New Noninvasive Method for Assessment of Left Ventricular Rotation

Speckle Tracking Echocardiography

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Background—Left ventricular (LV) torsion is due to oppositely directed apical and basal rotation and has been proposed as a sensitive marker of LV function. In the present study, we introduce and validate speckle tracking echocardiography (STE) as a method for assessment of LV rotation and torsion.

Methods and Results—Apical and basal rotation by STE was measured from short-axis images by automatic frame-to-frame tracking of gray-scale speckle patterns. Rotation was calculated as the average angular displacement of 9 regions relative to the center of a best-fit circle through the same regions. As reference methods we used sonomicrometry in anesthetized dogs during baseline, dobutamine infusion, and apical ischemia, and magnetic resonance imaging (MRI) tagging in healthy humans. In dogs, the mean peak apical rotation was $-3.7\pm1.2^\circ$ ($\pm$SD) and $-4.1\pm1.2^\circ$, and basal rotation was $1.9\pm1.5^\circ$ and $2.0\pm1.2^\circ$ by sonomicrometry and STE, respectively. Rotations by both methods increased ($P<0.001$) during dobutamine infusion. Apical rotation by both methods decreased during left anterior descending coronary artery occlusion ($P<0.007$), whereas basal rotation was unchanged. In healthy humans, apical rotation was $-11.6\pm3.8^\circ$ and $-10.9\pm3.3^\circ$, and basal rotation was $4.8\pm1.7^\circ$ and $4.6\pm1.3^\circ$ by MRI tagging and STE, respectively. Torsion measurement by STE showed good correlation and agreement with sonomicrometry ($r=0.94, P<0.001$) and MRI ($r=0.85, P<0.001$).

Conclusions—The present study demonstrates that regional LV rotation and torsion can be measured accurately by STE, suggesting a new echocardiographic approach for quantification of LV systolic function. (Circulation. 2005;112:3149-3156.)

Key Words: echocardiography ■ ventricles ■ torsion ■ magnetic resonance imaging ■ rotation

Left ventricular (LV) torsion (or twist) plays an important role with respect to LV ejection and filling.1-4 During the cardiac cycle, there is a systolic twist and an early diastolic untwist of the LV about its long axis because of oppositely directed apical and basal rotations. As viewed from the LV apex, systolic apical rotation is counterclockwise and basal rotation, clockwise. The magnitude and characteristics of this torsional deformation have been described in different clinical and experimental studies, and it is well established that LV rotation is sensitive to changes in both regional and global LV function.5-17 Therefore, assessment of LV rotation represents an interesting approach for quantifying LV function. However, so far, magnetic resonance imaging (MRI) tagging has been the only clinically available method,7,13-16,18-21 and implementation has therefore been limited by complexity and cost.

In the present study, we introduce and evaluate echocardiographic speckle tracking (STE) as a new, noninvasive method for assessment of LV rotation and torsion. Because of scattering, reflection, and interference of the ultrasound beams in myocardial tissue, speckle formations in gray-scale echocardiographic images represent tissue markers that can be tracked from frame to frame throughout the cardiac cycle. We hypothesized that STE could be an accurate and clinically applicable noninvasive method for estimating the magnitude and dynamics of LV rotation. In this study, torsion was estimated as the difference in apical and basal rotation, and the STE method was validated by comparison with sonomicrometry in a dog model and with MRI tagging in humans.

Methods

Experimental Study

Thirteen mongrel dogs of either sex and an average body weight of 23.2 kg were anesthetized with a bolus of thiopental 25 mg/kg,
followed by continuous infusion of morphine (3.5 mg · kg⁻¹ · h⁻¹) and pentobarbital (2 mg · kg⁻¹ · h⁻¹), the latter reduced to half the dose after 4 hours of infusion. The animals were artificially ventilated through a cuffed endotracheal tube with room air and 20% to 50% O₂. The ECG was monitored from limb leads. One femoral vein could be adjusted manually when the tracking appeared to be poor. Rarely was >1 crystal visible in the echocardiographic image. Therefore, it was not a major problem that nonphysiological speckle patterns would falsely improve tracking quality. Figure 1B shows representative recordings. The starting position of the ROIs could be adjusted manually when the tracking appeared to be poor. ROIs were excluded in regions of insufficient speckle quality because of dropouts of ultrasound data or severe reverberations.

