Assessment of Left Ventricular Torsional Deformation by Doppler Tissue Imaging
Validation Study With Tagged Magnetic Resonance Imaging

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Background—Left ventricular (LV) torsional deformation is a sensitive index for LV performance but difficult to measure. The present study tested the accuracy of a novel method that uses Doppler tissue imaging (DTI) for quantifying LV torsion in humans with tagged magnetic resonance imaging (MRI) as a reference.

Methods and Results—Twenty patients underwent DTI and tagged MRI studies. Images of the LV were acquired at apical and basal short-axis levels to assess LV torsion. We calculated LV rotation by integrating the rotational velocity, determined from DTI velocities of the septal and lateral regions, and correcting for the LV radius over time. LV torsion was defined as the difference in LV rotation between the 2 levels. DTI rotational and torsional profiles throughout systole and diastole were compared with those by tagged MRI at isochronal points. Rotation and torsion by DTI were closely correlated with tagged MRI results during systole and early diastole (apical and basal rotation, \( r = 0.87 \) and 0.90, respectively; for torsion, 0.84; \( P < 0.0001 \), by repeated-measures regression models). Maximal torsion showed even better correlation (\( r = 0.95, P < 0.0001 \)).

Conclusions—The present study has shown that DTI can quantify LV torsional deformation over time. This novel method may facilitate noninvasive quantification of LV torsion in clinical and research settings. (Circulation. 2005;111:1141-1147.)

Key Words: mechanics ■ echocardiography ■ ventricles ■ magnetic resonance imaging

Since William Harvey recognized the helical orientation of cardiac fibers, interest in fiber architecture and the resulting left ventricular (LV) torsional deformation during contraction has grown. The importance of LV torsional behavior as a sensitive indicator of LV performance has been previously corroborated by radiographic tracking of myocardial markers, optical devices, and 2D echocardiography. In the past decade, tissue tagging magnetic resonance imaging (MRI) has enabled noninvasive measurement of LV myocardial deformation in 3D space and prompted investigation of LV torsion in various cardiac diseases. More recently, it has been reported that LV torsion is closely related to alterations of sarcomeric proteins, like the transmural gradient of titin isoforms or myosin regulatory light chain in experimental cardiomyopathy models.

Simple and inexpensive methods for measurement of LV torsion could facilitate more widespread investigation of LV torsion, which might reveal significant relationships between torsional alterations and clinical outcomes and eventually lead to routine clinical application. Recently, Doppler tissue imaging (DTI) has been shown to accurately reflect myocardial velocity with better temporal resolution than MRI. We hypothesized therefore that DTI might be used for quantification of LV rotation and torsion of the human heart. The purpose of the present study was to examine the accuracy of a novel method with DTI for quantifying the LV torsion in humans and tagged MRI as the reference standard.

Methods

Study Sample

We assessed consecutive patients who satisfied the following criteria: (1) clinically indicated cardiac MRI and (2) satisfactory echocardiographic images on a previously performed study. The research echocardiographic study was performed on the same day as the MRI. Twenty patients with a variety of cardiac pathologies were recruited in an attempt to cover the full clinical range of LV torsion. Clinical diagnoses of the studied patients included aortic root disorder (n=11, including 3 patients with severe aortic stenosis, 3 patients with severe aortic insufficiency, and 3 patients after aortic valve replacement), ischemic heart disease (n=5), and cardiomyopathies (n=4). The institutional review board of the Cleveland Clinic Foundation

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approved the study protocol. Written, informed consent was obtained before the study from all patients.

**Echocardiography**

After a standard comprehensive 2D and Doppler echocardiography examination, we scanned apical and basal short-axis planes and a long-axis (from the apex) plane in DTI mode with a Vivid 7 ultrasound machine (GE Medical Systems) with an M3S probe. Axial resolution was 1 mm. The velocity range of DTI was set at 16 or 20 cm/s to avoid alias. We used the presence of the following anatomic landmarks throughout the cardiac cycle to define proper short-axis levels: at the basal level, the mitral valves; and at the apical level, the LV cavity (papillary muscles not visible). An effort was made to make the LV cross section as circular as possible.

