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# 4 Dimensional X-Strain Speckle Tracking Echocardiography: Assessment of Normal Values of Left Ventricular Rotation and Twist, in Healthy Indian Adults during Covid-19 Pandemic

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### *Abstract*

*Cardiac MRI and 2Dimensional speckle Tracking Echocardiography (2D STE) are the most sought-after methods to evaluate LV twist mechanics. LV rotational deformation resembles the wringing of a towel, and this deformation is referred as LV twist (LVT), and the subsequent recoil in diastole is known as LV untwist (LVUT). 2D/3D/4D twist mechanics assessment by STE is inherently associated with limitations. Recently introduced 4D XStrain STE has been used for evaluation of strain parameters because of better appraisal of contractile properties of LV, to analyse complex multi-dimensional LV rotational mechanics. This novel technology is a reliable, affordable, and simple tool for quantification of regional myocardial functions, particularly LV strain and rotation parameters. To evaluate and establish the normal values of LV rotation and twist by 4D XStrain STE in healthy Indian adults during the Covid-19 pandemic was the aim of the current study. 46 subjects were enrolled (34 males & 12 females). LA size, LV mass, CO, LVEDV and mitral E/A ratio were significantly greater in males (p<0.01) even though EF was higher in females (p<0.01). GLS, GCS, and GRS were increased in males (p<0.01). Peak basal rotation, peak twist, peak twist rate, and peak untwist rate were also greater in males (p<0.01), nonetheless, peak apical rotation and papillary muscle rotational velocity were greater in females (p<0.01). However, MV rotational velocity was increased in males (p<0.01). This is the first research publication of normal values of LV rotation and twists in healthy Indian adults by 4D XStrain STE.*

**Keywords:** *4Dimensional XStrain echocardiography, LV Rotational deformation, LV twist and Rotation, LV untwist.*

## Introduction

Lower, in 1669, was the first to describe the twisting motion of the left ventricle (LV) [1]. Experimental and clinical exploration on LV rotation, twist, and torsion have warranted the use of numerous techniques such as implanted radiopaque markers [2], biplane cine angiography [3], sonomicrometry [4, 5], optical devices [6], gyroscopic sensors [7], magnetic resonance imaging (MRI) [8-10], and echocardiography [11-14]. Speckle tracking echocardiography (STE) has gained popularity because of its wide availability. LV rotational deformation resembles the wringing of a towel (Figure 1, 2).

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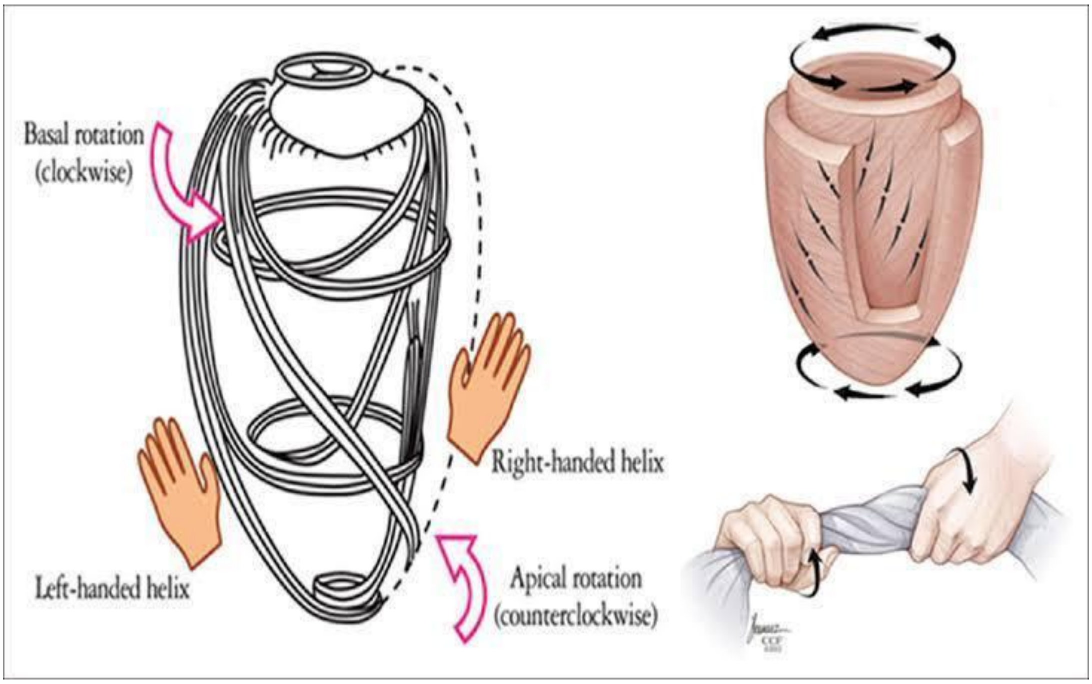


**Figure 1.** LV Twist (LVT)


**Figure 2.** 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) [15, 16]. LV untwist (UT), untwist rate (UTR) along with LV rotation, LV twist (LVT), and LV twist rate (LVTR) are commonly used terminologies for describing these important parameters. Definition of these terms is shown in Table-1 [17, 18, and 19].