Figure 1. A, Schematic representation of the LV with implanted crystals (filled circles) and directions of systolic rotations of the anterior wall are indicated (arrows). When viewed from the apex, LV rotation is counterclockwise and basal rotation, clockwise. B, End-diastolic and end-systolic apical, 2D, gray-scale echocardiographic images from an animal experiment. The ROIs (white squares) and best-fit circle are indicated. The thin, dashed arrows point to ROIs, and the thick solid arrows point to crystals. The change in position of arrows from end diastole to end systole confirmed the counterclockwise rotation.

Echocardiographic Recordings and Analysis
LV short-axis recordings were obtained by conventional 2D gray-scale echocardiography (Vivid 7 scanner, GE Vingmed). Transducer frequencies (1.7 to 2.0 MHz), sampling rates (70 to 110 frames per second), and sector width (as narrow as possible) were adjusted for optimal speckle quality of the recordings. Short-axis echocardiograms were recorded in the same plane as used for sonomicrometry with the anatomic crystals as a reference. Echocardiographic recordings were done immediately before the sonomicrometric recordings and analyzed with a Matlab-based program that uses the speckle patterns in the gray-scale images. The speckle tracking method, with minimum sums of absolute differences of the B-mode pixel data²⁶ was used to track the position of a kernel region (a selected region of interest [ROI] with a unique speckle pattern) frame by frame throughout the cardiac cycle. To avoid drift, the tracking algorithm was applied both forward and backward, and the results were averaged. The size of the ROI was 3×5 mm, and the limit for maximum displacement velocity was set to 12 cm/s for vertical and 7 cm/s for lateral velocities. Nine ROIs were automatically superimposed on the echocardiographic image at end diastole and positioned to fit the circle-shaped LV. In our experimental study, this superimposed circle was aligned with the subepicardial LV circumference at basal (n=3), equatorial (n=4), and apical (n=4) short-axis levels (Figure 1A). Anatomical layers were approximated by cubic Hermite interpolation (standard interpolation used in Matlab [The MathWorks Inc]). The center of rotation for each LV plane was determined as the center of a best-fit circle through the interpolated coordinates. For each plane, the angular movements of the interpolated coordinates were averaged, and LV torsion was estimated as the difference in angular movement between apical and basal planes at isochronal points. Apical and basal rotation was calculated by measuring the difference of the interpolated coordinates where rotation is known to be minimal,

Experimental Protocol
After baseline recordings (~2 hours after thoracotomy) were obtained, dobutamine was infused at a rate of 5 μg · kg⁻¹ · min⁻¹, and recordings were repeated. After the return of dP/dt to baseline values, the LAD was occluded for 10 minutes and recordings were obtained. Baseline data were obtained from 13 dogs, whereas dobutamine intervention was not performed in the first 4 experiments. In 5 dogs, recordings during ischemia could not be obtained because of sustained ventricular fibrillation shortly after LAD occlusion. In 6 dogs, short-axis recordings from multiple levels were obtained ~5 minutes before and 5 minutes after pericardiectomy. This was done to explore the importance of an intact pericardium for LV rotation.

Sonomicrometry
For estimation of LV torsion and apical and basal rotation, 1 sonomicrometric crystal was implanted at the tip of the apex, and 11 crystals were implanted along the LV circumference at basal (n=3), equatorial (n=4), and apical (n=4) short-axis levels (Figure 1A). Anatomy allowed only 3 crystals at the basal level. To minimize myocardial damage and to achieve reproducible and parallel planes, the crystals at each level were placed subepicardially and at distances ~20, 40, and 60 mm from the LV apex. With signals obtained from the 3D grid of crystals, the coordinates of each crystal were automatically determined in space as a function of time (200 Hz). Parallel apical, equatorial, and basal LV planes were constructed by interpolation of the corresponding crystal coordinates, and the in-plane positions were approximated by cubic Hermite interpolation (standard interpolation used in Matlab [The MathWorks Inc]). The center of rotation for each LV plane was determined as the center of a best-fit circle through the interpolated coordinates. For each plane, the angular movements of the interpolated coordinates were averaged, and LV torsion was estimated as the difference in angular movement between apical and basal planes at isochronal points. Apical and basal rotation was calculated by measuring the difference of the interpolated coordinates where rotation is known to be minimal,
Clinical Study

Twenty-nine healthy volunteers (15 men and 14 women; mean age, 33 ± 6 years) were included. The study protocol was approved by the National Committee for Medical Research Ethics of Norway. All participants gave written, informed consent.