**Data Analysis**

To assess LV torsion (a wringing behavior as the apex rotates with respect to the base about the LV long axis), LV rotation both at basal and apical levels was quantified. To obtain the LV rotation from the DTI data, we extracted the tangential velocity of the LV after elimination of the vector of whole cardiac motion (translation) and estimated the time-varying radius of the LV \( r(t) \) to convert the tangential velocity (cm/s) into angular velocity (radians/s).

To accomplish this, we measured the myocardial velocity in 4 separate regions in both the basal and apical short-axis LV planes (Figure 1). These sample volumes, a 4×8-mm ellipse for the lateral and septal regions (where only the tangential component of velocity is detected) and an 8-mm circular volume for the anterior and posterior ones (where only the radial component is detected), were semiautomatically tracked on the workstation by anchoring them to

**Figure 1.** Myocardial velocity sampling regions and velocity profiles for LV rotation measurements (apical level). Top panels: septal (Vsep) and lateral (lat) regions, difference of which yields rotational velocity (without radial component). Bottom panels: anterior (ant) and posterior (pos) regions, integral of which allows LV radius to be tracked (without any component of tangential motion). MVC and MVO indicate mitral valve closing and opening, whereas AVO and AVC indicate aortic valve opening and closing, which were determined by LV inflow and outflow Doppler profiles.
the LV inner and midwalls at end diastole, end systole and after early filling to keep the correct position. From these 4 velocity data sets, LV rotational velocity (Vrot, rad/s) was estimated from averaged tangential velocity corrected with r(t), as follows:

\[ V_{\text{rot}}(t) = \frac{[V_{\text{lat}}(t) - V_{\text{sep}}(t)]/2}{r(t)} \]

where \( r(t) \) is

\[ r(t) = r_0 + \int_0^t [V_{\text{ant}}(t) - V_{\text{pos}}(t)] \, dt \]

where Vlat, Vsep, Vant, and Vpos are myocardial velocity at lateral, septal, anterior, and posterior regions, and \( r_0 \) is end-diastolic radius. LV rotation and torsion (degrees) was calculated as follows:

\[ \text{LV rotation} = \int_0^t [V_{\text{rot}}(t)] \, dt, \]

where the integration is carried from end diastole to end systole (ts), and

\[ \text{LV torsion} = \text{Apical LV rotation} - \text{Basal LV rotation}. \]

This analysis of myocardial velocity was performed with a personal computer and customized software within the EchoPAC platform (GE Medical Systems). Plots of data of the myocardial velocity and ECG versus time over several cardiac cycles derived from each sample region were transferred to a spreadsheet program (Excel 2000, Microsoft Corp) for the aforementioned calculations. All of the calculations for LV rotation and torsion were averaged for at least 3 consecutive beats.

Magnetic Resonance Imaging

MRI examinations were performed with a 1.5-T scanner (Sonata, Siemens Medical Solutions). Scout images were acquired to identify the cardiac axes. Then, for purposes of this study, 2 levels of short-axis image loops (localized by using the same landmarks as for the echocardiography studies) were acquired during suspended respiration (duration, 12 to 15 seconds) with an ECG-triggered, segmented k-space, grid tagged gradient-echo imaging protocol (spatial modulation of magnetization; tag spacing, 8 mm; echo time, 2.5 ms; repetition time sequence, 75 ms; flip angle, 15°; temporal resolution, 45 ms; slice thickness, 8 to 10 mm; field of view, 300 to 360 mm; rectangular field-of-view 75%; and base resolution, 256×256).13

