Augmentation of Left Ventricular Apical Endocardial Rotation With Inotropic Stimulation Contributes to Increased Left Ventricular Torsion and Radial Strain in Normal Subjects

— Quantitative Assessment Utilizing a Novel Automated Tissue Tracking Technique —

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Background The difference in the left ventricular (LV) torsion of the endo- and epicardium (Endo, Epi) with inotropic stimulation and its relation to radial strain (RS) remain unclear.

Methods and Results LV basal and apical short-axis images were recorded in 13 normal subjects at rest and during dobutamine infusion (5, 10 μg·kg⁻¹·min⁻¹). A total of 8 points (anterior, lateral, posterior and septum in both Endo and Epi) were manually placed by 2-dimensional tissue tracking technique and the movement of these points during a cardiac cycle was tracked, after which the rotation angles and RS were calculated. LV torsion was defined as the net difference between the basal and apical rotations. In the LV apex, Endo-rotation increased (7.8±2.7 to 14.1±4.6 degrees, p<0.01), whereas Epi-rotation was unchanged, with dobutamine. The apical Endo-rotation was significantly greater than the Epi-rotation, although no difference was seen between the Endo and Epi in the LV base throughout the study. During dobutamine infusion, the LV Endo-torsion increased (9.5±2.8 to 19.3±4.8 degrees, p<0.01) and these values were greater than those for Epi. The apical RS increased with the dobutamine dose (39.0±9.3 to 61.9±15.5%, p<0.01), whereas basal RS initially increased at 5 μg·kg⁻¹·min⁻¹, but thereafter showed no further increase at 10 μg·kg⁻¹·min⁻¹ of dobutamine.

Conclusions Augmentation of LV rotation with inotropism was clearly observed in the apical Endo, thus causing increased LV Endo-torsion and apical RS. (Circ J 2007; 71: 661–668)

Key Words: Left ventricular torsion; Radial strain; Tissue tracking
myocardial wall thickening (ie, radial strain (RS)). Although the LV Endo contributes more than the Epi to RS,21-26 the difference between the Endo and Epi in LV torsion with inotropic stimulation and its relationship to RS still remain to be unelucidated. The aim of this study was to separately evaluate LV torsion in the Endo and Epi, and ascertain the effects of inotropic stimulation on both, and also clarify the relationship to RS.

Methods

Study Groups

We performed an echocardiographic analysis of 13 normal volunteers (mean age 30±2.6 years) under baseline conditions and during dobutamine infusion (Dob). In addition, 3 normal volunteers and 8 patients were also recruited to validate the LV torsion values against the tagged MRI findings.

The study protocol was approved by the Institutional Review Board of the Yamaguchi University Hospital. Written informed consent was given by all participants before the study. In addition, no complications resulted from these investigations.

Echocardiography

Echocardiography was performed using an EUB-8500 (Hitachi Medical Co, Tokyo, Japan) equipped with a 2- to 4-MHz sector transducer with the subject in the left lateral decubitus position at end-expiration. We scanned the LV basal and apical short-axis views at the mitral valve level and the LV cavity level with no visible papillary muscles, respectively.

All imaging data for 2 cardiac cycles were digitized and stored on a hard disk on the ultrasound machine and then transmitted to a personal computer (Sony Co Pentium 4, 3GHz, Tokyo, Japan) for further analysis. We scanned the LV basal and apical short-axis views at the mitral valve level and the LV cavity level with no visible papillary muscles, respectively.

All imaging data for 2 cardiac cycles were digitized and stored on a hard disk on the ultrasound machine and then transmitted to a personal computer (Sony Co Pentium 4, 3GHz, Tokyo, Japan) for further analysis. The images were acquired at both baseline and during Dob infusion (intravenously at a rate of 5μg·kg⁻¹·min⁻¹ during the first 5 min and then at 10μg·kg⁻¹·min⁻¹ during the next 5 min).

To quantify the LV volume and to evaluate systolic dynamics, a standard 2D echocardiographic examination was performed. LV end-diastolic dimension (LVEDd) and end-systolic dimension (LVESd) were measured in the parasternal long-axis view. The LV volume and stroke volume (SV) were obtained using the modified Simpson method from the apical 4- and 2-chamber views. The percent fractional shortening (%FS) at both the base and apex were also calculated as (LVEDd–LVESd)/LVEDd. The peak velocities of early (E) and late (A) mitral inflow, the E/A ratio, and deceleration time of E wave (DcT) were measured using pulse-wave Doppler.

