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Normal Value Ranges of LV Deformation, Rotation and Twist Parameters in Healthy Adults by 4Dimensional XStrain Speckle Tracking Echocardiography

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Abstract

XStrain 4D Speckle tracking echocardiography is a novel approach to address both the strain deformation and rotational mechanics of LV. The aim was to comprehensively present the normal value ranges of LV strain and rotational parameters of healthy Indian adults after assessment with this innovative technique. The study population comprising of 80 adults (58 males, 22 females; Group A < 30 years, Group B > 31 years) is revealing the values of Global longitudinal strain (GLS), Global longitudinal strain rate (GLSR), Transverse strain (TS), Transverse strain rate (TSR), Shear and Shear rate are greater in men than in women (p<0.01) and moreover in Group A, Global Circumferential strain (GCS), Global Circumferential strain rate (GCSR), Global Radial strain and Global Radial strain rate (GRSR) were similarly higher in men. Peak apical rotation, peak twist, twist rate and untwist rate values were again greater in men (p<0.01) and increased with advancing age. This is the first study to present a candid and comprehensive analysis of extensive parameters of LV strain and rotational mechanics in healthy Indian adults.

Keywords: *4Dimensional XStrain echocardiography, LV rotational mechanics, LV twist and torsion, Speckle tracking echocardiography*

Introduction

Global longitudinal strain (GLS) is the most-studied two-dimensional speckle tracking echocardiography (2D-STE) parameter and is now part of routine assessment of numerous echocardiographic laboratories worldwide. GLS varied from -15.9 % to -22.1% in a meta-analysis of 24 studies, which included 2597 healthy participants [1]. After reviewing the abundant data on GLS, the American society of echocardiography suggested a valve of above -20 ±2 % to be normal [2]. The three-dimensional (3D) STE techniques are feasible enough to measure real-time volumetric data, strain components, LV rotation, twist and torsion, in all LV segments, from a single acquisition [3]. Even though 3D-STE overcomes significant limitations of 2D-STE, neverthless 3D-STE is challenging, as both the temporal and spatial resolution of 3D data set are inferior to 2D imaging, and there is a possibility of speckle decorrelation between subsequent volumes [4, 5].

Lower, in 1669, was the first to describe the twisting motion of the left ventricle (LV) [6]. LV rotational deformation resembles the wringing of a towel (Figure 1).

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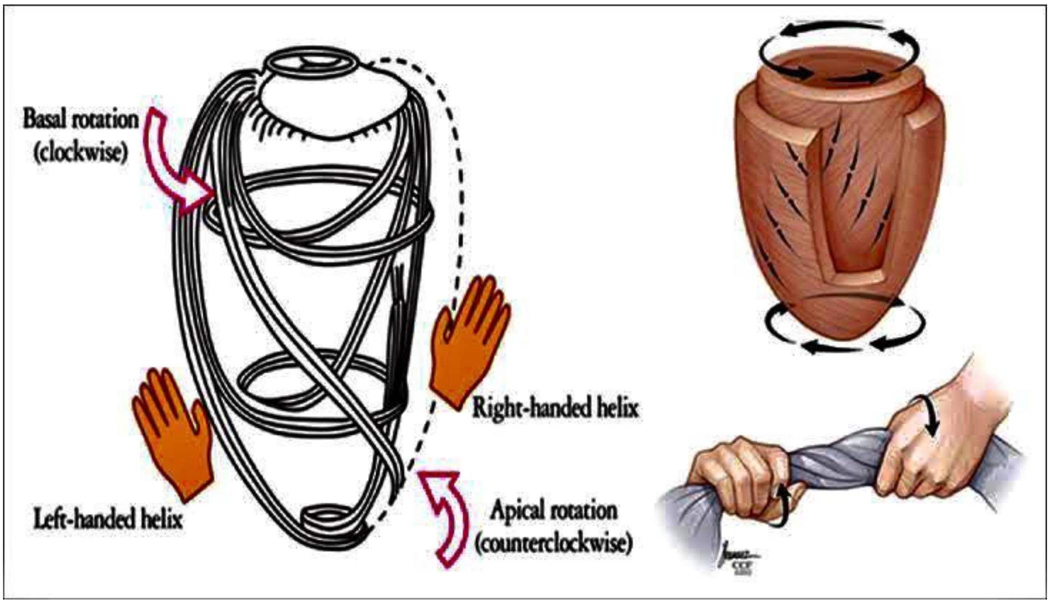

Figure 1. LV Twist

This wringing deformation is referred to as LV twist (LVT), and the subsequent recoil that occurs in diastole is referred to as LV untwist (LVUT) [7, 8]. Importantly, LV twist is the net difference between basal and apical rotation and LV torsion is derived by dividing the twist angle by the distance between LV apex and base (Figure 2).

