Defining Left Ventricular Apex-to-Base Twist Mechanics Computed From High-Resolution 3D Echocardiography
Validation Against Sonomicrometry

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OBJECTIVES To compute left ventricular (LV) twist from 3-dimensional (3D) echocardiography.

BACKGROUND LV twist is a sensitive index of cardiac performance. Conventional 2-dimensional based methods of computing LV twist are cumbersome and subject to errors.

METHODS We studied 10 adult open-chest pigs. The pre-load to the heart was altered by temporary controlled occlusion of the inferior vena cava, and myocardial ischemia was produced by ligating the left anterior descending coronary artery. Full-volume 3D loops were reconstructed by stitching of pyramidal volumes acquired from 7 consecutive heart beats with electrocardiography gating on a Philips IE33 system (Philips Medical Systems, Andover, Massachusetts) at baseline and other steady states. Polar coordinate data of the 3D images were entered into an envelope detection program implemented in MatLab (The MathWorks, Inc., Natick, Massachusetts), and speckle motion was tracked using nonrigid image registration with spline-based transformation parameterization. The 3D displacement field was obtained, and rotation at apical and basal planes was computed. LV twist was derived as the net difference of apical and basal rotation. Sonomicrometry data of cardiac motion were also acquired from crystals anchored to epicardium in apical and basal planes at all states.

RESULTS The 3D dense tracking slightly overestimated the LV twist, but detected changes in LV twist at different states and showed good correlation ($r = 0.89$) when compared with sonomicrometry-derived twist at all steady states. In open chest pigs, peak cardiac twist was increased with reduction of pre-load from inferior vena cava occlusion from $6.25° \pm 1.65°$ to $9.45° \pm 1.95°$. With myocardial ischemia from left anterior descending coronary artery ligation, twist was decreased to $4.90° \pm 0.85°$ ($r = 0.8759$).

CONCLUSIONS Despite lower spatiotemporal resolution of 3D echocardiography, LV twist and torsion can be computed accurately. (J Am Coll Cardiol Img 2010;3:227–34) © 2010 by the American College of Cardiology Foundation

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Left ventricular (LV) twist and torsion have been added to the battery of new indexes of cardiac performance (1). LV twist can be computed from the net difference of rotation at apical and basal LV level. To date, many studies have linked the dynamics of cardiac twist to systolic function of the heart (2–6). Similarly, rapid unwinding of systolic torsion also has been shown to have a significant contribution in early diastolic filling (7,8). Furthermore, alterations in the pattern or magnitude of LV rotation and torsion also have been associated with various cardiovascular diseases (9–12).

Recent advances in cardiac imaging have made it possible to quantify cardiac motion noninvasively. High-resolution 2-dimensional (2D) echo speckle tracking–based motion-detecting methods have been tested for computation of LV twist and have been validated (13,14). Selection of optimal imaging planes for such computation, however, is quite challenging because of limited acoustic windows and oblique orientation of the heart in the patient’s chest cavity. Torsion is a nonlinear function of ventricular length, and its magnitude depends critically on the measurement level relative to the LV base or other reference point. Nonuniform and variable selection of imaging plane levels and the angulation of the ultrasound beam causing variable transmural depth of the LV wall during 2D acquisition could result in a wide variation of results. Both of these factors are very difficult to optimize with 2D imaging. Because the 2D method computes twist directly from peak rotation values from apical and basal short axis views, it does not reflect true torsional deformation because the images are acquired separately from entirely different cardiac cycles and rotation at each level peaks at a different time in the cardiac cycle. Also, when short axis slices are acquired that are spatially fixed with respect to the static scanner coordinate system, the long-axis motion of the heart results in through-plane motion and leads to inaccurate results of the analysis because of in-plane decorrelation.

More recently, new generation matrix transducers have allowed the acquisition of 3-dimensional (3D) scanline data with a programmable degree of overlapping between successive volumes to suppress the through-plane motion, and with a resolution high enough to track speckle motion through the volumes for computation of mechanical functions at desired levels of 3D image loops. We quantified rotation in 3D ultrasound images at multiple levels of heart to allow computation of LV torsion.