**Table 1.** Basic Definition and Parameters Used to Assess LV Twist Mechanics [17]

| **Parameters** | **Definition** |
|---|---|
| **Systolic** | |
| Apical rotation(º) | Peak counterclockwise systolic rotation of the LV apical short-axis cross section as viewed from the apex |
| Apical rotation rate ($^{\circ}/_{s}$) | Peak velocity of apical counterclockwise rotation |
| Basal rotation(º) | Peak clockwise systolic rotation of the LV basal short-axis cross section level as viewed from the apex |

| | |
|---|---|
| Basal rotation rate ($^\circ/_s$) | Peak velocity of basal clockwise rotation |
| LV twist(°) | Peak difference in systolic rotation of LV apex and base as viewed from the apex |
| LV torsion $^\circ/_{cm}$ | Normalized twist: twist angle divided by the distance between the measured location of base and apex |
| LV twist rate **(**$^\circ/_s$) | Peak velocity of LVT |
| **Diastolic** | |
| Apical reverse rotation (°) | Peak clockwise diastolic reverse rotation of the LV apical short-axis cross section as viewed from the apex |
| Apical reverse rotation rate ($^\circ/_s$) | Peak velocity of apical diastolic reverse rotation |
| Basal reverse rotation (°) | Peak counterclockwise diastolic reverse rotation of the LV basal short-axis cross section as viewed from the apex |
| Basal reverse rotation ($^\circ/_s$) | Peak velocity of basal diastolic reverse rotation |
| LV untwist (°) | Difference in diastolic reverse rotation of LV apex and base as viewed from the apex, measured as percentage of untwist from aortic valve closure to mitral valve opening (% UT in IVR) |
| Untwist rate ($^\circ/_s$) | Peak velocity of UT |
| IVR indicated isovolumic relaxation; LV, left ventricular; LVT, LV twist; and UT untwist | |

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 3).

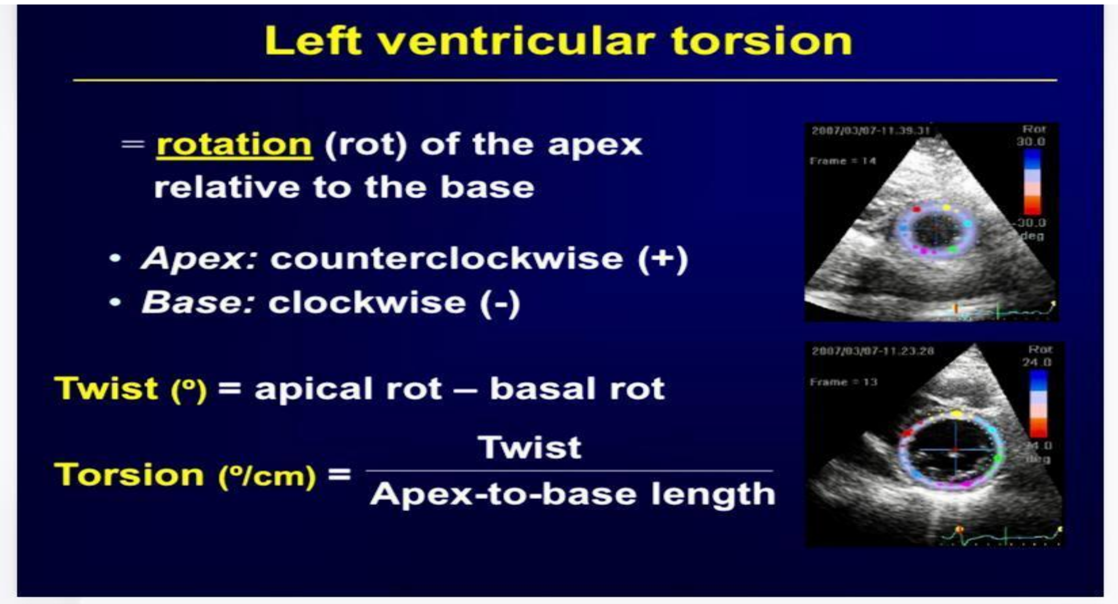


**Figure 3.** LV Torsion & LVT Calculation

Myocardial fibers are a 3-dimensional (3D) continuum that change orientation gradually from a subendocardial right-handed helix to a subepicardial left-handed helix (Figure 4, 5) [18].