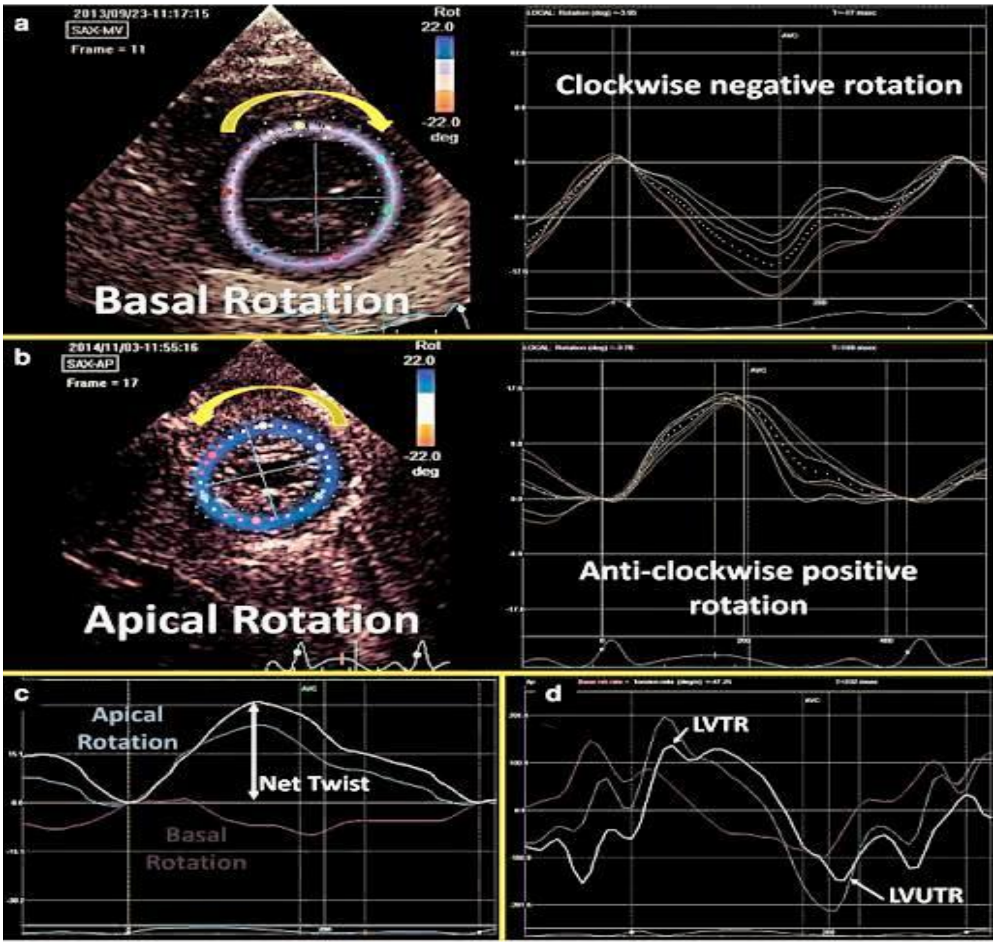

Figure 2. LV Apical, Basal Rotation, LVTR and LVUTR

XStrain 4D analysis is a novel approach that quantifies regional function from routine grayscale 2D echocardiographic images by fusing 2D speckle tracking information obtained from standard apical 4CH, 2CH, and LAX views and aims to make myocardial quantification imaging interpretation easier by the 3D/4D reconstruction of the LV. The user can freely rotate and zoom the Beutel and superimpose the echographic scanning planes to better evaluate the contractility properties of the LV, using a physiological tool to analyze the complex multi-dimensional LV mechanics [9] (Figure3).

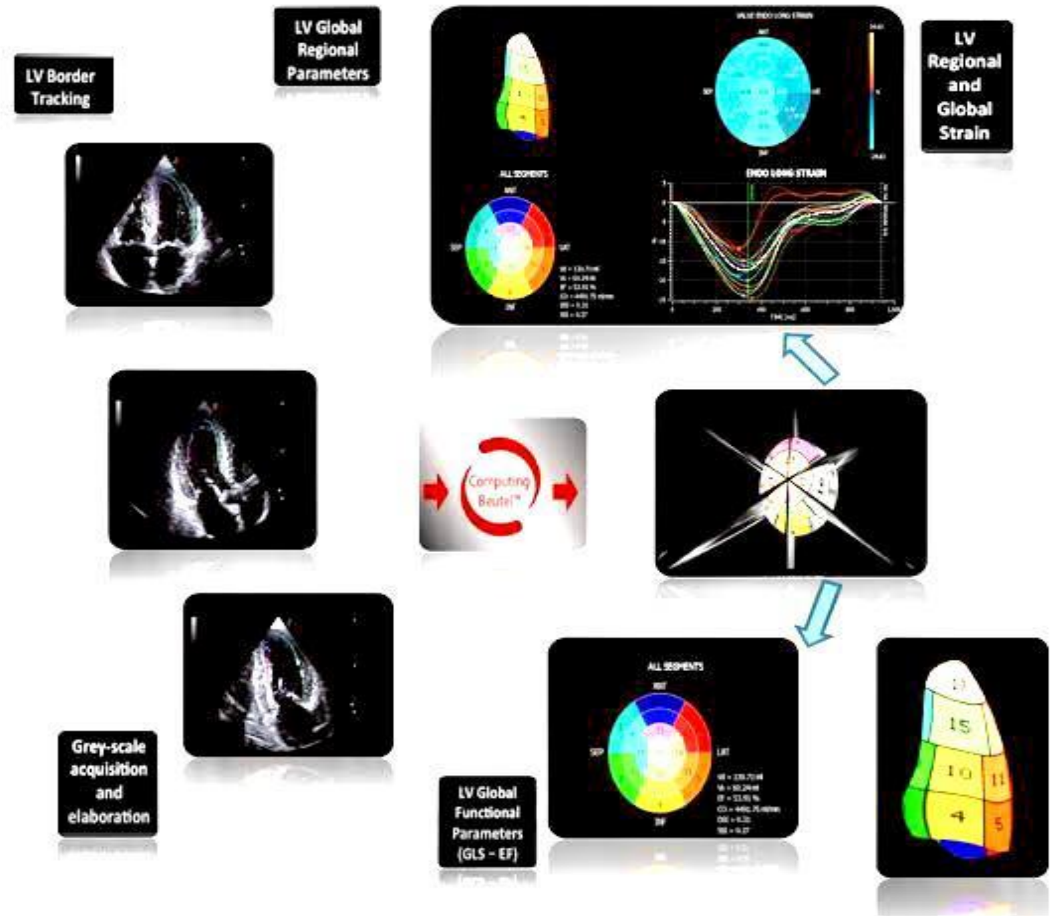

Figure 3. XStrain 4D global LV Strain Analysis

This innovative technology provides an additional effective and easy to use tool to add value to the traditional 2DE information and is especially emerging in this context. Utilizing LV border tracking XStrain4D delivers a more complete and intuitive picture of cardiac deformation behavior, providing temporal compensation for heart rate variations, spatial alignment of the 3 views in 3D space, and adaptation of a dynamic LV surface model. This tool, relying on the high spatial and temporal resolution of 2D imaging acquisitions, addresses and resolves the major limitations and criticalities currently related to the use of full-volume 3D STE [10-14]. Moreover, this advanced technique can analyse both deformation and rotational parameters meticulously, thoroughly, and accurately.