Data Analysis

Processing of tagged MRI images was accomplished with a harmonic-phase (HARP) analysis software (Diagnosoft Inc), the details of which have been described elsewhere. Garot et al reported that HARP MRI provided accurate measurement of 2D strain fields, including angular deformation, compared with the conventional method, which has been validated against a sonomicrometry method. In brief, HARP uses isolated spectral peaks in the frequency-domain representation of tagged images. The inverse Fourier transform of a spectral peak yields a complex image, the phase of which is related to cardiac motion in one direction. Analysis of 2 spectral peaks enables 2D cardiac motion to be determined, including tracking individual points within the myocardium. The LV midwall was specified by manually delineating the endocardium and epicardium at end systole at each short-axis level; the midwall was then located automatically in all other frames. Points lying on the midwall contour were tracked automatically by the HARP software from end diastole to end systole. Rotation of the LV about its central axis at each short-axis level was calculated on the basis of the average motion of midwall points. Counterclockwise LV rotation and torsion as viewed from the apex were expressed as positive values in both DTI and MRI analysis.

Figure 2. LV rotation profile by MRI and DTI in representative case. Blue, red, and black lines indicate apical rotation, basal rotation, and LV torsion, respectively.

Figure 3. Regression analysis by repeated-measures regression models and limits-of-agreement analysis for measurement of LV apical and basal rotation, assessed by tagged MRI and DTI. Blue and red indicate apical (triangle) and basal (square) rotations, respectively. Correlation (analyzed by repeated-measures regression models) and identity lines depicted as solid and dashed lines, respectively, in left panel. In right panel, solid line indicates mean, and dotted lines, 2-SD limits.
Statistical Analysis

For temporal analysis, the time sequence was normalized to the percentage of systolic duration (i.e., at end systole, t was 100%) in both modalities. End systole was determined from the LV outflow Doppler flow profile in the echocardiography examinations and from the smallest cavity observed in the MRI studies.

To assess the correlation of the measurements, LV rotation and torsion obtained by DTI were compared with those measured by tagged MRI by linear regression at isochronal time points, corresponding to the individual MRI frames. Analysis was conducted for the 400 ms after end diastole (8.8±1.4 frames) because reliable magnetic tagging persists for this period. To compare isochronal LV rotation and torsion data while accounting for repeated observations per subject, we applied the following repeated-measures regression models:

$$R_{DTI} = a + b \times R_{MRI} + \sum_{i=1}^{n} \delta_i + \epsilon,$$

where $R_{DTI}$ and $R_{MRI}$ are rotation (or torsion) by DTI and MRI, respectively; $\delta_i$ indicates dummy variables that code for individual subjects, a, b, and c are models of parameters; and $\epsilon$ is the error term. The goodness-of-fit was assessed by a within-subject correlation coefficient:

$$r = \sqrt{SS_{cov}/(SS_{cov} + SS_{res})}$$

where $SS_{cov}$ and $SS_{res}$ stand for the sum of squares attributed to covariates or residuals, respectively. To assess the correlation of peak torsion of the 2 modalities, simple linear regression analysis was performed. The accuracy of the DTI rotation and torsion measurements with respect to the MRI data was examined by a limits-of-agreement analysis. The bias was expressed as the mean difference between the 2 methods, and the limits of agreement were 2 SDs of the difference of the 2 methods. To determine whether the difference in the values between the 2 methods was statistically significant, a paired t test was performed. Interobserver and intraobserver variability was examined in a blinded fashion in 7 randomly selected patients and expressed as correlation coefficients and coefficients of variation (CV) between measurements of 2 investigators and 2 readings (>1 month apart) as well as the mean and SD of their differences. All of the statistical analyses were performed with Statistica 6.0 software (Statsoft). All values are presented as mean±SD. $P<0.05$ was taken to indicate statistical significance for all analyses.