METHODS

Animal preparation. We studied 10 adult pigs of both sexes (approximately 12 weeks of age; 18 to 22 kg). The pigs were placed in the supine position during the experiment and anesthesia was induced with 25 mg/kg intravenous thiopental and were maintained with an infusion of 25 mg/ml solution (100 ml/h) of fentanyl citrate. A median sternotomy was performed under hemodynamic monitoring and the pericardium was split from apex to base to expose the heart. Atraumatic vascular occluders were placed around the proximal third of the left anterior descending coronary artery. The inferior vena cava (IVC) was isolated by blunt dissection in posterior mediastinum, and a pneumatic occluder (14 to 16 mm; In-Vivo Metrics, Healdsburg, California) was placed on the IVC to decrease pre-load transiently (typically down to an LV end diastolic pressure of 3 to 4 mm Hg). At end expiration, the respirator was switched off for very short periods to allow for successive beats to be recorded without the effects of breathing.

For estimation of LV twist, 3 sonomicrometry (sono) crystals were implanted along the LV circumference close to the apex, and 4 were implanted close to the base in the short axis plane. Atraumatic surgical and fine suturing techniques were used to secure crystals subepicardially to minimize myocardial damage. To achieve reproducible and parallel planes, the crystals at each level were placed at fixed distances from LV apex (20% of LV length for apical plane and 80% of LV length for basal plane). Signals from crystals were acquired at a rate between 250 and 300 Hz after observing a clear, noise-free signal on the data display screen of SonoSoft (SonoMetrics, London, Ontario, Canada).

Three-dimensional image data were acquired on a Philips IE33 system (Philips Medical Systems, Andover, Massachusetts) with an X7–2 transducer placed directly on the cardiac apex separated only by a small piece of fresh liver as standoff (2 to 4 cm). Sector width and depth were adjusted to allow inclusion of LV walls within the pyramid. The frame rate was maximized to obtain an image loop of 24 to 38 pyramidal volumes representing a heart cycle. Frequency and focus places were optimized to obtain the best possible myocardial texture throughout the LV full volume (Fig. 1). Full-
volume 3D image loops were reconstructed by stitching of pyramidal volumes acquired through electrocardiography (ECG) triggering over 7 consecutive heart beats. After acquiring baseline data, pre-load to heart was altered by a controlled occlusion of the inferior vena cava for a short period. Sonomicrometry data and 3D apical long-axis full-volume images were acquired during this periodic occlusion. After releasing the IVC, another set of baseline data was acquired. The study then was repeated after ligating the left anterior descending coronary artery for 5 to 7 min to produce myocardial ischemia.

**Statistical analysis.** For speckle tracking-based motion analysis, envelope-detected 3D images in spherical coordinates were entered into a program implemented in MatLab (The MathWorks, Inc., Natick, Massachusetts). We used the free form deformation model to parameterize the nonrigid transformation, which had been used successfully for tracking of cardiac magnetic resonance (15). It has the advantage of being able to model complex nonrigid transformations using a small number of parameters (control points positions). The optimal locations of the control points were obtained by optimizing a similarity function that characterizes the speckle pattern variation between 2 volumes with a multiplicative Rayleigh noise model (16). The output of this algorithm is an estimation of the 3 components of a continuous, spatially dense displacement field \[ \mathbf{v}(x, y, z, t), \] between the \( t \)th and the \((t+1)\)th frame (Fig. 2). Quantitative measures like strain and torsion can be computed readily from the displacement field.

Cardiac twist is the rotation of the apical plane with respect to the basal plane or vice versa and is the result of the shape change experienced by the left ventricle during systole. For computation of twist, a plane of interest could be defined by fixing at least 3 uniformly spaced point markers around the LV circumference at a particular depth of 3D volume. We defined 2 planes of interest (apical and basal) for our twist analysis that were parallel to each other and were centered on a long axis line running in the center of the LV cavity from the apex to the base (Fig. 3). This resulted in the formation of a triangular cylinder (or prism) where the bottom surface would rotate with respect to the top surface, vice versa, or both, with cardiac motion depending on the setup of the measurement system. The location of the centroid within each plane was determined by the algebraic average of the \([x, y]\) coordinates of the 3 point markers. Having the average rotations from the apical and basal planes, we can calculate the twist through time as a difference in plane rotations.

For computation of twist from sono data, 3D coordinates of each crystal were determined by processing acquired data in Sono XYZ (Sono-Metrics, London, Ontario, Canada) as a function of time. Parallel apical and basal LV planes were reconstructed by interpolation of the corresponding crystal coordinates, and the in-plane positions were approximated. Using the crystal positions in each plane, we computed the twist similarly to the algorithm for point markers above (Fig. 4).