It has been advocated that eventually, a consolidated approach in which both changes in LV rotational mechanics and longitudinal shortening are vigorously evaluated and elucidated in an integrated way to establish the normal reference values [15-17]. The calculation of ventricular torsion from rotation and longitudinal strain by means of STE can provide complementary information about systolic ventricular function in relation to the traditional parameters used in daily practice, such as LVEF [18].

However, to be clinically useful, all these new parameters of myocardial and LV function need reference values that can be compared with data obtained from patients with suspected myocardial diseases. To date, reference values for deformation and rotational parameters are limited, heterogeneous, and sometimes inconsistent [19-22].

Accordingly, we present comprehensive values of strain and rotational mechanics obtained with STE by 4D XStrain speckle tracking echocardiography in healthy Indian adults and moreover to assess their relationship with sex and age.

Material and Methods

Study Population & Design

The present study was conducted at Prakash heart station and diagnostic, Lucknow, India, an approved centre of Texila American University for the current PHD Cardiology program of the author. The contemporary work was reviewed and approved by the Research Ethics Committee of our institution, and all subjects gave written informed consent. The study comprised of 107 healthy adults from which 27 cases were excluded due to inferior image quality, and finally, 80 participants were enrolled after a careful selection process during a period spanning for 9 months from June 2021-Feb 2022.

The study population consisted of 80 healthy adults of age group 18-60 years of either sex. The study group was arbitrarily divided into two groups: Group A containing subjects of 18-30 years of age, and Group B consisting of 31-60 years. Those participants were included if they were asymptomatic with a normal physical examination, BMI-23 or less, waist size 85 cm^2 or less in men and 80 cm^2 or less in women, free from overt cardiovascular disease, not receiving any drugs, non-smoker, non-tobacco chewer, non-diabetic, non-hypertensive according to JNC-8 guidelines, having normal thyroid and lipid profile, normal resting ECG in sinus rhythm with a normal 2DE and Treadmill Stress ECG. Those individuals were excluded if there was a presence of diabetes mellitus, neurological or psychiatric illness, malignancy, CAD, Aortic root abnormalities and aortic dilatation, thyroid disease, valvular heart disease, history of cardiac rhythm abnormalities, heart failure, systemic hypertension and significant pulmonary hypertension.

Methods

All the study population individuals underwent full history taking, clinical examination and a standard resting 12 lead ECG.

Biochemical & Hormonal Assessment

Blood samples were withdrawn, in the morning, after 12 hours of overnight fasting for HBAIC, T3, T4, TSH, Serum creatinine, Serum uric acid, Total cholesterol (TC), Triglycerides (TG) & high-density cholesterol (HDL-C). Serum Low-density Lipoprotein cholesterol (LDL-C) was calculated according to Freidwald’s formula [23].

Echocardiography

Echocardiographic examination was done employing My Lab X7 4D XStrain echocardiography machine of Esaote, Italy, equipped with a harmonic variable frequency (1-5 Mhz) electronic single-crystal array transducer, in left lateral decubitis position as recommended by American Society of Echocardiography [24] and connected to 3 lead ECG for continuous monitoring during the echocardiographic study.

Conventional Echocardiography

1. M-Mode: for measurements of wall thickness, dimensions, ejection fraction LV mass, LVEDV, LVESV, and Cardiac output (CO).
   a. LV mass was calculated using the Devereux formula [25].

2. Doppler flow: The mitral inflow velocities were recorded and the following.
   b. Velocities were measured: peak velocity of early diastolic wave velocity (E), late diastolic wave velocity (A) and E/A ratio.

Doppler Tissue Imaging

1.5-mm sample volume was placed at the lateral mitral of the mitral annulus in an apical 4-chamber view. Analysis was performed for the measurements of early diastolic wave velocity (E') and E/E' ratio.

1. 4D XStrain speckle tracking echocardiography.

A minimum of 3 consecutive cardiac cycles were acquired for STE analysis.

a. Measurements of the global strain of the LV

Three LV apical long-axis views: apical four-chamber, two-chamber, and apical three-chamber views were acquired; these views were taken at a frame rate ranging 40-75 frames/sec and stored digitally on hard disk for off-line analysis by software package XStrain™ advanced technology with TOMTEC GMGH 3D/4D rendering and Beutel ™ computation compabilities [9]. The endocardial border of the LV was semi-automatically tracked and then the software automatically generated a second, larger, concentric tracing at the epicardium so that all the LV myocardium became included. Then, the software automatically transformed each LV view into 6 equal segments and performed the speckle-tracking on a frame-to-frame basis [26]. After outlining the left ventricular endocardium in all recorded projections, the computer marked the left ventricle muscle area and divided it into 17 segments and then plotted the curves of left ventricular strain. Mitral and aortic flow velocities were recorded using pulsed-wave Doppler to measure the timing of cardiac events.

b. Measurements of LV twist

A short axis view at the level of the mitral valve was obtained by tilting the probe slightly upward until we got the characteristic fish mouth appearance of the mitral valve, and an apical short-axis view was acquired by tilting the probe further upwards until we got a cross-section of the LV apex. Speckle-tracking imaging analysis was performed using the available software as mentioned earlier [9].

