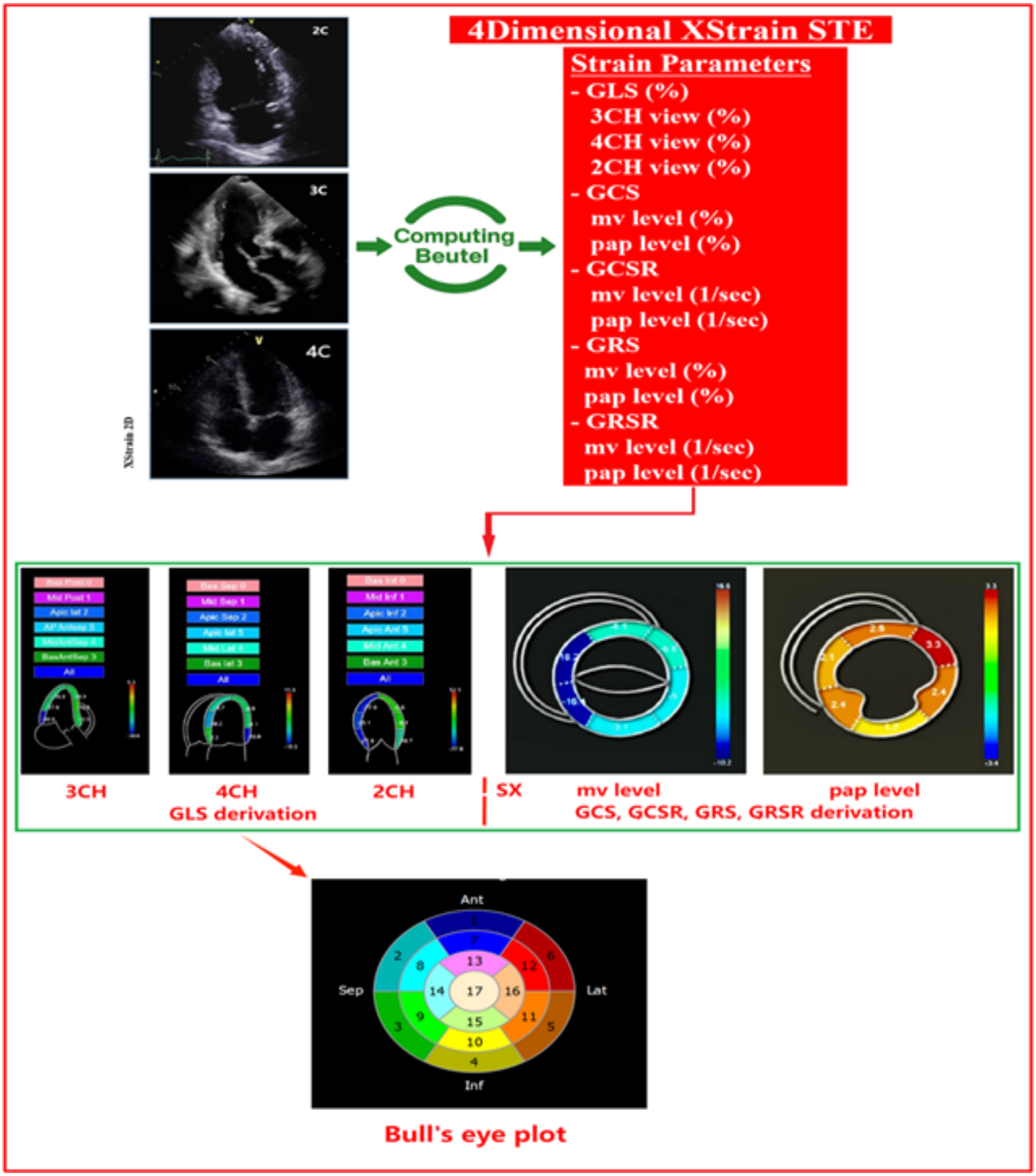

Figure 2: Illustration of 4DXStrain speckle tracking echocardiography. GLS, Global Longitudinal Strain; GCS, Global Circumferential Strain; GRS, Global Radial Strain; GCSR, Global Circumferential Strain Rate; GRSR, Global Radial Strain Rate.