**Statistical analysis.** Results are expressed as mean ± SD. Data were analyzed for variance using an analysis of variance to compare the degree of twist derived from sono and 3D echo. A p value <0.05 was considered significant. We used linear regression and Bland-Altman plots to assess the degree of agreement between the 3D echo-based twist method and sono-derived twist (17). Interobserver measurement variability was determined by having a second observer measure LV twist in 26 randomly selected 3D image loops. Intraobserver variability was determined by having 1 observer remeasure LV twist in 26 image loops that were reshuffled randomly 1 month after initial analysis. Interobserver and intraobserver variability were calculated as correlation coefficients that were obtained using Pearson product and Spearman rank correlation. Because LV twist is a continuous variable, we used an
**RESULTS**

At baseline, peak twist values were 6.25° ± 1.65° as detected by 3D echo and 5.25° ± 1.20° as detected by sono. With reduction of pre-load resulting from IVC occlusion, an increase in peak twist was seen (9.45° ± 1.95°; p = 0.02) by 3D echo and 7.85° ± 0.90° (p = 0.04) by sono. With anterior myocardial ischemia produced by atraumatic occlusion of left anterior descending coronary artery, peak global twist was reduced to 4.15° ± 0.75° (p = 0.03) by 3D echo and 3.65° ± 0.35° (p = 0.05) by sono (Fig. 5). Figure 6 shows a linear regression with correlation and agreement data for peak twist values derived by 3D echo and sono, which showed a strong linear correlation.

Figure 7 shows a Bland and Altman plot, with the difference between 3D echo and reference (sono) as the y-axis and the average of these 2 as the x-axis. The scatterplot of points is between the upper and lower limits of agreement defined by the 2 SDs that describes the range for 95% of comparison points. All data points were within the confidence limits; however, there was a bias. We used a regression approach to calibrate the bias and the systematic error. The bias was remedied using the least-square regression method that is used to obtain the predicted values of 3D echo through the line adjusted values of 3D echo.

Figure 8 shows a Bland-Altman plot after the calibration. There were no notable systematic trends or bias, and all data points were within the limits of agreement. So if the differences within the mean ± 2 SDs are not clinically important, the 2 methods may be used interchangeably. The results of the reproducibility analysis on 26 randomly selected image loops showed a good correlation (r = 0.88, with significant p < 0.0001) by the same observer and by 2 different observers (r = 0.76, with significant p value <0.0001). These correlation results were obtained using Pearson product correlation. Similar results were also obtained using Spearman rank correlation (intraobserver correlation, 0.88 [p < 0.0001]; interobserver correlation, 0.71 [p < 0.0001]).
The estimated ICCs of the intraobserver and interobserver comparisons were 0.89 and 0.75, respectively (Fig. 9). The ICC is interpreted as the proportion of total variance. The range of ICC is from 0 to 1, with 0 indicating no similarity and 1 showing perfect reproducibility. We used 1,000 bootstrap samples to construct the following confidence intervals. The 95% confidence interval for intraobserver intraclass correlation is 0.8154 to 0.9291, and that for interobserver intraclass correlation is 0.4866 to 0.8949. These 2 confidence intervals do not contain 0 value (no agreement), indicating that there exists significant reproducibility in intraobserver and in interobserver comparisons.

**DISCUSSION**

LV twisting motion is believed to be the consequence of oblique myocardial fiber orientation that induces rotation around the long axis during contraction. Because the magnitude of LV twist is determined by contractile force, it is suggested that measurement of LV twist could be implemented as a clinical index of contractility and may serve as a potential marker of myocardial dysfunction in the diseased heart. This concept is supported by experimental work, but none of the methods used in experimental work can be implemented in clinical routine for evaluation of cardiac twist. Difficulties with 2D methods led us to seek the possibility of using new 3D echo methods as an alternative. Speckle tracking in 3D echo image loops also offers unique challenges. Despite recent advances in technology, 3D ultrasound images are still of relatively low quality.
low spatiotemporal resolution, with artifacts like attenuation, shadows, and signal dropout. These factors result in a higher degree of inconsistency of speckles between successive volumes of a 3D image loop. Although it is encouraging that our method demonstrates its efficacy despite these difficulties, we believe that more accurate and robust results will be achieved with continuing improved spatial and temporal resolution in 3D echo that reduces the speckle pattern variability.