Using the average of LV rotations from the 6 segments, we measured the basal and apical rotation taking into consideration to measure the mean rotation at aortic valve closure. The apical rotation was expressed in positive values, while the basal rotation in negative values. LV twist equals the apical rotation minus the basal rotation. Rotation and twist are expressed in degrees. [26]. Following the acquisition, the parameters enumerated below will be evaluated:

Apical Long Axis

2CH View

a. Global longitudinal strain (%).
b. Global longitudinal strain Rate (1/s).
c. Longitudinal velocity (cm/s).
d. Transverse velocity (cm/s).
e. Transverse strain (%).
f. Transverse strain rate (1/s).
g. Shear (%).
h. Shear rate (1/s).

3 CH View

a. Global longitudinal strain (%).
b. Global longitudinal strain Rate (1/s).
c. Longitudinal velocity (cm/s).
d. Transverse velocity (cm/s).
e. Transverse strain (%).
f. Transverse strain rate (1/s).
g. Shear (%).
h. Shear rate (1/s).

4 CH View

a. Global longitudinal strain (%).
b. Global longitudinal strain Rate (1/s).
c. Longitudinal velocity (cm/s).
d. Transverse velocity (cm/s).
e. Transverse strain (%).
f. Transverse strain rate (1/s).

g. Shear (%).
h. Shear rate (1/s).

Short Axis

At LV apex

a. Apical Rotation - Peak (o).
b. Apical Rotation - Time to peak (ms).

At Mv level

a. Rotational velocity (^{o}/s).
b. Radial Velocity (cm/s).
c. Global Circumferential strain (GCS) (%).
d. Global Circumferential strain Rate (GCSR) (1/s).
e. Global Radial Strain (GRS) (%).
f. Global Radial Strain Rate (GRSR) (1/s).

At Pap. Muscle level

a. Rotational velocity (^{o}/s).
b. Radial Velocity (cm/s).
c. Global Circumferential strain (GCS) (%).
d. Global Circumferential strain Rate (GCSR) (1/s).
e. Global Radial Strain (GRS) (%).
f. Global Radial Strain Rate (GRSR) (1/s).

Twist Variables

a. Apical Rotation - Peak (o).
b. Apical Rotation -Time to peak (ms).
c. Basal Rotation - Peak (o).
d. Basal Rotation - Time to peak (ms).
e. Twist - Peak (o).
f. Twist -Time to peak (ms).
g. Twist Rate - Peak (^{o}/s).
h. Twist Rate -Time to peak (ms).
i. Untwist Rate -Peak (^{o}/s).
j. Untwist Rate -Time to peak (ms).
k. Rotational Velocity - (o/s)
l. Mv level
m. Pap. Muscle level.

Statistical Methods

The data were summarized as mean±SD. The 95% confidence interval (CI) of the mean was also calculated. The mean of male and female was tested by t-test for independent groups. The level of significance used was 0.05. A higher t-value having a probability smaller than 0.05 was marked significant. A p-value smaller than 0.01 was marked highly significant.

Results

Table 1 shows the demographic characteristics of the study population. A total of 80 healthy Indian adults were enrolled in the study, and males were 58 and females 22 mean age was 29.07±11.60 years in males and 34.64±10.42 years in females. Men had larger body surface area and body mass index than women.

Table 2 identifies the LA, LV geometry and function of the study population. The LA size was significantly higher in males as compared to females ($p<0.01$). LVEDV, LV mass, CO, Mitral E/A ratio, E/E' TDI ratio and 2D-EF % were significantly greater in males in comparison to females ($p<0.01$).

The 4Dimensional volumetric data presented in Table 3 also illustrates that LVEDV, 4D-EF, CO and CI are increased in males ($p<0.01$) along with sphericity index in diastole and systole ($p<0.01$).

The normal values of comprehensively accomplished strain parameters are expressed in Table 4. Global Longitudinal strain (GLS), Global longitudinal strain rate (GLSR), longitudinal velocity, Transverse velocity, Transverse strain (TS), Transverse strain rate (TSR), shear and shear rate are significantly greater in males in comparison to females, in apical 2CH, 3CH and 4CH views ($p<0.01$). Similarly, the majority of these parameters are higher in Group A, comprising of subjects < 30 years of age, when compared to Group B, which consisted of > 31 years of age.

Table 5 demonstrates in short-axis views at the mitral valve and papillary muscles level the Global Circumferential Strain (GCS), Global Circumferential Strain rate (GCSR), Global Radial Strain (GRS), Global Radial Strain rate (GRSR), Radial and rotational velocity were higher in men as compared to women, even though GCSR, GRS, GRSR and rotational velocity valves were homogenous (p = NS) in Group A and Group B at the mitral valve level. Moreover, these values are significantly greater in Group A in comparison to Group B (p<0.01) at the papillary muscle level.

Despite 80 healthy adults being enrolled in the current study, LV rotation and twist parameters could be satisfactorily procured in 65 subjects from short-axis views, at the level of LV apex, mitral valve, and papillary muscles (Table 6). Peak apical rotation, peak twist, peak twist and untwist rate and their Time to peak were significantly increased (p<0.01) in males in comparison to females. In Group B, values of basal rotation, twist and untwist rate was higher in comparison to Group A (p<0.01). Thus, the twist was greater is normal healthy men and the values increased with increasing age (p<0.01).