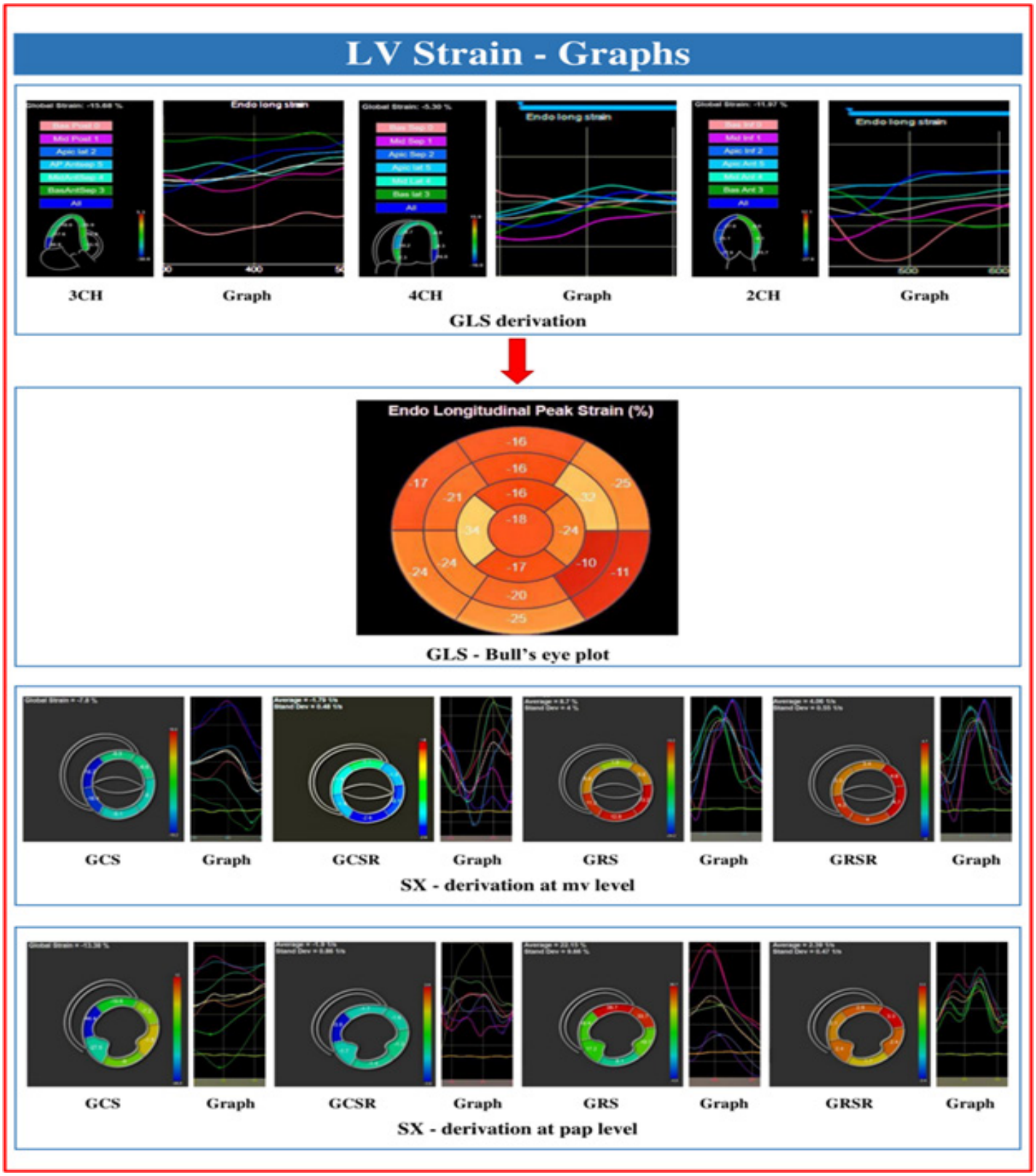

Figure3: Graphical representation of the nine LV strain parameters. GLS, Global Longitudinal Strain; GCS, Global Circumferential Strain; GRS, Global Radial Strain; GCSR, Global Circumferential Strain Rate; GRSR, Global Radial Strain Rate; mv, mitral valve; pap, papillary muscle; CH, chamber; SX, short axis view.

Statistical Analysis

Study subjects were categorized as follows:

- **Category 1:** Healthy individuals without CVRFs (Healthy group)
- **Category 2:** Individuals with only one CVRF
- **Category 3:** Individuals with two CVRFs
- **Category 4:** Individuals with three or more CVRFs

NB: The data of categories 2, 3, & 4 were pooled together for statistical analysis in Table 1 (Pooled group).

Statistical analyses were conducted using IBM SPSS Statistics, Version 26.0 (IBM Corp., Armonk, NY, USA). Graphical representations for trend analysis were created using Microsoft Excel 2013 (Version 15.0.558.1000; MSO 15.0.5589; 32-bit), included in Microsoft Office Professional Plus 2013.

- The **Shapiro–Wilk** test was conducted to assess the normality of distribution for continuous variables.
- Variables with normal distributions were expressed as **mean ± standard deviation**. The **Student's t-test** was applied to normally distributed data to determine the significance of differences between groups and risk categories (95% confidence intervals). Multiple independent t-tests comparing Risk Category 1 with Categories 2, 3, and 4 across various variables were conducted.
- For data that were not normally distributed, the **Mann–Whitney U test** was employed.
- **Levene's test** was applied to assess the homogeneity of variances.
- The **Tukey–Kramer** post hoc analysis was used to evaluate differences between parameters across CVRF risk categories.
- The **Kruskal–Wallis** test was utilized for data exhibiting unequal variances between groups.
- **Pearson's correlation coefficient** was calculated to measure the linear correlation between two data sets.
- **Trend & Multivariate regression analysis** was performed across Risk Categories 1–4.
- Continuous variables are expressed as mean ± standard deviation, whereas categorical variables are presented as frequencies and percentages (Table 1).