We used envelope-detected image data in the raw spherical coordinates in this study. The main benefit of using image data in spherical coordinates is the avoidance of information loss associated with scan conversion and interpolation. The envelope-detected data in spherical coordinates have much higher resolution in the axial direction and take 11 times less operative memory when compared with the Cartesian format, which greatly improves the speed of processing. Because of the above-mentioned approach, we are able to track individual 3D image voxels with much higher spatial resolution, as compared with a Cartesian data format, and yield a spatially dense displacement field. The displacement field is dense in the sense that it can provide a displacement vector for all voxels on the myocardium by tracking the actual intramural speckle patterns, instead of interpolations from faraway points in B-mode tracking or on the boundary in border tracking methods. A spatially dense displacement field allows tracking of virtually any material point in the myocardium and computation of both segmental and global cardiac mechanics.

We used sono as a reference method because it has superior resolution compared with other experimental methods. Although echo-derived twist values showed slight overestimation, both methods detected the changes in LV twist at different steady states and showed a good correlation between sono- and echo-derived twist values. Both motion detecting methods (sono and echo) use different ultrasound frequencies, sampling rates, coordinate systems, and methods to compute twist, which may explain the bias between their results. We believe that the major reason for the difference in twist values between both methods is the result of the location of sampling points. We secured sono crystals on the epicardial surface to minimize the trauma to the myocardium. For echo analysis, however, we placed the sampling points in the myocardium. This finding of slightly higher twist in the inner myocardial layer as compared with the outer epicardial layer is consistent with earlier observations (19).

**Study limitations.** The results of this study are derived from analysis of very high-resolution images acquired directly from the surface of the heart. Acquiring such uniform and artifact-free images may not be possible in clinical examinations through poor acoustic windows. We selected the minimum number of points of interest at each level to simplify analysis and to minimize the procedural difficulties of anchor-
ing crystals on the exposed pig hearts, because instrumented pigs under anesthesia are prone to ventricular fibrillation. This simplified approach resulted in the reconstruction of a triangular prism rather than the actual elliptical cylinder of the LV.

Our current algorithm is designed to evaluate the feasibility of twist computation and is not optimized for speed. Currently, it is offline and typically takes approximately 5 to 6 min to register 2 volumes, which translates to up to 2 h total, depending on the loop size. We can reduce the computation time by using C/C++ programming language instead of MatLab, by optimizing the code efficiency, or by parallel processing. However, we believe the biggest reduction in computation time will come from using customized hardware such as field programmable gate array, in which case real-time or near real-time speed can be achieved.

This study used the 3D images that were acquired from 7 consecutive cardiac cycles of a steady state with ECG gating during single acquisition and stitched to reconstruct a full-volume loop. Although the twist values were not derived from 1 cardiac cycle, they were derived from similar cycles.

Figure 8. Bland Altman Method on 3D Echo Versus Sono After the Calibration
Bland-Altman plot after the calibration. Bias was determined by regression method because both methods showed a positive linear correlation. There were no notable trends, and all data points were within the limits of agreement.

Figure 9. Scatterplots Showing Interobserver and Intraobserver Variability
Scatter plots that were obtained with respect to each observer to determine intraobserver and interobserver variability. The data were spread out within a reasonably similar range to 3-dimensional (3D) echocardiography (echo)-derived twist values (intraobserver interclass correlation coefficient [ICC], 0.89; interobserver ICC, 0.75). The confidence intervals of these ICCs confirm the inferential conclusion about the reproducibility of the 3D echo method to compute left ventricular twist.
Use of ECG gating for acquisition also is a concern in patients with cardiac arrhythmias. Future development of single beat image acquisition technology without ECG triggering will overcome these limitations. Currently available 3D echo has relatively low time resolution as compared with 2D echo, which may limit its accuracy in computing mechanical indexes like strain rate and untwisting velocity. However, lower temporal resolution may not be significant for many quantitative measures, which integrate the measurement over a certain period or use peak values like strain and twist.

**REFERENCES**


**CONCLUSIONS**

Dense speckle tracking-based computation of LV twist is feasible in apical long-axis 4-dimensional full-volume image loops. This methodology is highly reproducible and provides a robust method for evaluation of cardiac twist.

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**Key Words:** left ventricular twist ♦ myocardial ischemia ♦ validation study ♦ 3-dimensional echocardiography.

**APPENDIX**

For supplementary videos and their legends, please see the online version of this article.