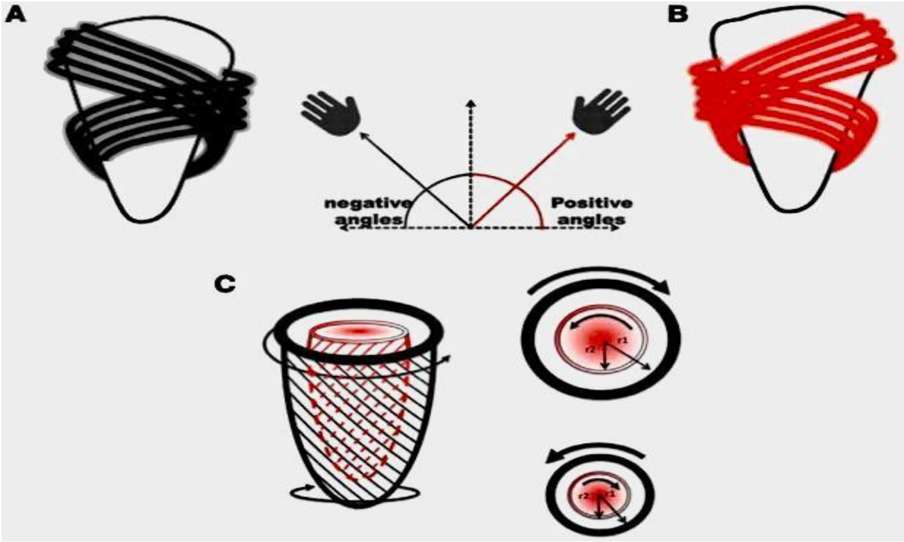


**Figure 4.** Myocardial Fiber Orientation in LVT

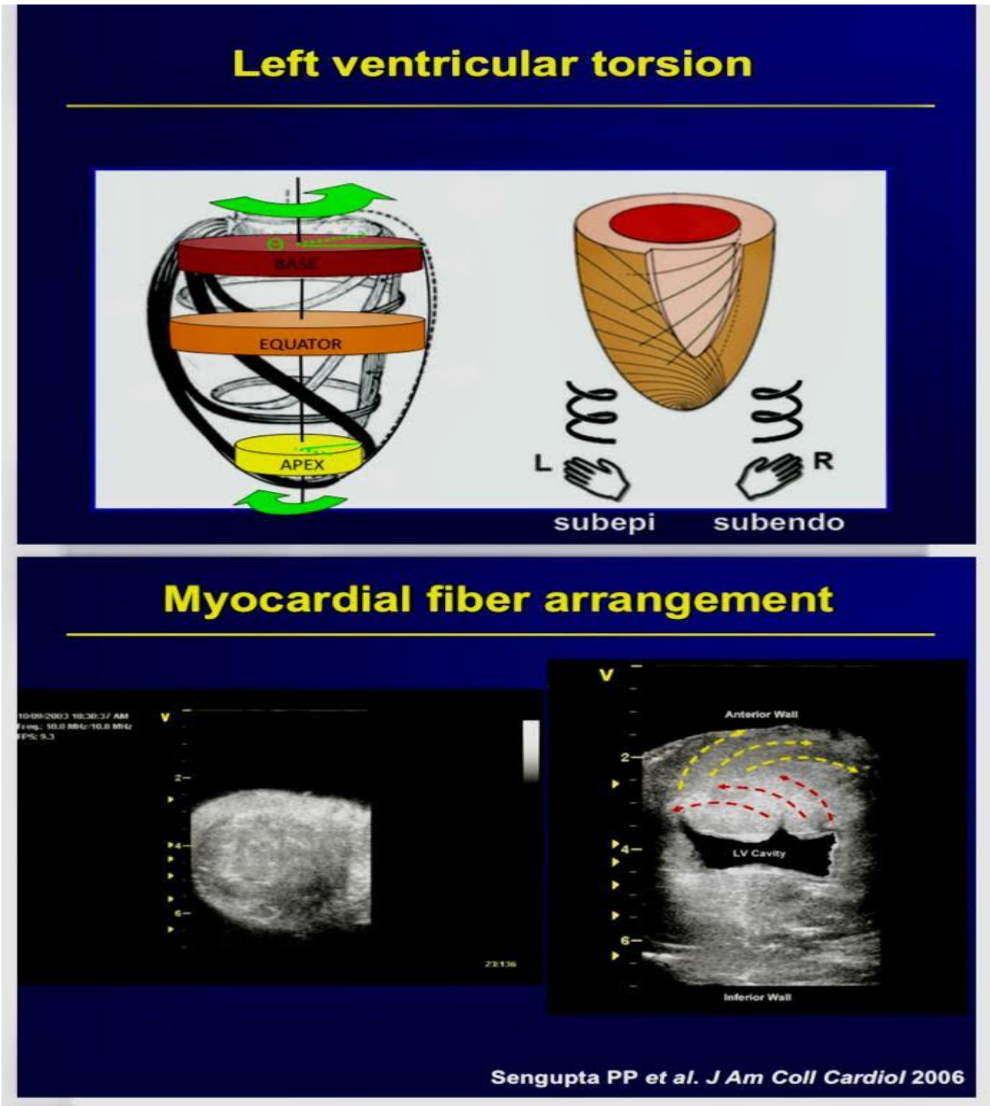


**Figure 5.** Myocardial Fiber Arrangement

The counter-directional helical arrangement of fibers results in sliding or shear deformation. The largest shear deformation occurs in the circumferential-longitudinal plane, also known as LVT [20].

LVT mechanics can be assessed noninvasively using echocardiography [21] and cardiac magnetic resonance (CMR) [22]. Tissue tagging and phase-contrast velocity mapping are assessment methods by CMR. For several years, CMR was considered the reference standard for the non-invasive assessment of cardiac biomechanics. The need for multiple breath-holding, however, significantly affects the temporal resolution. This limitation has been addressed by the development of a respiratory-gated free-breathing tissue phase mapping, resulting in a temporal resolution comparable to tissue Doppler imaging [23]. The contraindication in patients with a pacemaker or internal cardioverter defibrillator remains a major limitation of all CMR techniques.

## Speckle-Tracking Echocardiography

2D-STE for assessment of LVT mechanics has especially gained considerable publicity because of its versatility and wide availability at the bedside [21]. Images are obtained from the short axis of the LV base at the mitral valve level and apex for evaluation of LV rotation and twist (Figure 4). The accuracy of 2D-STE has been validated against sonomicrometry and tagged CMR [22].

The major limitation in 2-dimensional (2D) STE for determination of rotation is transducer angulation [21], the true apex is often poorly identified, and LV twist is significantly underestimated when compared with CMR [24]. It can be foreseen that all these limitations can be overtaken by using a 3D/4D/4D XStrain echocardiography with a single acquisition and a comprehensive LV reconstruction.

By fusing 2D speckle tracking information obtained from standard apical 4CH, 2CH, and LAX views, XStrain$^{TM}$ four-dimensional (4D) 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 [25]. Because of the paucity of LV twist data and moreover its assessment not done till date by 4D XStrain echocardiography, is distinctly encouraging for a compelling research study.

Hence, the aim of our study was to evaluate the LV rotational mechanics in healthy Indian adults by 4Dimensional XStrain Speckle Tracking Echocardiography. Perhaps, this is the first publication of normal values of LV Rotation and twist parameters in healthy Indian adults by 4D XStrain STE during the Covid-19 pandemic.

# Material & Methods

## Study Population & Design

The present study was performed at Prakash Heart Station & Diagnostic, Lucknow, India, an approved centre of Texila American University for the current Phd Cardiology program of the author. The current study was reviewed and approved by the Research Ethics Committee of Prakash Heart Station & Diagnostic, Lucknow, India.

The study comprised of 310 healthy adult subjects study group from which 254 cases were excluded due to inferior image quality, and 46 participants were enrolled after a careful selection process during a period spanning for 9 months from May 2021- to January 2022.

Thus, the study population consisted of a study group of 46 healthy adults of age group 18-60 years of either sex. 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 2Dimensional color echocardiography 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. A negative Covid-19 RT-PCR report, conducted within 72 hours prior to the date of enrollment and echocardiography imaging, was the essential requirement.