Statistical significance was defined as **p<0.05**, with **p<0.01** considered highly significant. Values with **p>0.05** were deemed not significant.

Results

Demographic Data

In Category 1 (Table 1), 152 healthy individuals were enrolled (103 males, 49 females). The mean age was 29.5 ± 10.24 years for males and 34.16 ± 9.95 years for females, with females being significantly older than males ($p < 0.01$). Males exhibited significantly greater weight, height, BMI, blood pressure (BP), and heart rate (HR) compared to females ($p < 0.01$).

In the pooled data, there were 348 participants (204 males, 144 females). The mean age of males was 49.85 ± 12.73 years, and that of females was 54.92 ± 12.58 years. Males had significantly higher weight, height, BMI, and diastolic BP (DBP) than females ($p < 0.01$), whereas systolic BP (SBP) and HR were significantly higher in females ($p < 0.01$).

Conventional Echocardiography Data

Routine two-dimensional echocardiography was employed to obtain conventional measurements.

In male subjects of Category 1 (Table 1), left atrial size, interventricular septal diameter (IVS d), left ventricular internal diameter in diastole (LVID d), left ventricular posterior wall diameter (LVPW d), left ventricular end-diastolic volume (LVEDV), LV mass in diastole (LV Mass d), cardiac output (CO), mitral E/A ratio, lateral wall tissue Doppler imaging (TDI) E′ velocity, and 2D fractional shortening (FS) were significantly greater than in females ($p < 0.01$). Conversely, E-point septal separation (EPSS), lateral wall TDI E/E′ ratio, and 2D left ventricular ejection fraction (2D-LVEF) were greater in females ($p < 0.01$, $p > 0.05$, and $p < 0.05$, respectively).

Pooled data values for EPSS, IVSd, LVID d, LVPW d, LVEDV, LV Mass d, CO, TDI E′, and TDI E/E′ ratio were significantly higher in males ($p < 0.01$, $p < 0.05$). In contrast, left atrial size, mitral E/A ratio, 2D-LVEF, and 2D-FS were significantly higher in females ($p < 0.01$).

4-Dimensional XStrain Speckle Tracking Data

LV Strain Data

A comparative analysis of LV strain parameters between category 1 and the pooled category (Table 1) revealed a significant reduction in GLS and GCS at the pap level in the pooled category ($p < 0.001$ and $p = 0.01$, respectively), although GCSR at the pap level showed borderline significance ($p = 0.06$). Nevertheless, GCS at the mv level, global GRS at both mitral and papillary levels, and GCSR at the mv level were also lower in the pooled category; however, these differences did not reach statistical significance ($p > 0.05$). Meanwhile, GRSR at both the mitral and papillary levels was marginally higher in the pooled category, though this increase was not statistically significant ($p > 0.05$).

Demograhpic Data								
Variable	**Category 1 (N-152)**				**Pooled category (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	**Category 1 (N-152)**				**Pooled category (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	**
Variables	**Categories**				**p**			
	Category 1 (N-152)		**Pooled category (N-348)**		**value**		**sign.**	
	mn ± sd		**mn ± sd**					
GLS (%)	-19.03 ± 3.14		-17.33 ± 3.16		0.00000005		p<0.001	
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		p 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	BS
GRSR				
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

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; *, significant; ** , highly significant; NS, not significant; 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; BS, borderline significant.

Table1: Demographic, Conventional Echocardiography & Strain Data

Trend Analysis of Multiple Left Ventricular Strain Parameters

Trend analysis of MLVSP across ascending CVRF categories (Table 2, Figure 4) demonstrated a strong and statistically significant downward trajectory in GLS and GCS at the pap level ($p < 0.01$), indicating progressive deterioration in myocardial deformation with increasing cardiovascular risk. GCSR at the mv level also exhibited a mild yet statistically significant decline ($p < 0.05$), whereas GCSR at the papillary level showed borderline significance ($p = 0.09$). Other parameters, including radial strain and their respective strain rates, did not display significant trends ($p > 0.05$), suggesting relative preservation of these strain dimensions across risk categories.