Table 1. Demographic Data(n=80)

Variables	**Male(N-58)**	**Female(N-22)**	**Age wise Group (Years)**	
	Mean ± SD	**Mean ± SD**	**Group A***	**Group B***
			(n=45)	**(n=35)**
Age (YRS)	29.07 ± 11.60	34.64 ± 10.42	22.47 ± 4.14	41.06 ± 9.21
Weight (kg)	64.40 ± 10.56	56.55 ± 10.65	59.67 ± 10.22	65.54 ± 11.44
HT (cm)	167.76 ± 6.15	159.18 ± 8.84	165.04 ± 6.35	165.86 ± 9.67
BSA(M2)	1.73 ± 0.15	1.57 ± 0.18	1.65 ± 0.15	1.73 ± 0.19
BMI	22.80 ± 2.94	22.17 ± 2.87	21.81 ± 2.94	23.66 ± 2.58
SBP (mmhg)	118.38 ± 10.70	118.45 ± 11.38	114.93 ± 10.59	122.86 ± 9.52
DBP (mmhg)	76.66 ± 6.84	76.82 ± 6.46	74.58 ± 6.56	79.43 ± 5.91
Heart Rate (bpm)	77.16 ± 12.04	84.77 ± 15.68	78.69 ± 12.41	79.97 ± 14.89
NS=Not Significant(p>0.05)				
** Highly Significant=(p<0.01)				
* Significant=(p<0.05)				
Group A:18 to 30 years of age				
Group B:31 to 60 years of age				

Table 2. Conventional Echocardiography Data (n=80)

Variables	**Male(N-58)**	**Female(N-22)**	**P**		**Age wise Group (Years)**		**P**	
	Mean ± SD	**Mean ± SD**	**P-Val.**	**Sign.**	**Group A* (n=45)**	**Group B* (n=35)**	**P-Val.**	**Sign.**
EPSS (mm)	0.57 ± 0.25	0.66 ± 0.40	<0.01	**	0.58 ± 0.32	0.61 ± 0.26	0.12	NS
Left Atrium (cm)	2.81 ± 0.56	2.72 ± 0.49	<0.01	**	2.63 ± 0.44	2.97 ± 0.61	0.14	NS
IVS d (cm)	0.76 ± 0.17	0.73 ± 0.13	<0.01	**	0.72 ± 0.17	0.79 ± 0.15	0.07	NS
LVID d (cm)	4.80 ± 0.41	4.45 ± 0.47	<0.01	**	4.65 ± 0.46	4.77 ± 0.45	<0.01	**
LVPW d (cm)	0.80 ± 0.14	0.73 ± 0.13	<0.01	**	0.73 ± 0.13	0.83 ± 0.13	0.13	NS
LVEDV (ml)	76.02 ± 51.94	32.64 ± 44.94	<0.01	**	80.17 ± 46.94	43.43 ± 54.96	<0.01	**
LV MASS d (gm)	124.09 ± 32.38	101.14 ± 30.91	<0.01	**	108.87 ± 27.84	129.23 ± 36.76	0.42	NS
C.O.(L/min)	5.20 ± 1.42	5.31 ± 2.02	<0.01	**	4.98 ± 1.39	5.56 ± 1.79	0.17	NS
E/A RATIO	1.58 ± 0.58	1.34 ± 0.54	<0.01	**	1.79 ± 0.54	1.16 ± 0.39	<0.01	**
Lateral TDI E’	10.68 ± 7.15	5.09 ± 6.62	<0.01	**	12.34 ± 6.94	5.03 ± 5.85	<0.01	**
Lateral TDI E/E’ Ratio	0.23 ± 0.30	0.50 ± 0.48	0.55	NS	0.19 ± 0.33	0.46 ± 0.38	<0.05	*
2D-EF (%)	0.63 ± 0.07	0.69 ± 0.07	<0.01	**	0.64 ± 0.08	0.64 ± 0.08	<0.01	**
NS=Not Significant(p>0.05)								
** Highly Significant=(p<0.01)								
* Significant=(p<0.05)								
Group A:18 to 30 years of age								
Group B:31 to 60 years of age								

Table 3. 4-Dimensional Volumetric Data (n=80)

Variables	Male(N-58)	Female(N-22)	P		Age wise Group (Years)		P	
	Mean ± SD	Mean ± SD	P-Val.	Sign.	Group A* (n=45)	Group B* (n=35)	P-Val.	Sign.
Sphericity Index d	0.46 ± 0.11	0.43 ± 0.10	<0.01	**	0.46 ± 0.12	0.44 ± 0.10	<0.01	**
Sphericity Index s	0.38 ± 0.11	0.36 ± 0.12	<0.01	**	0.39 ± 0.12	0.36 ± 0.10	<0.01	**
LVEDV (ml)	74.47 ± 17.88	72.10 ± 16.96	<0.01	**	72.08 ± 19.09	76.06 ± 15.34	0.03	*
LVESV (ml)	32.93 ± 9.39	31.95± 10.06	<0.01	**	32.61 ± 9.93	32.73 ± 9.11	<0.01	**
EF (%)	56.33 ± 5.56	56.45 ± 6.44	<0.01	**	55.47 ± 5.58	57.51 ± 5.89	<0.01	**
CO(L/min)	3.17 ± 0.82	3.23 ± 0.95	<0.01	**	3.07 ± 0.82	3.33 ± 0.89	0.08	NS
Cardiac Index(L/mm/m2)	1.84 ± 0.47	2.05 ± 0.52	<0.01	**	1.86 ± 0.47	1.94 ± 0.51	0.03	*
NS=Not Significant(p>0.05)								
** Highly Significant=(p<0.01)								
* Significant=(p<0.05)								
Group A:18 to 30 years of age								
Group B:31 to 60 years of age								

Table 4. LV Strain Parameters-Part-1(n=80)