### 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 [26].

## Echocardiography

Echocardiographic examination was done using My Lab X7 4D XStrain echocardiography machine of Esaote, Italy, equipped with a harmonic variable frequency (1-5 Mhz) electronic single-crystal array transducer, while the participant was in left lateral decubitus position as recommended by American Society of Echocardiography [27] and connected to 3 lead ECG for continuous monitoring during echocardiographic study.

## Conventional Echocardiography

1. **M-Mode:** for measurements of wall thickness, dimensions, ejection fraction LV mass, LVEDV, LVESV, Cardiac output (CO), LV mass was calculated using the Devereux formula [28].
2. **Doppler flow:** The mitral inflow velocities were recorded and the following

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/a' ratio.

## 4D XStrain Speckle Tracking Echocardiography

### Measurements of Global Longitudinal 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 50-80 frames/sec and stored digitally on hard disk for off-line analysis by software package XStrain$^{TM}$ advanced technology with TOMTEC GMGH 3D/4D rendering and Beutel $^{TM}$ computation compabilities [25]. Mitral and aortic flow velocities were recorded using pulsed-wave Doppler to measure the timing of cardiac events.

### Measurements of LV Twist

The short axis view at the level of mitral valve was obtained by tilting the probe slightly upward until we got the characteristic fish mouth appearance of the mitral valve apical short axis view was obtained by tilting the probe more upward until we got a cross section of the LV apex. Speckle-tracking imaging analysis was performed using the available software as mentioned earlier [25]. 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 performed the speckle-tracking on a frame-to-frame basis and calculated the LVT of 6 equal segments [29].

Using the average of LV rotations from the 6 segments, we measured the basal and apical 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. [29]. The pulsed wave Doppler tracing from the LV outflow tract was used to identify the timing of aortic valve opening and closure that marks systole.

## Statistical Analysis

Data was statistically analyzed by using the well-known program statistical package for social science (SPSS) version 20 (IBM Corp, Armonk, NY). Two types of statistics were used.

Descriptive statistic. e. g. percentage (%), mean (x), and standard deviation (SD).

Analytic statistic: e. g. A student's t-test is a test of significance used for comparison between two groups having quantitative variables. A p-value was considered statistically significant below 0.05.

## Result

The study comprised of 310 healthy adult subjects, from which 254 cases were rejected due to inferior image quality, and only 46 participants in good health were enrolled, study group. Table 2. Shows the demographic characteristics of study population. In the study group, there are 34 males of age 29.38 ±11.07 years and 12 females of age 34.38 ± 11.48 years. The values of weight, height, BSA, BMI, SBP, and DBP were greater in males as compared to females (p<0.01). On the contrary, age and heart rate were greater in females when compared to males (p<0.01).

**Table 2**. Demographic Data (n=46)

| **Variables** | **Male (n-34)** | **Female (N-12)** | **t-test** | **P** | |
|---|---|---|---|---|---|
| | **Mean±SD** | **Mean±SD** | | **P-Val.** | **Sign.** |
| Age (yrs) | 29.38 ± 11.07 | 34.58 ± 11.48 | 4.73 | <0.01 | ** |
| Weight (kg) | 65.38 ± 11.71 | 49.83 ± 7.04 | 10.26 | <0.01 | ** |
| HT(cm) | 166.76 ± 6.41 | 154.17 ± 8.58 | 8.71 | <0.01 | ** |
| BSA(M2) | 1.73 ± 0.17 | 1.46 ± 0.14 | 9.67 | <0.01 | ** |
| BMI | 23.34 ± 2.86 | 20.90 ± 1.76 | 8.80 | <0.01 | ** |
| SBP (mmhg) | 119.71 ± 10.73 | 117.50 ± 13.35 | 7.80 | <0.01 | ** |
| DBP (mmhg) | 77.82 ± 6.41 | 75.83 ± 6.69 | 7.93 | <0.01 | ** |
| Heart Rate (bpm) | 78.76 ± 12.82 | 86.25 ± 18.41 | 6.26 | <0.01 | ** |
| **NS=Not Significant(p>0.05)** | | | | | |
| *** Significant=(p<0.05)** | | | | | |
| **** Highly Significant=(p<0.01)** | | | | | |

Table 3. On assessing the conventional-Echocardiography data LA size, Interventricular septal thickness in diastole left ventricular posterior wall thickness in diastole, left ventricular end-diastolic volume and LV mass were significantly greater in males as compared to females (p<0.01). On studying the diastolic function, mitral E/A ratio and Lateral mitral annulus TDI E' was found to be higher in comparison to females (p <0.01), even though lateral mitral annulus TDI E/E' ratio of females was higher in comparison for males (p<0.01). Moreover, EF was significantly higher in females (p<0.01).

**Table 3.** Conventional Echocardiogrpahy Data (n=46)

| Variables | Male (N-34) | Female (N-12) | t-test | P | |
|---|---|---|---|---|---|
| | **Mean ± SD** | **Mean ± SD** | | **P-Val.** | **Sign.** |
| EPSS(mm) | 0.57 ± 0.28 | 0.58 ± 0.20 | 5.18 | <0.01 | ** |
| Left Atrium (cm) | 2.80 ± 0.54 | 2.65 ± 0.31 | 7.72 | <0.01 | ** |
| IVS d (cm) | 0.76 ± 0.15 | 0.70 ± 0.13 | 7.96 | <0.01 | ** |
| LVID d (cm) | 4.73 ± 0.85 | 4.26 ± 0.43 | 8.38 | <0.01 | ** |
| LVPW d (cm) | 0.81 ± 0.14 | 0.70 ± 0.08 | 8.87 | <0.01 | ** |
| LVEDV(ml) | 112.70 ± 24.91 | 80.97 ± 20.83 | 10.2 | <0.01 | ** |
| LV MASS d (gm) | 126.18 ± 32.40 | 88.58 ± 23.47 | 9.97 | <0.01 | ** |
| C.O.(L/min ) | 5.42 ± 1.36 | 5.05 ± 2.04 | 6.99 | <0.01 | ** |
| E/A RATIO | 1.48 ± 0.49 | 1.35 ± 0.63 | 6.52 | <0.01 | ** |
| Lateral TDI E’ | 1.35 ± 0.39 | 1.36 ± 0.50 | 6.18 | <0.01 | ** |
| Lateral TDI E/E’ RATIO | 0.21 ± 0.27 | 0.33 ± 0.35 | 1.51 | <0.01 | NS |
| 2D-EF (%) | 0.62 ± 0.07 | 0.70 ± 0.06 | 6.26 | <0.01 | ** |
| **NS=Not Significant(p>0.05)** | | | | | |
| **** Highly Significant=(p<0.01)** | | | | | |
| *** Significant=(p<0.05)** | | | | | |