Variables	**Category 1 (n=152)**	**Category 2 (n 130)**	**Category 3 (n 143)**	**Category 4 (n 75)**	**Trend\p value**	**sign.**
	mn ± sd	**mn ± sd**	**mn ± sd**	**mn ± sd**		
GLS(%)	-19.03 ± 3.14	-16.33 ± 2.17	-15.99 ± 3.53	-14.09 ± 1.58	p=0.001	p<0.01
GCS						
at mv level (%)	-15.91 ± 6.06	-14.95 ± 6.96	-15.37 ± 7.98	-15.62 ± 5.94	p=0.70	p>0.05
at pap level (%)	-23.27 ± 6.81	-21.32 ± 8.05	-20.32 ± 8.32	-20.31 ± 7.81	p=0.005	p<0.01
GRS						
at mv level (%)	21.88 ± 10.25	23.16 ± 11.81	21.77 ± 10.73	21.94 ± 10.82	p=0.71	p>0.05
at pap level (%)	25.67 ± 11.32	25.05 ± 10.84	24.46 ± 10.93	24.91 ± 10.31	p=0.82	p>0.05
GCSR						
at mv level (1/sec)	-2.14 ± 0.79	-1.99 ± 0.65	-1.94 ± 0.69	-1.92 ± 0.62	p=0.04	p<0.05
at pap level (1/sec)	-2.22 ± 1.75	-2.01 ± 0.89	-1.96 ± 0.64	-1.86 ± 0.65	p=0.09	BS
GRSR						
at mv level (1/sec)	3.14 ± 0.97	3.09 ± 1.19	3.59 ± 3.77	2.96 ± 0.93	p=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	p=0.87	p>0.05

sd, standard deviation; sign, significance; BS, borderline 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.

Table2: Trend of LV strain parameters in cardiovascular risk factor categories

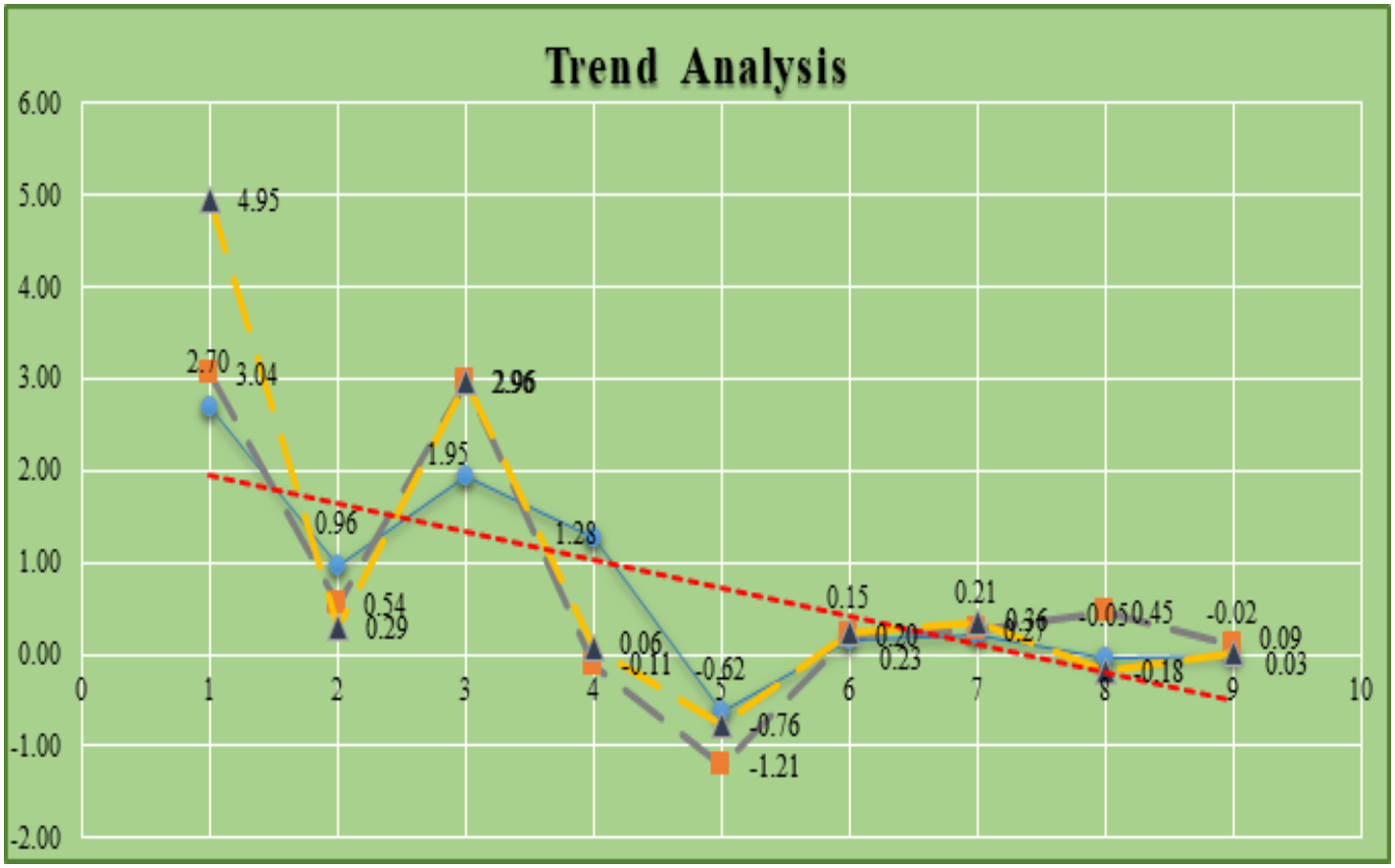

Figure4: Graphical illustration of the trend analysis of MLVSP across cardiovascular risk categories 1–4, highlighting the progressive decline in GLS and GCS at pap level with increasing risk burden.