Results

The temporal resolution of the images acquired by MRI and DTI was 40±13 and 136±19 frames per second, respectively. LV rotation and torsion profile curves by the 2 modalities in a representative case are shown in Figure 2. Regression analysis for the measurement of LV rotation at apical and basal levels (Figure 3, left) at isochronal time points, analyzed by repeated-measures regression models, indicated a strong correlation ($r=0.87$ and 0.90, respectively; $P<0.0001$ for both levels) between the 2 methods, with an SEE of 1.65 and 1.06 (regression slope coefficient). The results of regression for LV torsion (Figure 4, left) also demonstrated very good correlation ($r=0.84$; $P<0.0001$, repeated-measures regression models; SEE, 1.42). The limits-of-agreement analysis demonstrated a minimal but statistically significant mean difference in measurement of apical LV rotation (Figure 3, right) and torsion (Figure 4, right); the bias is 0.79±1.91° for apical rotation ($P<0.001$), 0.20±1.37° for basal rotation ($P=0.09$), and 0.57±1.98° for LV torsion ($P<0.001$). In a comparison of the maximal torsion during systole only, there was also a strong correlation between DTI and MRI ($r=0.95$, $P<0.0001$) and good agreement (MRI−DTI: $\Delta$torsion = −0.35±1.30°, $P=0.24$; Figure 5).

Figure 4. Regression analysis by repeated-measures regression models and limits-of-agreement analysis for LV torsion. Solid, dashed, and dotted lines indicate same as in Figure 3.

Figure 5. Simple linear regression analysis and limits-of-agreement analysis for maximal LV torsion. Solid, dashed, and dotted lines indicate same as in Figure 3.
Reproducibility of the Method

Interobserver variability expressed as the correlation between measurements of 2 investigators was \( r = 0.90 \) for peak torsion (8.8 ± 3.8° versus 9.4 ± 4.1°, CV = 12.4%) and \( r = 0.96 \) for timing of peak torsion (93 ± 11% versus 95 ± 13% of systolic duration, CV = 3.8%). The error was random with no systematic trend observed. Intraobserver variability was lower than interobserver variability, with correlation coefficients of \( r = 0.93 \) for peak torsion (9.1 ± 3.9° versus 9.4 ± 4.1°, CV = 9.9%) and \( r = 0.97 \) for timing of peak torsion (97 ± 12% versus 95 ± 13%, CV = 3.1%). Thus, overall reproducibility of the measurement for LV torsion by DTI was sufficient. According to current-generation processing software, the time required to complete the analysis for a patient, once the DTI files were on the workstation, was 29 ± 6 minutes.

Discussion

In this study, we have developed a novel echocardiography method that can assess the time course of LV rotation and torsion. The method yielded LV torsion data that were correlated closely with the results from tagged MRI studies, the current “gold standard” for cardiac torsional deformation analysis, with acceptable bias and variability.

Prior Pathophysiological Studies by MRI of LV Torsion

MRI is an excellent way to study intramural wall motion and myocardial kinematics by myocardial tagging and has revealed important physiological findings. MRI LV torsion measurement has been reported in patients with hypertrophic cardiomyopathy, has revealed diastolic dysfunction in aortic stenosis due to delayed diastolic untwisting, and has demonstrated persistent abnormal torsion after partial ventriclectomy. MRI technique has been introduced to overcome this problem, which may ultimately be feasible for ultrasound imaging.