Table 4: On analysis of the 4Dimensional volumetric data, sphericity index in diastole and systole, LVEDV, LVESV, and CO were significantly greater in males as compared to females (p<0.01), none the less EF was higher in females (p<0.01).

**Table 4.** 4-Dimensional Volumetric Data (n=46)

| Variables | Male (N-34) | Female (N-12) | t-test | P | |
|---|---|---|---|---|---|
| | **Mean ± SD** | **Mean ± SD** | | **P-Val.** | **Sign.** |
| Sphericity Index d | 0.47 ± 0.13 | 0.44 ± 0.11 | 7.13 | <0.01 | ** |
| Sphericity Index s | 0.39 ± 0.13 | 0.38 ± 0.12 | 6.52 | <0.01 | ** |
| LVEDV d (ml) | 77.80 ± 16.45 | 65.83 ± 13.79 | 8.65 | <0.01 | ** |
| LVESV s (ml) | 34.92 ± 9.05 | 28.39 ± 8.85 | 8.42 | <0.01 | ** |
| EF (%) | 55.62 ± 4.74 | 57.75 ± 7.62 | 7.15 | <0.01 | ** |
| CO(L/min) | 3.37 ± 0.80 | 2.97 ± 0.86 | 7.88 | <0.01 | ** |
| Cardiac Index(L/mm/m2) | 1.96 ± 0.48 | 2.03 ± 0.51 | 6.39 | <0.01 | ** |
| **NS=Not Significant(p>0.05)** | | | | | |
| **** Highly Significant=(p<0.01)** | | | | | |
| *** Significant=(p<0.05)** | | | | | |

Table 5: On the evaluation of strain parameters by STE, it was observed that all the variables of strain parameters, global longitudinal strain (GLS), Global Circumferential Strain (GCS) at the mitral valve and papillary muscle level, and Global Radial Strain (GRS) at the mitral valve and papillary muscle level were significantly higher in males when compared to females (p<0.01).

**Table 5.** 4-Dimensional X strain parameters (n=46)

| **Variables** | **Male (N-34)** | **Female (N-12)** | **t-test** | **P** | |
|---|---|---|---|---|---|
| | **Mean ± SD** | **Mean ± SD** | | **P-Val.** | **Sign.** |
| GLS (%) | 18.79 ± 2.82 | 20.11 ± 3.92 | 6.55 | <0.01 | ** |
| GCS-MV level (%) | 16.52 ± 6.72 | 17.67 ± 5.14 | 5.31 | <0.01 | ** |
| GCS-pap level (%) | 22.25 ± 9.47 | 22.57 ± 7.68 | 5.50 | <0.01 | ** |
| GRS-MV level (%) | 23.69 ± 9.39 | 20.85 ± 10.04 | 6.36 | <0.01 | ** |
| GRS-pap level (%) | 23.74 ± 10.57 | 20.41 ± 9.88 | 6.19 | <0.01 | ** |
| **NS=Not Significant(p>0.05)** | | | | | |
| **** Highly Significant=(p<0.01)** | | | | | |
| *** Significant=(p<0.05)** | | | | | |

Table 6: By performing 4D XStrain Speckle Tracking on apical and basal levels of LV to assess the rotational mechanics (Figure 6, 7, 8), we found that peak basal rotational, peak twist, peak twist rate, and peak untwist rate were significantly higher in males as compared to females (p<0.01), even though peak apical rotation and papillary muscle rotation velocity were greater in females (p<0.01). Moreover, apical rotation time to peak, peak twist time to peak, twist rate time to peak, untwist rate time to peak, and MV rotational velocity was significantly increased in males as compared to females (p<0.01) nonetheless basal rotation time to peak was increased in females (p<0.01).

**Table 6.** Rotation and Twist Data (n=46)

| **Variables** | **Male (N-34)** | **Female (N-12)** | **t-test** | **P** | |
|---|---|---|---|---|---|
| | **Mean ± SD** | **Mean ± SD** | | **P-Val.** | **Sign.** |
| Apical rotation peak(o) | 5.40 ± 4.06 | 5.64 ± 2.45 | 3.77 | <0.01 | ** |
| Time to Peak (ms) | 281.73 ± 195.63 | 271 ± 92.07 | 4.34 | <0.01 | ** |
| Basal rotation peak(o) | -6.84 ± 3.80 | -6.56 ± 2.79 | -4.89 | <0.01 | ** |
| Time to Peak (ms) | 357.73 ± 173.38 | 361.17 ± 101.07 | 5.11 | <0.01 | ** |
| Twist peak(o) | 10.26 ± 5.55 | 10.18 ± 3.99 | 4.82 | <0.01 | ** |
| Time to Peak (ms) | 323.58 ± 186.97 | 318.25 ± 84.23 | 4.81 | <0.01 | ** |
| Twist Rate peak(o/s) | 125.10 ± 73.29 | 96.23 ± 20.98 | 5.89 | <0.01 | ** |
| Time to Peak (ms) | 181.12 ± 173.38 | 137.17 ± 97.52 | 3.88 | <0.01 | ** |
| Untwist Rate peak(o/s) | -109.64 ± 47.80 | -108.25 ± 40.92 | -5.37 | <0.01 | ** |
| Time to Peak (ms) | 355.45 ± 190.38 | 352.83 ± 183.84 | 4.69 | <0.01 | ** |
| MVRotational Vel(o/s) | -118.26 ± 58.19 | -107.75 ± 98.31 | -4.67 | <0.01 | ** |
| Pap Mus.Rotational Vel.(o/s) | 99.03 ± 40.71 | 119.07 ± 54.76 | 4.11 | <0.01 | ** |
| **NS=Not Significant(p>0.05)** | | | | | |
| **** Highly Significant=(p<0.01)** | | | | | |
| *** Significant=(p<0.05)** | | | | | |