Pearson's Correlation (Bivariate Analysis)

Pearson's correlation analysis revealed predominantly weak to moderate linear relationships among the strain parameters, suggesting generally mild associations (Table 3, Figure 5):

- **Moderate negative correlations** were observed between:
  - GCS and GRS at the mv level (r = –0.463)
  - GCS and GRS at the pap level (r = –0.528)

These findings suggest a notable inverse relationship, wherein increased GCS may correspond with reduced GRS at the respective anatomical levels.

- Most of the remaining correlations were **weakly positive or weakly negative**, indicating limited linear dependency among the majority of strain parameters.

Despite the small effect sizes, **several of these correlations were statistically significant**, as supported by corresponding *p-values*.

		GLS (%)	GCS mv level	GCS pap level	GRS mv level	GRS pap level	GCSR mv level	GCSR pap level	GRSR mv level	GRSR pap level
GLS (%)	**r**	1	0.013	0.180	-0.045	-0.063	0.070	0.113	0.034	0.012
	Sig. (2-tailed)		0.764	0.0001	0.318	0.161	0.116	0.011	0.443	0.793
GCS mv level	**r**	0.013	1	0.300	-0.463	-0.166	0.252	0.082	-0.085	-0.092
	Sig. (2-tailed)	0.764		0.0000 00000 01	0.00000 0000000 0000000 00000001	0.0002	0.0000 0001	0.066	0.057	0.039

GCS pap level	**r**	0.180	0.3	1	-0.136	-0.528	0.198	0.359	-0.002	-0.113
	Sig. (2-tailed)	0.0001	0.00000000001		0.002	0.0000000000000000000000000000000000003	0.00001	0.0000000000000001	0.963	0.011
GRS mv level	**r**	-0.045	-0.463	-0.136	1	0.219	-0.171	-0.007	0.121	-0.034
	Sig. (2-tailed)	0.318	0.0000000000000000000000000001	0.002		0.000001	0.0001	0.880	0.007	0.442
GRS pap level	**r**	-0.063	-0.166	-0.528	0.219	1	-0.093	-0.149	-0.078	0.141
	Sig. (2-tailed)	0.161	0.0002	0.0000000000000000000000000000000000003	0.000001		0.038	0.001	0.081	0.002
GCSR mv level	**r**	0.070	0.252	0.198	-0.171	-0.093	1	0.194	-0.262	-0.104
	Sig. (2-tailed)	0.116	0.00000001	0.00001	0.0001	0.038		0.00001	0.000000003	0.020
GCSR pap level	**r**	0.113	0.082	0.359	-0.007	-0.149	0.194	1	-0.055	-0.216
	Sig. (2-tailed)	0.011	0.066	0.0000000000000001	0.880	0.001	0.00001		0.224	0.000001
GRSR mv level	**r**	0.034	-0.085	-0.002	0.121	-0.078	-0.262	-0.055	1	0.130
	Sig. (2-tailed)	0.443	0.057	0.963	0.007	0.081	0.000000003	0.224		0.004
GRSR pap level	**r**	0.012	-0.092	-0.113	-0.034	0.141	-0.104	-0.216	0.13	1
	Sig. (2-tailed)	0.793	0.039	0.011	0.442	0.002	0.020	0.000001	0.004	

	Strong Negative Correlations	r ≤ –0.70
	Moderate Negative Correlations	r = –0.40 to –0.69
	Weak Negative Correlations	r = –0.10 to –0.39
	Weak Positive Correlations	r = +0.10 to +0.39
	Moderate Positive Correlations	r = +0.40 to +0.69
	Strong Positive Correlations	r ≥ +0.70

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; sig., significance;

Table3: Pearson's correlation coefficient (Bivariate analysis)