Apical long axis views	Variables	Male(N-58)	Female(N-22)	P		Age wise Group (Years)		P	
		Mean ± SD	Mean ± SD	P-Val.	Sign.	Group A*	Group B*	P-Val.	Sign.
2 CH View	Global longitudinal strain (%)	-20.83 ± 4.16	-20.72 ± 3.51	<0.01	**	-21.13 ± 3.39	-20.37 ± 4.62	<0.01	**
	Global longitudinal strain Rate (1/s)	-1.79 ± 0.49	-1.75 ± 0.42	<0.01	**	-1.84 ± 0.49	-1.70 ± 0.44	<0.01	**
	Longitudinal velocity (cm/s)	0.43 ± 0.11	0.42 ± 0.13	<0.01	**	0.45 ± 0.10	0.40 ± 0.13	<0.01	**
	Transverse velocity (cm/s)	0.38 ± 0.08	0.36 ± 0.07	<0.01	**	0.38 ± 0.07	0.38 ± 0.09	<0.01	**
	Transverse strain (%)	24.29 ± 8.83	29.62 ± 10.79	<0.01	**	25.05 ± 8.84	26.67 ± 10.65	0.09	NS
	Transverse strain rate (1/s)	2.82 ± 0.94	2.69 ± 0.72	<0.01	**	2.72 ± 0.86	2.86 ± 0.91	<0.05	*
	Shear (%)	0.12 ± 0.06	0.13 ± 0.06	<0.01	**	0.13 ± 0.06	0.11 ± 0.05	<0.01	**

	Shear rate (1/s)	2.26 ± 0.99	1.99 ± 0.68	<0.01	**	2.20 ± 0.76	2.17 ± 1.10	<0.05	*
3 CH View	Global longitudinal strain (%)	-17.38 ± 3.17	-18.92 ± 3.42	<0.01	**	-17.52 ± 2.92	-18.16 ± 3.73	<0.05	*
	Global longitudinal strainRate (1/s)	-1.67 ± 0.39	-1.60 ± 0.38	<0.01	**	-1.68 ± 0.38	-1.61 ± 0.39	<0.01	**
	Longitudinal velocity (cm/s)	0.43 ± 0.13	1.42 ± 5.04	0.79	NS	0.95 ± 3.52	0.37 ± 0.08	0.21	NS
	Transverse velocity (cm/s)	0.35 ± 0.07	0.34 ± 0.08	<0.01	**	0.33 ± 0.07	0.35 ± 0.07	<0.05	*
	Transverse strain (%)	25.15 ± 7.54	27.42 ± 9.65	<0.01	**	23.35± 8.67	28.89 ± 6.33	0.71	NS
	Transverse strain rate (1/s)	2.48 ± 0.58	2.50 ± 0.64	<0.01	**	2.39 ± 0.63	2.62 ± 0.52	0.09	NS
	Shear (%)	0.10 ± 0.04	0.12 ± 0.07	<0.01	**	0.11 ± 0.06	0.10 ± 0.04	<0.01	**
	Shear rate (1/s)	2.24 ± 0.76	2.14 ± 0.71	<0.01	**	2.29 ± 0.82	2.12 ± 0.63	<0.01	**
4 CH View	Global longitudinal strain (%)	-19.12 ± 3.91	-18.59 ± 4.97	<0.01	**	-19.00 ± 3.56	-18.94 ± 4.96	<0.01	**
	Global longitudinal strainRate (1/s)	-1.64 ± 0.32	-1.49 ± 0.41	<0.01	**	-1.62 ± 0.36	-1.58 ± 0.33	<0.01	**
	Longitudinal velocity (cm/s)	0.42 ± 0.10	0.39 ± 0.13	<0.01	**	0.44 ± 0.11	0.37 ± 0.09	<0.01	**
	Transverse velocity (cm/s)	0.36 ± 0.07	0.33 ± 0.08	<0.01	**	0.34 ± 0.08	0.35 ± 0.07	<0.01	**
	Transverse strain (%)	24.04 ± 8.83	26.94 ± 11.15	<0.01	**	23.95 ± 8.79	25.98 ± 10.46	0.14	NS
	Transverse strain rate (1/s)	2.50 ± 0.78	2.71 ± 1.59	<0.01	**	2.41 ± 0.76	2.74 ± 1.34	0.31	NS
	Shear (%)	0.15 ± 0.06	0.14 ± 0.06	<0.01	**	0.15 ± 0.06	0.15 ± 0.06	0.07	NS
	Shear rate (1/s)	2.07 ± 0.51	1.92 ± 0.72	<0.01	**	2.08 ± 0.57	1.95 ± 0.59	<0.01	**
NS=Not Significant(p>0.05)									
** Highly Significant=(p<0.01)									
* Significant=(p<0.05)									
Group A:18 to 30 years of age									
Group B:31 to 60 years of age									

Table 5. LV Strain Parameters-Part-2(n=80)