Measurement of LV Rotation and Torsion

Image analysis was performed using a newly developed customized software program with 2DTT (US Image Viewer 05-01, Hitachi Medical Co, Tokyo, Japan). If 1 selects the tracking point in the first frame of the 2D echocardiographic image, the algorithm searches the next frame for the region that is assumed to be the closest to the selected point, according to the information of pixel intensity distribution. By repeating this process frame by frame, the total movement of the selected point can thus be determined as a coordinate.15 Four points (anterior, lateral, posterior and septum) on both the Endo and Epi were manually placed on the LV short-axis views at end-diastole (Fig 1) and the movement of these points during the cardiac cycle was tracked. The loci of these 8 points were confirmed (Fig 1). After finishing the tracking, the total movement of the selected point can be expressed as a coordinate. The center of the points was determined as the center of rotation in each frame using US Image Viewer, and then the rotation angles were calculated (Fig 2). LV torsion was defined as the net difference between the basal and apical rotation angles, and these profile curves were also obtained (Fig 2).

Strain Analysis by 2DTT

To calculate the RS, the same points for measuring LV rotation on the LV basal and apical short-axis images were used for an off-line analysis. If the pattern-matching algorithm is applied to a pair of selected points on the surface of each of the Endo and Epi, then the change in the distance between the 2 surfaces (ie, endo- and epicardium) during 1 cardiac cycle can be measured.15 The movement of these points during a cardiac cycle was tracked and then the strain profile was extracted.

Fig 1. Loci of the tracking points (anterior, lateral, posterior and septum) in both the endocardium (Endo) and epicardium (Epi), overlaid on 2-dimensional echocardiographic image. ED, end-diastole; ES, end-systole; orange line, the locus during systole; yellow point, the location. Apical level (Left): the left ventricle rotates counterclockwise as viewed from apex. Basal level (Right): the left ventricle rotates clockwise.
Assessment of LV Rotation and Radial Strain

Validation of LV Torsion Against Tagged MRI

The study group comprising 5 patients with cardiomyopathy, 3 others undergoing clinically indicated cardiac MRI and 3 healthy volunteers with a normal resting LV systolic function underwent the echocardiographic study on the same day as the MRI (1.0-T scanner, Harmony, Siemens Medical Solutions). The LV torsion in both the Endo and Epi were obtained as previously described.\textsuperscript{18-20}

Statistical Analysis

The results are expressed as the mean value ± SD. The hemodynamic values, 2D and Doppler echocardiographic values, rotation angles and torsion values for the 3 different stages (baseline, 2 Dob doses) were compared by 1-way analysis of variance followed by the Bonferroni/Dunn posthoc test. The torsion measured by 2DTT and by tagged MRI was compared by a least-squares linear-regression method. Statistical significance was accepted at p<0.05.

Inter- and intra-observer variabilities were assessed for LV torsion (Endo, Epi) in 10 randomly selected participants and calculated as the SD of the differences between 2 measurements and expressed as a percent of the average value.

Results

The hemodynamic data and conventional echocardiographic...
graphic measurements are shown in Table 1. The heart rate and systolic blood pressure significantly increased with 10 μg·kg⁻¹·min⁻¹ Dob infusion compared with baseline. LVEDd and volume with inotropic stimulation did not differ substantially from the baseline values. The LVESd decreased significantly with both doses of Dob. The %FS of the LV apex increased with Dob infusion, but that in the LV base decreased significantly with both doses of Dob. The %FS (apex) (%) 32±6.6 to 44±7.2, p<0.01. There was no difference between the Endo and Epi in the LV base throughout of the study (Fig 7).

The E wave increased and the DcT shortened during the Dob infusion. Regional differences in the rotation of the Endo were smaller than in the lateral or IVS regions during Dob infusion. Regional differences in basal rotation in the Endo were greater than in the LVEDd and LVESd (mm) 49±2.8, 50±3.6, 51±3.2. The LV Rotation Angle and Torsion in the Endo and Epi

The apical rotation angle in the Endo was greater than in the Epi, but there was no difference in the basal rotation angles of the Endo and Epi at baseline (Table 2). Fig 4 shows representative traces of the apical and basal rotations and LV torsion at baseline and during Dob infusion. In the LV apex, the Endo-rotation increased at both doses of Dob (7.8±2.7 to 12.4±4.5 degrees with 5 μg·kg⁻¹·min⁻¹; 14.1±4.6 degrees with 10 μg·kg⁻¹·min⁻¹, p<0.01), whereas in the LV base, rotation did not change (Table 2, Fig 5A). In the LV base, although both Endo- and Epi-rotation unchanged at 5 μg·kg⁻¹·min⁻¹ Dob infusion, both rotations increased at 10 μg·kg⁻¹·min⁻¹ (Endo: 2.6±1.9 to 5.7±2.9 degrees; Epi: 2.4±1.4 to 5.0±2.6 degrees, p<0.01). There was no difference between the Endo and Epi in the LV base throughout of the study (Table 2, Fig 5B). The LV torsion in the Endo increased as the dose of Dob increased (9.5±2.8 to 16.0±3.5 degrees with 5 μg·kg⁻¹·min⁻¹; 19.3±4.8 degrees with 10 μg·kg⁻¹·min⁻¹, p<0.01) and the values were greater than for the Epi (Fig 5C). LV torsion in the Epi increased only at 10 μg·kg⁻¹·min⁻¹ Dob infusion.