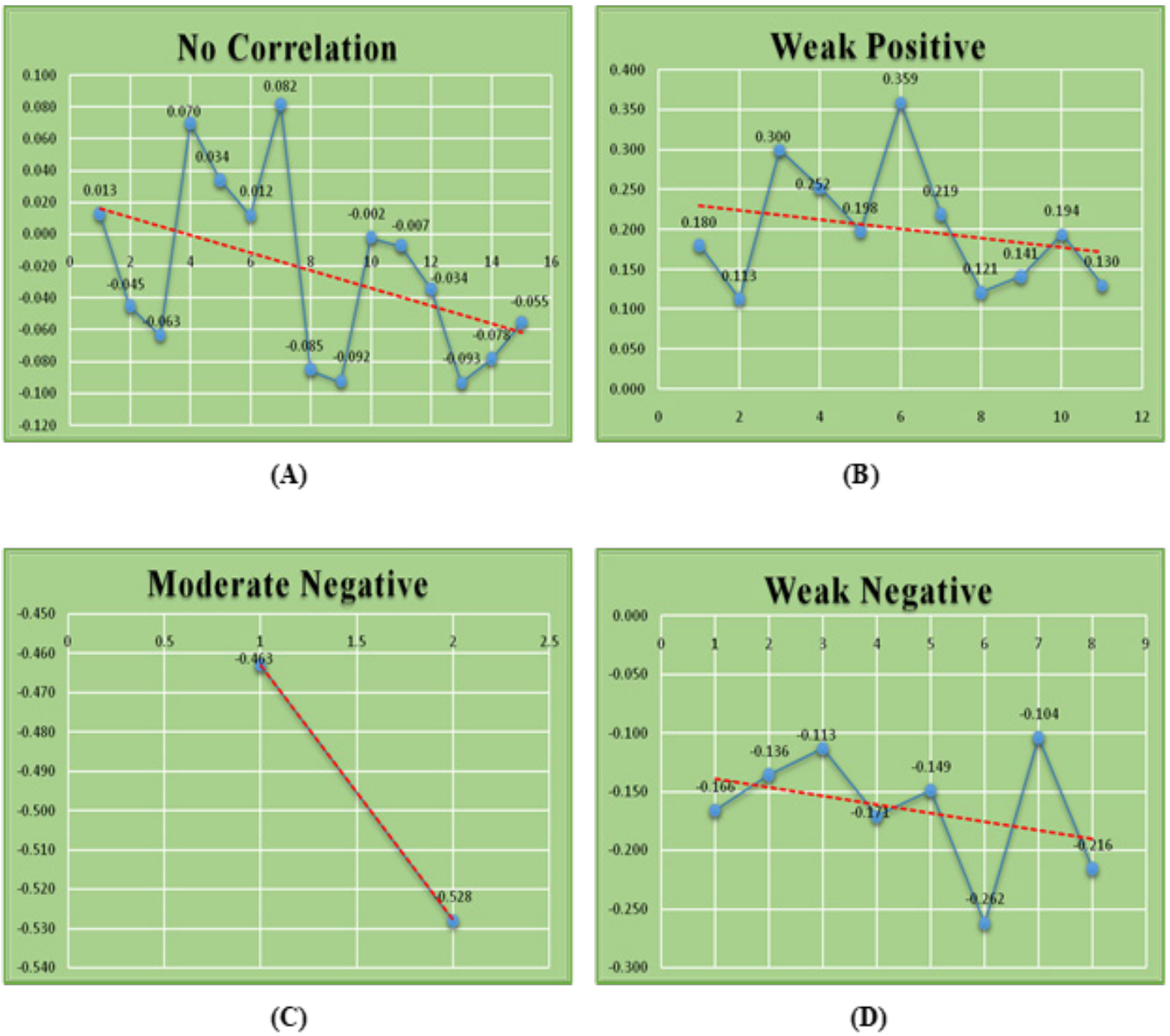

Figure5: Pearson's correlation: (A), No correlation; (B), Weak Positive; (C), Moderate Negative; (D), Weak Negative.

Multivariate Regression Analysis

On multivariate regression analysis, the following significant associations were identified (Table 4, Figure 6):

- Risk Category 3 – GLS (β = –0.164, p = 0.043),
- Risk Category 2 – GCSR at mv level (β = –0.174, p = 0.032), and
- Risk Category 4 – GCSR at mv level (β = –0.188, p = 0.021),

all demonstrated statistically significant associations with Risk Category 1 – GLS.

Other LV strain parameters did not exhibit any independent significant associations.

Parameters		Multivariate (β)	Correlations	p-values
GLS (%)	Risk category 2	0.130	0.126	0.109
	Risk category 3	-0.164	-0.160	* 0.043
	Risk category 4	-0.068	-0.064	0.397
GCS mv level	Risk category 2	0.69	0.103	0.410
	Risk category 3	-0.103	-0.125	0.214
	Risk category 4	-0.102	-0.122	0.215
GCS pap level	Risk category 2	0.056	0.070	0.499
	Risk category 3	-0.124	-0.131	0.138
	Risk category 4	-0.007	-0.018	0.933
GRS mv level	Risk category 2	-0.027	-0.032	0.745
	Risk category 3	0.045	0.048	0.588
	Risk category 4	0.034	0.033	0.677
GRS pap level	Risk category 2	-0.121	-0.144	0.144
	Risk category 3	-0.038	-0.025	0.641
	Risk category 4	0.037	0.032	0.654
GCSR mv level	Risk category 2	-0.174	-0.151	* 0.032
	Risk category 3	-0.027	-0.026	0.733
	Risk category 4	0.188	0.168	* 0.021
GCSR pap level	Risk category 2	0.033	0.029	0.693
	Risk category 3	0.025	0.021	0.768
	Risk category 4	0.011	0.010	0.896
GRSR mv level	Risk category 2	0.080	0.079	0.331
	Risk category 3	-0.010	-0.008	0.905
	Risk category 4	0.075	0.075	0.359
GRSR pap level	Risk category 2	-0.002	-0.003	0.981
	Risk category 3	0.038	0.038	0.644
	Risk category 4	0.018	-0.017	0.828

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; *, $p<0.05$.