Short axis views	**Variables**	**Male(N-58)**	**Female(N-22)**	**P**		**Age wise Group (Years)**		**P**	
		Mean ± SD	**Mean ± SD**	**P-Val.**	**Sign.**	**Group A* (n=45)**	**Group B* (n=35)**	**P-Val.**	**Sign.**
At LV apex	Apical Rotation - Peak (o)	Values Presented in Table 6							
	Apical Rotation - Time to peak (ms)								
At mv level	Rotational velocity (°/s)	-111.61 ± 57.23	-93.96 ± 60.67	<0.01	**	-106.52 ± 68.37	-107.06 ± 43.14	0.09	NS
	Radial Velocity (cm/s)	0.41 ± 0.12	0.38 ± 0.12	<0.01	**	0.39 ± 0.13	0.42 ± 0.10	<0.05	*
	Global Circumferential strain (GCS) (%)	-16.71 ± 6.55	-15.88 ± 6.01	<0.01	**	-15.46 ± 6.44	-17.79 ± 6.16	0.34	NS
	Global Circumferential strain Rate (GCSR) (1/s)	-2.21 ± 0.79	-2.12 ± 0.82	<0.01	**	-2.16 ± 0.84	-2.23 ± 0.73	<0.05	*
	Global Radial Strain (GRS) (%)	23.11 ± 11.75	18.33 ± 6.70	<0.01	**	20.99 ± 11.51	22.83 ± 9.82	0.21	NS
	Global Radial Strain Rate (GRSR) (1/s)	3.12 ± 0.87	3.01 ± 1.04	<0.01	**	2.97 ± 0.95	3.25 ± 0.84	0.10	NS
At pap. muscle level	Rotational velocity (°/s)	96.47 ± 39.37	99.30 ± 29.79	<0.01	**	97.88 ± 38.54	96.44 ± 35.02	<0.05	*
	Radial Velocity (cm/s)	0.38 ± 0.09	0.40 ± 0.13	<0.01	**	0.39 ± 0.09	0.39 ± 0.11	<0.01	**
	Global Circumferential strain (GCS) (%)	-23.13 ± 6.52	-22.76 ± 7.06	<0.01	**	-23.66 ± 6.74	-22.22 ± 6.49	<0.01	**
	Global Circumferential strain Rate (GCSR) (1/s)	-1.95 ± 0.46	-2.03 ± 0.47	<0.01	**	-1.99 ± 0.47	-1.95 ± 0.46	<0.01	**
	Global Radial Strain (GRS) (%)	25.10 ± 9.93	23.54 ± 11.07	<0.01	**	24.80 ± 9.72	24.50 ± 10.95	<0.05	*
	Global Radial Strain Rate (GRSR) (1/s)	2.63 ± 0.96	2.78 ± 1.06	<0.01	**	2.71 ± 1.03	2.63 ± 0.92	<0.01	**
NS=Not Significant(p>0.05)									
** Highly Significant=(p<0.01)									
* Significant=(p<0.05)									
Group A:18 to 30 years of age									
Group B:31 to 60 years of age									

Table 6. Rotation and Twist Data(n=65)

Variables	**Male(N-51)**	**Female(N-14)**	**P**		**Age wise Group (Years)**		**P**	
	Mean ± SD	**Mean ± SD**	**P-Val.**	**Sign.**	**Group A* (n=39)**	**Group B* (n=26)**	**P-Val.**	**Sign.**
Apical rotation peak(o)	6.32 ± 3.95	5.64 ± 2.28	<0.01	**	6.45 ± 4.03	5.74 ± 3.01	<0.01	**
Time to Peak (ms)	267.09 ± 166.26	266.86 ± 85.37	<0.01	**	252.83 ± 158.40	288.35 ± 141.96	0.12	NS
Basal rotation peak(o)	-6.51 ± 3.63	-6.76 ± 2.81	<0.01	**	-6.44 ± 4.02	-6.75 ± 2.44	<0.05	*
Time to Peak (ms)	345.33 ± 172.25	345.07 ± 101.66	<0.01	**	362.25 ± 179.69	319.81 ± 120.46	<0.01	**
Twist peak(o)	10.89 ± 5.50	10.67 ± 3.94	<0.01	**	10.77 ± 5.86	10.94 ± 4.04	<0.01	**
Time to Peak (ms)	309.75 ± 169.76	307.43 ± 82.24	<0.01	**	305.21 ± 178.07	315.31 ± 113.57	<0.05	*
Twist Rate peak(o/s)	124.38 ± 61.87	99.96 ± 23.37	<0.01	**	127.70 ± 67.17	106.26 ± 32.53	<0.01	**
Time to Peak (ms)	197.09 ± 185.30	138.00 ± 90.50	<0.01	**	206.53 ± 189.89	151.12 ± 133.18	<0.01	**
Untwist Rate peak(o/s)	-116.35 ± 51.71	-107.57 ± 38.35	<0.01	**	-113.67 ± 49.06	-115.65 ± 49.86	<0.01	**
Time to Peak (ms)	364.29 ± 168.25	347.21 ± 170.35	<0.01	**	314.36 ± 156.92	430.00 ± 161.44	0.55	NS
NS=Not Significant(p>0.05)								
** Highly Significant=(p<0.01)								
* Significant=(p<0.05)								
Group A:18 to 30 years of age								
Group B:31 to 60 years of age								

Discussion

We are presenting a comprehensive assessment of LV mechanics in healthy Indian adults, including data about the myocardial strain and rotational mechanics, and the impact of age and sex on these parameters, by employing a novel method of 4Dimensional XStrain speckle tracking echocardiography. In this way, we intend to provide an extensive picture of the physiological components involved in ventricular contraction. STE has been widely studied in recent times and has been found to be a pragmatic, convenient, and highly effective tool for the analysis of cardiac functions [27], enabling every myocardial segment to be visualized as a distinctive and exclusive speckle pattern and thus allowing to discriminate from other segments during the cardiac cycle. STE is distantly related to LV myocardial function, and thus the mechanism of contraction components are described as longitudinal, circumferential shortening, radial thickening, and rotational alteration [28].

Several studies have underlined that cardiac torsion is because of the presence of unique obliquely oriented muscle fibers in the subendocardium, which with the cardiac contraction, gradually place themselves in the opposite direction to the subepicardium [29, 30]. This peculiar spiral double helix-like structure, seems to be fundamental for both cardiac systolic and diastolic function [31-33]. Torrent-Guasp in the 1960s, highlighted simultaneous systolic rotation in the opposite direction between LV apex and base, around the longitudinal axis [33]. Ventricular torsion is induced by the synchronous movement of the ventricular base towards the apex [34]. Therefore, simultaneous and combined action of ventricular rotation and longitudinal shortening gives rise to ventricular contraction [34]. LV dysfunction may not affect these two mechanisms in the same way [35], and their assessment may be important in clinical practice because they may be detected early in pathological states where the classical hemodynamic parameters and unable to identify them [36-38].