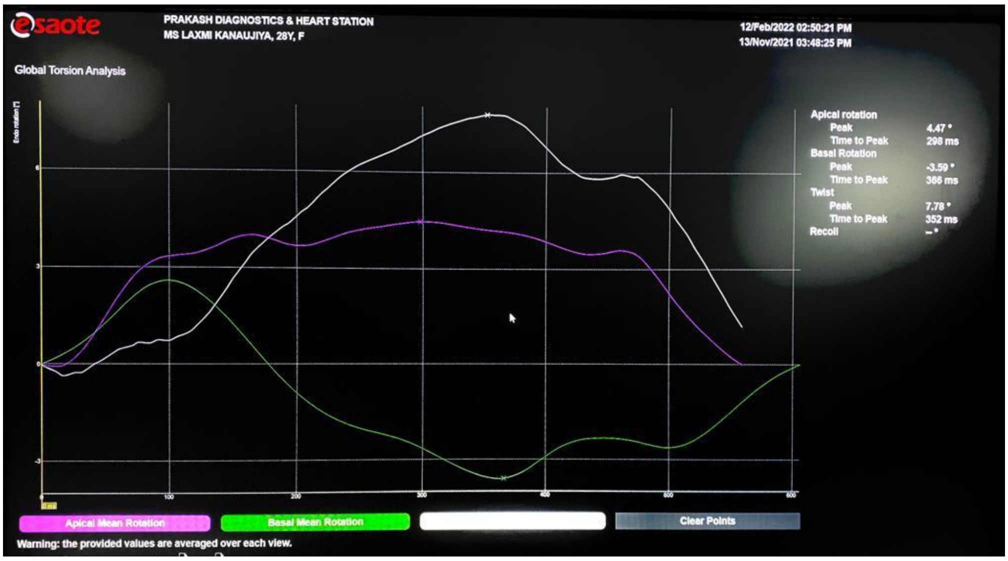


**Figure 6.** Apical Rot, Basal Rot & Twist

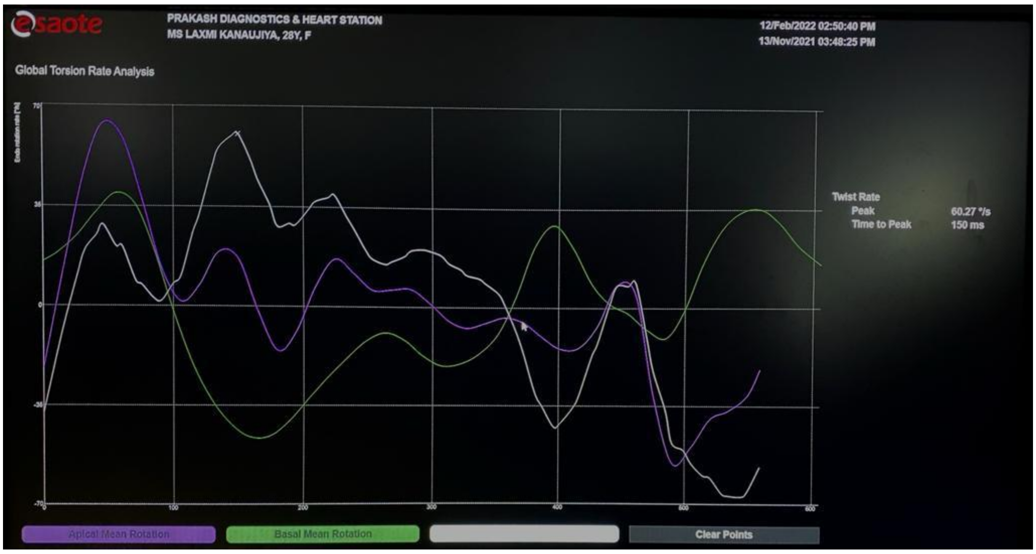


**Figure 7.** Twist Rate

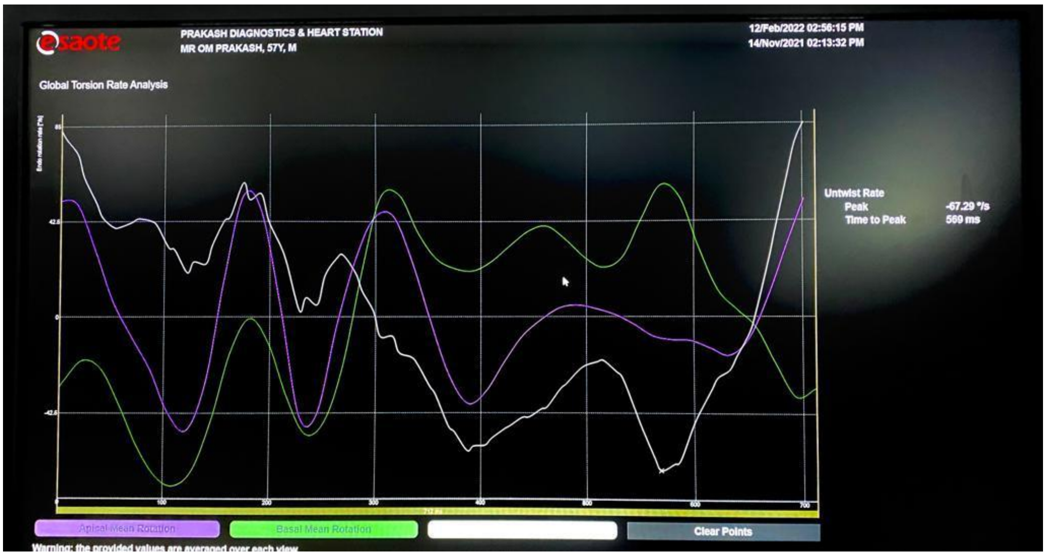


**Figure 8.** Untwist Rate

## Discussion

LV has a special helical 3D structure. LV base and apex rotate in a towel-wringing-like motion called LV twist, which is the net difference between the rotation of the LV base and apex [30, 31]. The prognostic role of LV twist is not yet confirmed [31, 32]. LV volumes deformation and rotation can be assessed simultaneously by 3D STE. Recently introduced 4D XStrain STE has been used for evaluation of strain parameters because of better appraisal of contractile properties of LV, to analyze multi-dimensional LV strain and rotational variables. This novel technology is a reliable, affordable, and simple tool for quantification of regional myocardial functions [25]. The current study aimed to establish normal values of LV rotation and twist by 4D XStrain speckle tracking echocardiography in healthy Indian adults. The summary of LV rotation and twist data of our study is being presented in Table 7.

**Table 7.** Summary of Normal Values of Twist Parameters (n=46)

| Variables | Total Study Group (n=46) | Gender wise Study Group (n=46) | |
|---|---|---|---|
| | Mean ± SD | Male (n=34) | Female (n=12) |
| | | Mean ± SD | Mean ± SD |
| Apical rotation(o) | 5.46 ± 3.67 | 5.43 ± 3.76 | 5.31 ± 3.67 |
| Basal rotation(o) | -6.76 ± 3.53 | -6.71 ± 3.48 | -6.46 ± 3.60 |
| Peak Twist(o) | 10.23 ± 5.14 | 10.18 ± 5.23 | 9.71 ± 4.91 |
| Peak Twist Rate(o/s) | 117.40 ± 64.67 | 118.15 ± 66.00 | 117.42 ± 68.34 |
| Peak Untwist Rate(o/s) | -109.26 ± 45.61 | -109.28 ± 45.93 | -109.84 ± 46.89 |
| Rotational velocity MV(o/s) | -115.45 ± 70.00 | -117.47 ± 70.92 | -113.75 ± 72.88 |
| Rotational velocity Pap Mus(o/s) | 104.37 ± 45.11 | 102.70 ± 45.10 | 106.48 ± 46.09 |

Table 7: In our study apical rotation, basal rotation, peak twist are 5.43 ±3.76 (o), -6.71 ± 3.48 (o), 10.23 ± 5.14 (o) in males respectively and 2.31 ± 3.67 (o), -6.46 ± 3.60 (o), 9.70 ± 4.9 (o) in females, respectively ($p<0.01$).

Table 8: is a 2D study of reference values of LV rotation and twist, in a large cohort of 247 healthy caucasian volunteers of Italy and Romania [33], the apical rotation, basal rotation, and twist in males was 13.2 ± 6.3 (o) -6.6 ± 3.4 (o) 20.1 ± 7.4 (o) respectively and 12.8 ± 6.8 (o), -7.1 ± 3.5 (o), 19.9 ± 7.2 (o) in females, respectively. The overall LV twist was 20.0 ± 7.3 (o).