Table4: Multivariate regression analysis

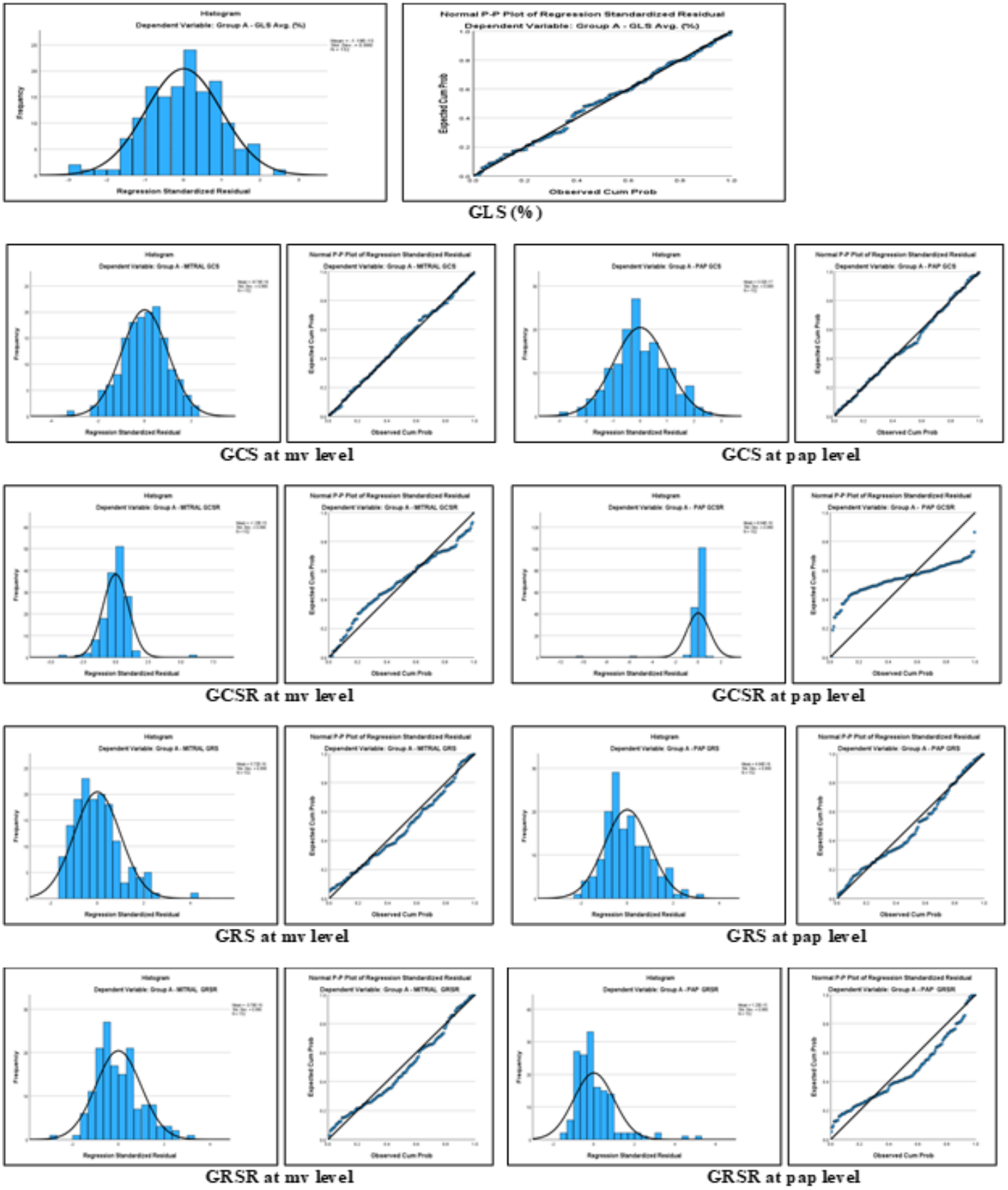

Figure6: Graphical Illustration of multivariate regression analysis of MLVSP across risk categories.

Discussion

Two-dimensional speckle tracking echocardiography (2D STE) remains a widely employed, non-invasive modality for evaluating left ventricular (LV) systolic function, as well as strain, volumetric indices, and rotational mechanics—including twist, torsion, and rotation [17,18]. However, inherent limitations persist across 2D, 3D, and 4D STE platforms [17]. The most recent innovation, XStrain™ 4D, was developed to improve the precision of LV contractile function assessment [17], although its adoption in routine clinical practice remains limited.

4Dimensional/3Dimensional versus 2Dimensional Speckle Tracking Echocardiography

Prior studies have demonstrated that real-time three-dimensional echocardiography (RT3DE) and four-dimensional STE (4D STE) offer superior accuracy in quantifying LV ejection fraction (LVEF) and strain parameters compared to conventional 2D echocardiography [19-21]. This advantage largely stems from the geometric assumptions inherent to 2D-derived LVEF calculations [22]. Indeed, several reports have shown that LVEF and LV volumes measured by 2D imaging tend to be overestimated relative to RT3DE or 4D modalities [23, 24]. In the present study, we employed 4DXStrainSTE to perform LVEF and volumetric assessments within a true 3D/4D analytical framework.