MRI Tagging

Images were obtained with a 1.5 T scanner (Magnetom Vision Plus, Siemens). To standardize short-axis image planes between individuals, the basal cine image was defined just distal to the fibrous mitral ring, and the apical level, just proximal to the level with luminal closure at end systole. Striped tags were prescribed separately in 2 orthogonal orientations (45° and 135°) with spatial modulation of magnetization in a grid pattern with an 8-mm distance between tags and a time resolution of 35 ms. Images were acquired during 12- to 18-second breath-holds and triggered by ECG. Consistent with STE measurements, rotation by MRI tagging was calculated as the average of measurements obtained in the midendocardial and subendocardial layers. Recordings were analyzed by Harmonic Phase Imaging (HARP version 1.0, Diasonost Inc) at an experienced MRI reading center (Johns Hopkins University).

Echocardiographic Recordings and Analysis

Short-axis echocardiographic recordings were obtained with the volunteers in a supine left lateral position. The same scanner and acquisition settings were used as for the experimental recordings. Short-axis recordings at the basal level were obtained from a standard parasternal probe position, and recordings at the apical level, from a more distal anterior or anterolateral position. Short-axis images were acquired at approximately the same levels as the MRI cine images. Echocardiographic recordings were taken within 5 to 10 minutes before or after MRI examinations during breath-holds, and an effort was made to make the LV cross section as circular as possible. The quality of the speckles improved progressively from the epicardium to the endocardium, and in many cases, the subepicardial speckle quality was suboptimal. Therefore, we limited the study to assessment of rotation of the midendocardial and subendocardial layers. Criteria for adjustments or rejections of ROIs were the same as for the experimental study.

Reproducibility of the STE Method

All echocardiographic analyses were done without knowledge of the results from the reference methods. To assess interobserver variability, 6 experimental and 6 clinical echocardiographic recordings were randomly selected and then independently analyzed by 2 different observers (including selection of the cardiac cycle, placement of the ROIs, and deriving the results).

Statistical Analysis

Data are presented as mean ± SD unless otherwise stated. The rotation and torsion measurements obtained by STE and reference methods were compared by a least-squares linear-regression method and by the Bland-Altman method. In the experimental study, we used a 1-way repeated-measures ANOVA followed by the Bonferroni correction for predefined comparisons of baseline versus dobutamine and baseline versus ischemia (SPSS version 12). Statistical differences were considered significant at \( P < 0.05 \). Interobserver variability was assessed by the intraclass correlation coefficient and the Bland-Altman method.

Results

LV Rotation and Torsion by STE Versus Sonomicrometry: Experimental Study

Figure 2 shows representative traces of LV apical and basal rotation and torsion by STE and sonomicrometry at baseline, during dobutamine infusion, and during acute LAD occlusion (apical ischemia; Table 1). By convention, the direction of rotation was referenced to apical views as clockwise (positive values) or counterclockwise (negative values). By both methods, an early systolic clockwise followed by a counterclockwise rotation during ejection was seen at the apical level, with corresponding counterclockwise-clockwise rotations at the basal level. At baseline, peak apical rotation increased with dobutamine, from \(-4.1 ± 1.2°\) to \(-6.7 ± 0.9°\) \((P < 0.001)\) and from \(-3.7 ± 1.2°\) to \(-6.2 ± 0.9°\) \((P = 0.001)\) as measured by STE and sonomicrometry, respectively. Peak basal rotation increased from \(2.0 ± 1.2°\) to \(4.5 ± 1.2°\) \((P < 0.001)\) and from \(1.9 ± 1.5°\) to \(4.8 ± 2.0°\) \((P < 0.001)\). Apical rotation decreased during LAD occlusion, to \(-1.8 ± 1.3°\) \((P < 0.001)\) and \(-2.0 ± 1.9°\) \((P = 0.007)\) by STE and sonomicrometry, respectively, whereas basal rotation was unchanged with either method. Correspondingly, LV torsion increased during dobutamine infusion \((P < 0.001)\) and decreased during LAD occlusion \((P = 0.003\) by STE and \(P = 0.055\) by sonomicrometry).