**Table 8.** 2D LV Rotation & twist in healthy adults [33]

| Variables | Overall | Men | Women | P-value |
|---|---|---|---|---|
| Basal rotation, degrees, n = 225 | -6.9(3.5) | -6.6(3.4) | -7.1(3.5) | 0.269 |
| Apical rotation, degrees, n = 202 | 13.0(6.5) | 13.2(6.3) | 12.8(6.8) | 0.704 |
| Twist, degrees, n = 194 | 20.0(7.3) | 20.1(7.4) | 19.9(7.2) | 0.89 |

Table 9: is a 2D study of 127 black adult African populations of Johannesburg, South Africa [34]. Apical rotation, basal rotation, and twist was 5.74 ± 2.04 (o), -3.39 ± 0.94 (o), and 8.87 ± 2.21 (o), respectively in overall 127 healthy subjects. The authors found that overall twist increases with age.

**Table 9.** 2D Rotational & Twist in African Healthy Adults [34]

| Variables | Total |
|---|---|
| Number of Subjects | 127 |
| AR (degrees) | 5.56 ± 1.98 |
| Subendocardial AR (degrees) | 5.74 ± 2.04 |
| Subepicrdial AR (degrees) | 5.44 ± 1.96 |
| BR (degrees) | -3.31 ± 0.92 |
| Subendocardial BR (degrees) | -3.39 ± 0.94 |
| Subepicardial BR(degrees) | -3.16 ± 1.12 |
| Time to peak rotation (ms) | 357 ± 41 |
| Net twist(degrees) | 8.87 ± 2.21 |
| Untwist rate (degrees) | 52.19 ± 5.56 |
| Data reported as mean standrad deviation | |
| AR, apical roattaion; BR, basal rotation | |

**Table 10.** 3D Rotational & Twist in Healthy Adults [35]

| Variables | 18-29yrs age group | | |
|---|---|---|---|
| | **All Subject (n=94)** | **Male (=45)** | **Female (n=49)** |
| LV rotational parameters(deg) | | | |
| LV basal rotation (deg) | -4.2 ± 2 | -4.3 ± 2.9 | -4 ± 1.8 |
| LV apical roattaion(deg) | 9.3 ± 3.6 | 9.7 ± 3.2 | 8.9 ± 3.9 |
| LV twist (deg) | 13.5 ± 3.7 | 14.1 ± 3.8 | 13 ± 3.6 |
| LV twist time (deg) | 350 ± 84 | 341 ± 86 | 359 ± 82 |

Table 10: is a 3Dimensional study of normal values of LV rotation and twist in 175 healthy Caucasian adults of Hungary of the age group 18-29 years [35]. Apical rotation, basal rotation and twist was 9.7 ± 3.2 (o) -4.3 ± 2.9 (o), 14.1 ± 3.8(o) in males, respectively and 8.9 ± 3.9 (o), -4.0 ± 1.8 (o), 13.0 ± 3.6 (o) in females, respectively. The authors were of the opinion that 3D STE seems to be a reasonably viable tool for quantification of LV rotation and twist. LV basal rotation, apical rotation, and LV twist increase with aging, regardless of gender.