Advantage of the Current DTI Method for LV Torsion Assessment

Previous studies with 2D and color tissue Doppler echocardiography reported only the peak value of systolic torsion, not its temporal evolution. DTI possesses an intrinsic advantage in that it can directly detect myocardial velocity continuously through several cardiac cycles with high temporal resolution. The current method, therefore, provides not only peak rotation and torsion but also the profile curve during systole and subsequent early diastole, something that the tagged MRI protocol used in this study cannot achieve because of fading of the tagging after 400 ms. This later limitation of MRI could be overcome by retagging at end systole or steady-state free precession with myocardial tagging, which can analyze LV deformation during the diastolic phase. The method used in this study was optimized for assessment of systolic function and early diastole. These advantages of the DTI method may facilitate assessment of LV torsional dynamics, including the relationship between systolic torsion and diastolic suction, and may give insight into tissue molecular aspects of ventricular mechanics. Diastole is a very complex process that cannot be separated from the preceding systole. It is hypothesized that ventricular twisting in systole stores potential energy, perhaps via titin, the giant springlike molecule that resists both excessive shortening and elongation of the sarcomere (comprehensively reviewed recently in Granzier and Labeit). With the end of active contraction, titin may force rapid untwisting (which we and others have shown occurs mainly during isovolumic relaxation in the normal condition), thus lowering pressure in the ventricle, particularly the apex, and effectively sucking blood into the ventricle once the mitral valve opens. Exaggerated transmural variation in titin isoforms and titin-to-myosin heavy-chain ratios seen in rapid-pacing canine cardiomyopathy may contribute to changes in large-scale deformation, including twisting and untwisting, observed in that model. Thus, the simple noninvasive assessment of LV torsional behavior by the current method may have significant impact for both clinical and research assessment of the failing heart.

Limitations

An inevitable drawback of DTI is the angle dependency of the acquired myocardial velocity data. We sought to minimize this issue by extracting tangential velocity from 2 sampling points (lateral and septal regions) of the LV. Prior detailed MRI work has demonstrated in humans that peak strain and torsional components were typically greatest in the anterolateral wall and minimal in the septum. Because of this regional inhomogeneity, DTI velocity data in the 2 regions observed could represent LV rotational velocity while simultaneously correcting for cardiac translation. There was no way to guarantee absolute congruity of the short-axis levels used to assess LV torsion between echocardiography and MRI; however, the mitral valve and papillary muscles were used as landmarks in both modalities. We also should address the issue of through-plane motion, particularly at the basal slice. Although the MRI technique had almost enough thickness (8 mm in the current study) for the long-axis shortening motion (typically ~10 mm), it may affect DTI assessment of the basal slice. Fortunately, LV torsion increases nonlinearly toward the apex (where through-plane motion is minimal), thus limiting the impact of through-plane motion at the base where the gradient in twist is minimal. In depressed LV systolic function, long-axis shortening is less than in the normal heart, further limiting the impact of through-plane motion on the DTI results. Even in this situation, assessment of the basal slice rotation by DTI underestimated the MRI measurements more than at the apex (the regression slope was 0.92 in apical and 0.75 in basal), possibly because of the through-plane motion impact on DTI assessment. In addition, we should mention that the reported value of LV rotation and torsion by both DTI and MRI in the current study was likely underestimated because of through-plane motion. Recently, a 3D tagging MRI technique has been introduced to overcome this problem, which may ultimately be feasible for ultrasound techniques as well. The close agreement between MRI and echocardiography further suggests that this misalignment.
was not large enough to cause clinical concern. We should note, however, that the difference between tagged MRI and DTI values were relatively large in individual subjects, although the overall rotational profiles were quite similar. Developments in 3D echocardiography may help to make this more reproducible. Noise in the DTI data and the use of only 2 sampling points for rotation calculation may have contributed to the underestimation of apical LV rotation and torsion by the current method compared with MRI. Although this underestimation was statistically significant, the mean error was much less than 1° and the temporal profile was strongly correlated with MRI results. We therefore believe that the current method is clinically applicable.

The current DTI method cannot assess regional LV rotational behavior, although LV torsion is a global LV index of systolic and diastolic performance. Buchalter et al. reported that LV rotation was affected regionally during ischemia. Although we tried to include patients with a variety of cardiac pathologies, the studied population was biased toward patients who had an indication for MRI examination. It may be problematic to apply the current method to a severely deformed LV. An alternative algorithm of tissue velocity/displacement measurement in echocardiography, which is completely free from the angle dependency of the ultrasound beam line, should be used to overcome these problems.

Conclusions

The present study has validated the ability of DTI to assess LV torsional deformation against MRI tissue tagging. This novel method may promote noninvasive serial evaluations of the LV torsional behavior in clinical settings and provide unique and valuable information to patients with heart disease.

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