Figures 3 and 4 are scatterplots, with correlation and agreement data, for peak rotation and torsion by STE and sonomicrometry. Separate regression analyzes of pooled data for apical and basal rotation by STE and sonomicrometry demonstrated good correlation \((r = 0.92, P < 0.001,\) and \(r = 0.76, P < 0.001,\) respectively), and as shown by Bland-Altman analyses, there were no systematic differences between the methods. There was also good correlation and agreement between STE and sonomicrometry for the time to peak rotation at the apex \((y = 0.79x + 46, r = 0.58, P = 0.006,\) and mean difference \(-10 ± 49\) ms) and at the base \((y = 0.96x + 23, r = 0.9, P < 0.001,\) and mean difference \(-13 ± 23\) ms). For LV torsion, the results were equally good for magnitude and timing \((y = 0.92x - 0.83, r = 0.94, P < 0.0001\) and mean difference \(0.3 ± 1.2°,\) and \(y = 0.90x + 23, r = 0.90, P < 0.0001\) and mean difference \(2 ± 26\) ms, respectively).
TABLE 1. Results From the Experimental Study

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n=13)</th>
<th>Dobutamine (n=9)</th>
<th>Ischemia (n=8)</th>
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<tr>
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<td>Early Systole</td>
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<td>Early Systole</td>
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<td>Heart rate, bpm</td>
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<td>LV peak systolic pressure, mm Hg</td>
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<td>118±3*</td>
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<td>LV dP/dt\text{max}, mm Hg/s</td>
<td>1515±102</td>
<td>2818±265*</td>
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<td>Apical rotation, °, by</td>
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<td>0.8±0.6</td>
<td>1.5±1.1</td>
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<tr>
<td>STE</td>
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<td>Time to peak apical rotation, ms, by</td>
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<tr>
<td>Sonomicrometry</td>
<td>58±34</td>
<td>33±16</td>
<td>26±27</td>
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<tr>
<td>STE</td>
<td>45±22</td>
<td>45±8</td>
<td>34±39</td>
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<td>Basal rotation, °, by</td>
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<tr>
<td>STE</td>
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<td>Torsion, °, by</td>
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<td>Time to peak torsion, ms, by</td>
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<td></td>
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</tr>
<tr>
<td>Sonomicrometry</td>
<td>57±33</td>
<td>34±13</td>
<td>31±17</td>
</tr>
<tr>
<td>STE</td>
<td>55±30</td>
<td>50±17</td>
<td>33±27</td>
</tr>
</tbody>
</table>

Values are mean±SD.
*P<0.05 vs baseline (1-way repeated-measures ANOVA; P value after Bonferroni correction).

There was no significant change in heart rate or time to peak rotation from baseline to interventions. However, there was a tendency toward increased heart rate during both ischemia and dobutamine infusion, and a reduced time to peak rotation during dobutamine infusion. Short-axis recordings from the time of crystal implantation confirmed minimal rotation at the equatorial level (−0.2±0.3°).

**LV Rotation and Torsion by STE Versus MRI Tagging: Healthy Humans**

Figure 5 shows representative examples of rotation and torsion by STE and MRI tagging in healthy subjects, and Table 2 summarizes the findings. Consistent with the experimental study, LV apical rotation during ejection was counterclockwise by STE and MRI, and basal rotation was clockwise. Early systolic basal rotation was counterclockwise by both methods, whereas early systolic apical clockwise rotation was confirmed only by STE.

Figure 6 displays correlation and Bland-Altman plots for STE and sonomicrometry data. The correlation and agreement between the 2 methods were good for both peak apical rotation (r=0.91, P<0.001) and peak basal rotation (r=0.67, P<0.001). There were also good correlations and agreements for time to peak apical rotation (y=0.62x+132, r=0.47, P<0.012, and mean difference −14±46 ms) and for the time to peak basal rotation (y=0.82x+62, r=0.61, P<0.001, and mean difference 0±33 ms). For the magnitude of peak torsion and time to peak torsion, correlation and agreement were also good (y=0.85x−1.6, r=0.85, P<0.001, and mean difference −1.4±2.0°, and y=0.56x+154, r=0.49, P<0.008, and mean difference −10±30 ms, respectively).