**Table 11.** 3D Rotation and Twists in Healthy Pediatric Population [36]

| Variables | Group 1 (<1 y) | Group 2 (≥1 -<5y) | Group 3) (≥5 -<9y | Group 4 (≥9 -<13y) | Group 5 (≥13 -<18y) | P |
|---|---|---|---|---|---|---|
| **Rotation apical (o)** | 8.2 ± 5.22 | 5.63 ± 3.58 | 6.52 ± 3.86 | 5.64 ± 3.91 | 5.91 ± 3.41 | 0.0726 |
| **Rotation basal (o)** | -3.68 ± 153 | -4.5 ± 2.09 | -4.19 ± 2.24 | -4.31 ± 1.87 | -3.91 ± 1.99 | 0.0943 |
| **Twist (o)** | 11.89 ± 4.96 | 10.14 ± 4.14 | 10.71 ± 4.52 | 9.96 ± 4.37 | 9.82 ± 3.29 | 0.2343 |
| **Torsion (o/cm)** | 3.08 ± 0.97 | 2.01 ± 0.89 | 1.64 ± 0.81 | 1.3 ± 0.87 | 0.97 ± 0.72 | 0.0001 |

Table 11: is a real-time 3D STE study of normal ranges of LV rotation and twist in a Chinese pediatric population of 307 consecutive healthy subjects of mean age of 7.12 ± 5.3 years. Apical rotation varied from 5.63 ± 3.589 (o) to 8.20 ± 5.22 (o), being highest in the age group of <1 year. Basal rotation varied from -3.68 ± 1.53 (o) to -4.50 ± 2.09 (o), being

highest in the age group <1 year. Similarly, LV twist was also showing the highest value in the age group< 1 year. The authors of this large study concluded that the analysis of LV rotation and twist is feasible and reproducible in the pediatric population. Moreover, there is no maturational change in these variables.

**Table 12.** 2D Rotation and Twist in <40years & >40 years [37]

| Variables | Age Group | |
|---|---|---|
| | **<40years (n=40)** | **>40years (n=35)** |
| **LV Rotation Parameters** | | |
| Apical rotation | 3.3 ± 2.4 | 4.4 ± 2.9 |
| Basal rotation | -5.2 ± 3.3 | -4.1 ± 2.7 |
| LV Twist | 8.5 ± 4.1 | 8.7 ± 3.3 |

Table 12: This is a 2D Turkish study of 75 healthy subjects regarding age-related changes in LV rotation and twist. In this study, the participants were divided into 2 groups: < 40-year age group and >40 year age group. The authors concluded that LV twist slightly increased with age, and increased twist may also be used as a marker of early-stage diastolic dysfunction even in the presence of normal systolic function.

Hence, we can infer from the above Tables 7 – 12 that the normal values of LV rotation and twist have considerable variability, and therefore the values are to be used cautiously in clinical settings. These normative ranges must be interpreted in context to:

1. The echocardiographic machinery used in the study, whether it is a 2D/3D/RT3D/ 4D/4D XStrain speckle tracking echocardiography study?
2. The population studied- whether Caucasians, African blacks, Chinese, Turkish, or Indians?
3. The age of the population-whether pediatric or adult population, < 40 years or > 40 years age group?
4. And, of course, the software specification of the STE package, because different vendors tend to use different software and algorithm, thereby the normal value ranges are differing from vendor to vendor.

We recommend a large randomised controlled trial involving multiple tertiary care centres, in multiple regions of the world-Europe, Africa, Asia, North America, etc., including hundreds of participants of various age groups to find a definitive answer to the normal value ranges of LV rotation and twist, so that these values can be effectively used to differentiate normal healthy population from those with abnormal values in various disease states.

## Conclusion

In the present work, we have provided normal reference values of rotation, twist, and untwist data in a healthy adult Indian population by 4D XStrain STE. LV rotation mechanics evaluation may lead to the furtherance of understanding of an elementary contractile function of the heart.

Based on the 4D XStrain STE technique, the novel method is feasible to assess LV twist deformation, potentially bringing new insights into this complex ventricular motion. Whereas further investigations applying 4D XStrain STE are needed to validate this promising technology.

## Limitations

Despite the growing evidence, the routine clinical use of these measurements has not yet been recommended. [38] This is related to the lack of standardization between various software and the challenges in obtaining basal and apical cross-sectional views, leading to remarkable variability in the normal values of the various parameter of LV twist. 2D-STE measurements cannot be performed in single image acquisition. 3D-STE is a definitive answer for this problem [39]. However, the 3D acquisition is currently limited by low frame rates and reduced temporal resolution. This may be overcome by utilizing highly advanced state of the art high-frequency echocardiography machines with high temporal and spatial resolutions [40]. The sample size of the present study is small, and 4D XStrain STE derived LV twist, and rotation parameters may require more extensive validation by sincere efforts toward tracking accuracy with future research studies. Moreover, the twist parameters should be compared with cardiac MRI rotational data. We are all aware that the human heart has an oblique orientation in the chest cavity, because of which the selection of optimal planes is quite challenging due to limited acoustic windows. Correct measurements of LV twist at the apical and basal levels is crucial because the subjectivity of the echocardiography can bring quantification biases. In essence, measurements of LV twist by STE is contingent on high-quality recordings, high tracking quality, and the correct recognition of anatomic structures that identity the basal and apical short-axis levels.

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## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this manuscript.

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