Trials in patients with heart failure with preserved ejection fraction (HFpEF) have shown that LVEF and global circumferential strain, the chief predictor of LV twist, is conserved suggesting it acted as a compensatory mechanism [39, 40, 41]. Moreover, longitudinal strain (LS) is the most important prognosticator of CV death and/or heart failure [42, 43]. Hence, considering the fact that both LV myocardial strain and rotational mechanics are harmoniously involved in the dynamic functions of LV. Thus integration of complementary parameters of pumping (EF) and myocardial function (strain and twist) must be attempted to comprehensively bring forward the normal value ranges of these essential parameters of LV contractile function.

There is a lot of inconsistencies in the reference values for GLS, GCS, and GRS. Marwick et al. [21] enrolled 242 healthy individuals and found normal global LV GLS of – 18.6%. [20] demonstrated regional reference values for global GLS and found that GLS was lower in basal segments and showed a significant increase from base to apex. The authors concluded a global GLS of-20.6% in their cohort of a normal healthy population. According to a recent meta-analysis that included 24 studies with a total of 2597 subjects' normal values of GLS were -19.7%, normal GLS were -23.2 %, and GRS was 47.3 %. Moreover, they found that all directional components of strain showed heterogeneity and inconsistency between studies. We found similar values of GLS and GCS reported in the literature. Our GRS data are lower to those reported in the literature but there was a large inconsistency of data in the earlier studies. This may be explained by technical rather than biological factors. The GRS is a rather inaccurate measure, especially in lateral and basal segments, because the distance between the endocardium and epicardium is small and the spatial resolution in this tracking direction is reduced.

The effects of age on myocardial deformation remains controversial, while some studies have shown reduced strain values with increasing age [24, 25]. Others have reported no change [20, 46, 47]. In a very recent study, [48] reported that GLS became less negative with aging while GCS became more negative, and the GRS remained unchanged. Similarly, [49] reported that GLS became less negative in elderly patients, but there was no significant change in GRS and GCS. Another study used three-dimensional magnetic resonance imaging using tissue tagging and compared healthy adults by age and reported less negative GLS and GCS in the elderly with a change that was larger at the apex than at the base [50]. In our study population, GLS was having higher in Group A in comparison to Group B. GCS and GRS were higher In Group B at the mitral valve level, and conversely, at the papillary muscle level, GCS and GRS were higher in Group A.

The effect of sex on LV myocardial deformation remains controversial. Several studies found no difference in strain measurements between men and women [21, 46, 47, 51]. However, [44] reported higher GRS in women than in men. Recently, [52] found that, on average, GLS was more negative in women than in men. [22] found that global GLS and GCS were significantly more negative in women than in men. These findings were confirmed by [20], who reported more negative GLS in women. Finally, the HUNT study showed that myocardial deformation was consistently higher in women [45]. On the contrary, our data shows that GLS, GCS and GRS values were higher in men.

Both LV rotation and torsion have been demonstrated to be important determinants of LV function [53]. Apical rotation is usually greater than basal rotation and more strictly correlated with global LV function [54]. [19] reported normal values in different age groups. They found that basal and apical rotation were $4.9 \pm 2.0^{\circ}$ and $10.1 \pm 1.9^{\circ}$, respectively in 20 normal individuals between 33 years and 40 years old. Our data show higher values of LV rotation at the apex and lower values of basal rotation. The reasons for these differences are difficult to explain, however, an ethnic factor cannot be excluded.

A Study [20] have emphasized the importance of acquisition of LV apical short-axis view because the measurements can vary if the view is taken few millimeters more towards the LV apex. We have taken great care to obtain the most apical (just before the right ventricular apex disappears) and circular view. A study [55] reported that the twist changed substantially after 40 years to age. In our study, the LV twist values were $10.89 \pm 5.50^{\circ}$ in males and $10.67 \pm 3.94^{\circ}$ in females ($p<0.01$), and these values increased significantly in the 31 – 60-year age group ($p<0.01$), similar to the finding of Maharaj et al. This increase is likely related to an imbalance between subendocardial and subepicardial layers, with a greater preponderance of epicardial fibers with increasing age [56]. The authors recommend, in future, studies need to adopt a combined approach in which changes in LV rotational mechanics and longitudinal shortening are considered and interpreted together. Additionally, the integration of complementary parameters of pumping and myocardial function should be considered for a more accurate evaluation of the LV systolic function.

Conclusion

After a comprehensive assessment of myocardial deformation LV rotational mechanics in a modest cohort of healthy Indian adults, we are displaying the normal value ranges of the abundant data available in the present research work. In our study, GLS was higher in <30 years age group and GCS and GRS were higher in >31 years age group at the mitral valve level. Moreover, GLS, GCS and GRS values were increased in men. Furthermore, LV twist values were higher in males, and they significantly increased in the 31-60 years age group.

The novel method of 4D XStrain speckle tracking echocardiography is feasible to assess the LV myocardial deformation and rotational mechanics, bringing new insights into this complex ventricular motion. Whereas further investigations are needed to validate this promising technology.

Limitations

The current study has a few limitations. All the participants are of Indian ethnicity, and therefore, the normal values ranges of the present study cannot be anticipated to be identical with other ethnic groups. The echocardiography machine used has an important bearing for the evaluation of deformation values, and these values may change according to the echocardiography system and the offline software being employed for tracking the endocardial border [57]. Other concerning limitation is the non standardisation of the speckle tracking deformation values across different vendors, because of which the strain and rotational values acquired will vary [58]. Moreover, we did not validate the accuracy of strain measurements against the reference standards, such as MRI.

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Conflict of Interest

There are no conflicts of interest.

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