In our clinical study, ROIs were rejected in only 10% of the recordings (1 ROI in 6% and 2 ROIs in 4% of the recordings). In the experimental study, ROIs were rejected in 18% of the recordings (1 ROI in 10% and 2 ROIs in 8% of the recordings).

**Effect of Pericardiotomy on LV Rotation and Torsion**

Pericardiotomy caused no change in LV apical or basal rotation (−5.7±0.5 and −5.5±0.4° [P=NS], and 3.1±0.6 and 3.0±1.2° [P=NS], respectively). During the 2- to 3-hour period before the baseline recording, however, apical and basal rotation decreased (to −4.2±0.6, P<0.05, and 1.8±0.7°, P=NS, respectively). Furthermore, LV dP/dt\text{max} and LV pressure, which were unaffected by pericardiotomy (2138±485 and 2134±453 mm Hg/s, P=NS, and 120±7 and 120±6 mm Hg, P=NS, respectively), decreased to 1644±319 (P=NS) and 104±5 (P=0.040), respectively, at the time of baseline recordings. Similarly, torsion was unaffected by pericardiotomy (−8.7±1.8° before versus −8.6±2.0° after) and was reduced at the time of baseline recordings (−6.0±1.5°, P<0.002).

**Interobserver Variability**

Measurements by STE of peak rotation by 2 independent observers showed a mean difference between the 2 analyses...
of 0.4±1.6°. The intraclass correlation coefficient between the 2 observers was 0.99. The typical time spent for data analysis was <1 minute.

Discussion

Echocardiography is one of the cornerstones for diagnosing and monitoring cardiac diseases. However, angle-independent assessment of LV deformation and rotation has only been possible by MRI tagging. The present study demonstrates that STE can measure LV torsional deformation noninvasively by automated tracking of speckles from apical and basal short-axis recordings. The validity of our approach was tested with sonomicrometry as a reference method in an animal model and MRI tagging in humans. With sonomicrometry, the implanted myocardial crystals served as anatomic landmarks that ensured that the LV cross-sectional planes studied by the 2 methods were the same, and measurements could be performed only a few seconds apart. Furthermore, in the animal model, comparison between the methods could be completed under a wide range of experimental settings known to alter LV rotation. The STE method showed dynamics, magnitudes, and timing of peak basal and apical rotation and torsion that were closely related to measurements by sonomicrometry. The same relation was found when STE was compared with MRI in healthy volunteers.

Apical Rotation

In the present study, counterclockwise rotation during LV ejection was demonstrated at the apical level in healthy individuals and was found in the dog model. During dobutamine infusion, there was an increase in apical rotation and a tendency toward a decrease in the time to peak rotation, whereas during LAD occlusion, apical rotation was reduced. These changes in apical rotation by dobutamine and apical ischemia are concordant with the findings from previous studies that have used other methods.2,8,10,11,29

Although systolic apical rotation was predominantly counterclockwise, there was a small, clockwise rotation during isovolumic contraction. The oppositely directed rotation was demonstrated by both sonomicrometry and STE but not by MRI (see Figures 3 and 5). This phenomenon has been described previously and might be attributed to earlier activation of subendocardial fibers (right-handed helix) than subepicardial fibers.1,6,30,31 The reason why this motion was not recognized by MRI tagging is probably the relatively low temporal resolution of the method (35 ms).

Basal Rotation

Consistent with previous studies,14–16,19–21,23–25 LV rotation at the base was predominantly clockwise. During early systole, however, there was a counterclockwise rotation that gradually changed into a more substantial clockwise rotation during ejection. Dobutamine infusion caused a significant increase in basal clockwise rotation, with no change in the time to peak rotation. To our knowledge, no previous studies exist of basal rotation during dobutamine infusion. Apical ischemia caused no significant change in basal rotation.14
reflecting the fact that there was no impairment of LV function between equator and base.

Some studies have indicated that basal LV rotation is minimal. However, in patients with aortic stenosis, a reduced magnitude of basal rotation compared with normal hearts has been observed. Furthermore, in patients with chronic heart failure, 6 months of treatment was associated with an increase in basal rotation, whereas apical rotation was unchanged, indicating that measurement of basal rotation may be clinically relevant. However, compared with the reference methods, assessment of rotation by STE was less accurate for the basal level than for the apical level. Therefore, deviations in basal rotation could be difficult to assess by STE, and larger clinical studies will need to be performed to answer this question.