Earlier work by Takahashi et al. [9] and the STAAB cohort [25] examined the influence of CVRFs on LV strain using 2D echocardiographic platforms. However, 2D-based methods may compromise strain accuracy due to spatial and geometric limitations. In contrast, our study leveraged 4DXStrainSTE-a technologically advanced and potentially more precise modality [7,26].

Clinical Significance of Cardiovascular Risk Factors on LV Strain

GLS has emerged as a sensitive and prognostically valuable marker of adverse cardiovascular outcomes, often surpassing GCS and GRS in predictive capacity. This superiority likely reflects the vulnerability of subendocardial, longitudinally oriented myocardial fibers to early pathological insults during the initial stages of myocardial dysfunction [27,28]. Conversely, circumferential strain-reflecting mid-wall circumferential fibers-typically remains preserved until later disease stages [29]. Radial strain, representing myocardial wall thickening in the radial dimension, is comparatively less sensitive to early changes [30]. Strain rate parameters provide complementary insights into the velocity of myocardial deformation, thereby refining the characterization of contraction and relaxation kinetics.

CVRFs are highly prevalent among older adults and, if unaddressed, predispose individuals to overt cardiovascular disease (CVD) [31]. The cumulative presence of multiple CVRFs has been implicated in the development of subclinical myocardial dysfunction [32]. Importantly, impaired GLS has been reported even in individuals with preserved LVEF, underscoring its value as an early marker of myocardial impairment [33]. Moreover, multiple studies have linked an increasing burden of CVRFs with stepwise elevations in cardiovascular mortality risk [34,35].

Although prior investigations have explored the relationship between CVRFs and strain-primarily GLS-using 2D STE [9,25], our study, employing 4DXStrainSTE, detected significantly lower GLS and GCS at the papillary level in pooled CVRF categories compared with the low-risk group ($p < 0.01$). While reductions in GCS at the mitral level, GRS at both mitral and papillary levels, and GRSR were also observed in the CVRF group, these differences did not achieve statistical significance ($p > 0.05$).

Furthermore, trend analysis and linearity testing via Pearson's correlation and multivariate regression demonstrated a significant, progressive decline in GLS and GCS at the papillary level across ascending CVRF categories, consistent with worsening myocardial deformation. GCSR at the papillary level showed borderline significance ($p = 0.09$). Pearson's bivariate correlation revealed predominantly mild linear associations among strain indices, while multivariate regression identified significant associations between GLS and GCSR at the mitral level with GLS.

GLS remains the most widely adopted strain parameter in both clinical and research settings [36]. However, there is a notable paucity of studies systematically evaluating the impact of CVRFs on GCS and GRS. To our knowledge, this is the first study to comprehensively examine the clinical implications of CVRFs on GCS, GRS, GCSR, and GRSR using an advanced 4DXStrainSTE platform.

Conclusion

This study provides comprehensive normative data on LV strain parameters in healthy Indian adults and individuals with CVRFs, assessed using advanced 4DXStrainSTE. The presence of CVRFs was significantly associated with reduced GLS and GCS at the papillary level ($p < 0.01$), while GCSR at the papillary level showed a borderline reduction ($p = 0.06$). In contrast, GRSR values were marginally higher but not statistically significant ($p > 0.05$).

A robust statistical approach-including trend analysis, Pearson's correlation, and multivariate regression-demonstrated that ascending CVRF categories were associated with a significant stepwise decline in GLS and GCS at the papillary level ($p < 0.01$), GCSR at the mitral level ($p < 0.05$), and borderline significance for GCSR at the papillary level ($p = 0.09$), indicating progressive myocardial dysfunction. Other parameters showed non-significant or inconsistent patterns ($p > 0.05$). Pearson's correlation revealed predominantly mild linear associations among strain parameters, while mul-

tivariate regression identified significant associations of GLS and GCSR at the mitral level with GLS.

To the best of our knowledge, this is the first single-center investigation to comprehensively evaluate MLVSP in the context of CVRFs using 4DXStrainSTE. The results highlight distinct differences in LV strain profiles between CVRF-affected individuals and healthy controls, supporting the clinical utility of XStrain™ 4D STE as a cost-effective and sensitive tool for detailed ventricular mechanics assessment, particularly for GLS and related strain parameters.

Limitations of the Present Research

1. This was a single-center study conducted on healthy Indian adults. Therefore, the reference values generated cannot be extrapolated to other ethnic groups such as Africans, Europeans, or Americans.
2. The specific ultrasound system used plays a significant role in strain evaluation, and values may differ when using other echocardiographic platforms due to software algorithm variability [37].
3. A major limitation lies in the lack of standardization of GLS values across vendors, which can affect strain measurements [38,39].
4. The study did not incorporate validation against cardiac magnetic resonance tagging (CMR-TAG) or feature tracking (CMR-FT) [40], which remain the gold standards for strain analysis.

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