Comparison With Previous Studies
The magnitudes of LV apical and basal rotation and torsion, as reported in previous experimental and clinical studies, differ substantially and a number of factors may explain this variance. As demonstrated by Henson et al, apparent differences in torsion between mice and humans are due to the different sizes of their ventricles. When systolic torsion angle was normalized for LV length, torsion was essentially similar in the 2 species. Furthermore, because torsion angle is a nonlinear function of ventricular length, its magnitude depends critically on the measurement level relative to the LV base or other reference point. The relatively high values of apical rotation measured by Gibbons Kroeker et al are most likely explained by their measurement technique, which recorded rotation at the distal part of the LV apex. Another factor that may explain some of the variance in torsion magnitude in different studies is the existence of a marked transmural gradient, with subendocardial values almost twice those of subepicardial values. In the dog model, we measured subepicardial rotation, and during baseline conditions, torsion was about 6°. These values are in the same range as reported by Buchalter et al, who measured both subepicardial and subendocardial torsion in anesthetized dogs by MRI tagging. Furthermore, the hemodynamic and contractile status of the heart in different animal models may vary and give rise to differences in torsion. A significant reduction in rotation at the apical level and a trend toward a reduction at the base was found at the time of baseline recordings. This was associated with reductions in LV pressure and LV dP/dt max, indicating that there was some reduction in LV systolic function. Most likely the decrease in rotation reflects impairment of LV function owing to the extensive surgical instrumentation.

Limitations
Several important factors may influence the accuracy of STE. The quality of the recordings must be high to achieve correct tracking, and it requires proper adjustment of frame rate, probe frequency, and focus. In the present study, tracking quality was evaluated visually, and ROIs of poor tracking were either manually moved to areas of better speckle quality or deleted. Because rotational displacement is relatively homogeneously distributed around the LV circumference in healthy myocardium, deletion of 1 or a maximum of 2 ROIs will have a minimal effect on average rotation.

A fundamental problem with STE in LV short-axis images is that longitudinal motion of the LV causes the myocardium
displacement, according to our results, was most pronounced at the LV base, where the longitudinal cross-sectional levels during the cardiac cycle. This problem thickness) will represent the myocardium from different speckles generated from the ultrasound beam (2 to 3 mm of to move in and out of the image plane. As a consequence, this phenomenon. A limitation in the clinical study was that speckle quality in some cases was suboptimal in the subepicardial layer of the LV. Therefore, for validation against MRI, we compared measurements from the middle and inner wall layers. Hopefully, technical developments in ultrasound technology will resolve this problem. In the dog study, we had direct access to the heart via sternotomy, and by using ultrasound gel as a standoff, we obtained satisfactory tracking quality in all layers of the LV wall.

One limitation of clinical routine use of STE is the selection of reproducible anatomic landmarks for measuring apical rotation. One approach was to move the cross-sectional image plane as far distally as possible. Another approach could be to measure at the most distal level that does not have luminal closure during systole. At the basal level, reproducible image planes were easier to obtain with the fibrous mitral ring for orientation. Selection of imaging plane is a challenge, and clinical testing of STE in patients is needed to determine whether reproducible measurements can be obtained from ventricles that may change in size and geometry over time.

In contrast to STE, which provides a measure relative to a stationary reference point outside the heart (the echocardiographic transducer), sonomicrometry provides no direct measure of rotation. Because apical and basal rotations are in opposite directions, somewhere between them there exists a level where rotation changes from one direction to the other. A number of studies in dogs, mice, and humans have confirmed that the short-axis level approximately one third from the base to apex (LV equator) shows minimal rotation. Taking into account the good relation between STE and sonomicrometry, this finding indicates that our methodological approach was adequate. Furthermore, for strict methodological comparison of STE with sonomicrometry, assessment of LV torsion was sufficient, and the correlation and agreement between torsion by the 2 methods were very good.

Conclusions
This study demonstrates that the magnitude, timing, and dynamics of regional LV rotation and torsion can be measured accurately by STE. When MRI and sonomicrometry were used as reference methods, STE showed good correlation and agreement, suggesting that STE has the potential to become a fast and accurate noninvasive clinical tool.

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