Regional Differences in LV Rotation and Torsion

In the LV apex, regional differences in the rotation of the Endo and Epi were not seen throughout the study (Fig 6A), whereas in the LV base, rotation in the anterior regions of the Endo were smaller than in the lateral or IVS regions during Dob infusion. Regional differences in basal rotation in the Epi were similar to those in the Endo; namely, rotation in the anterior regions of the Epi was less than in the lateral region (Fig 6B). No regional differences were observed in either LV Endo- or Epi-torsion throughout the study (Fig 7).

Table 1 Hemodynamic Data and Echocardiographic Measurements

<table>
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<th>Baseline</th>
<th>Dobutamine</th>
<th>Dobutamine</th>
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<tbody>
<tr>
<td></td>
<td>5 μg·kg⁻¹·min⁻¹</td>
<td>10 μg·kg⁻¹·min⁻¹</td>
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<tr>
<td><strong>Hemodynamic</strong></td>
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<tr>
<td>Heart rate (beats/min)</td>
<td>60±6.6</td>
<td>64±6.4</td>
<td>83±10.3 *≤</td>
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<td>Systolic BP (mmHg)</td>
<td>112±12.8</td>
<td>121±16.4</td>
<td>136±26.9 *</td>
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<tr>
<td>Diastolic BP (mmHg)</td>
<td>63±12.1</td>
<td>63±15.7</td>
<td>67±17.5</td>
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<td><strong>2-dimensional echocardiography</strong></td>
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<tr>
<td>LVEDd (mm)</td>
<td>49±2.8</td>
<td>50±3.6</td>
<td>51±3.2</td>
</tr>
<tr>
<td>LVESd (mm)</td>
<td>33±5.3</td>
<td>29±5.7 *</td>
<td>28±3.9 *</td>
</tr>
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<td>%FS (base) (%)</td>
<td>32±3.7</td>
<td>41±3.9 *</td>
<td>45±5.1 *</td>
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<tr>
<td>%FS (apex) (%)</td>
<td>32±6.6</td>
<td>44±7.2 *</td>
<td>52±8.3 *</td>
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<tr>
<td>EDV (ml)</td>
<td>115±15.2</td>
<td>122±20.1</td>
<td>124±17.5</td>
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<td>SV (ml)</td>
<td>64±3.4</td>
<td>77±6.1 *</td>
<td>85±6.1 *</td>
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<td><strong>Pulsed-wave Doppler</strong></td>
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<tr>
<td>Peak E velocity (m/s)</td>
<td>0.74±0.15</td>
<td>1.0±0.2 *</td>
<td>1.1±0.24 *</td>
</tr>
<tr>
<td>Peak A velocity (m/s)</td>
<td>0.4±0.8</td>
<td>0.44±1.0</td>
<td>0.49±1.2</td>
</tr>
<tr>
<td>E/A</td>
<td>1.9±0.6</td>
<td>2.5±0.9</td>
<td>2.5±0.9</td>
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<td>DcT (ms)</td>
<td>188±20</td>
<td>176±20</td>
<td>165±19</td>
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</table>

BP, blood pressure; LVEDd, left ventricular end-diastolic dimension; LVESd, left ventricular end-systolic dimension; FS, fractional shortening; EDV, end-diastolic volume; SV, stroke volume; E velocity, the early velocity of mitral inflow; A velocity, the late velocity of mitral inflow; DcT, deceleration time of the early diastolic wave of mitral inflow.

*p<0.05 vs baseline, †p<0.05 vs 5 μg·kg⁻¹·min⁻¹.

Table 2 Rotation Angle, LV Torsion, and Radial Strain

<table>
<thead>
<tr>
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<th>Baseline</th>
<th>Dobutamine</th>
<th>Dobutamine</th>
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<tbody>
<tr>
<td></td>
<td>5 μg·kg⁻¹·min⁻¹</td>
<td>10 μg·kg⁻¹·min⁻¹</td>
<td></td>
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<tr>
<td><strong>Apical rotation (degree)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endo</td>
<td>7.8±2.7 *</td>
<td>12.4±4.5 *</td>
<td>14.1±4.6 *</td>
</tr>
<tr>
<td>Epi</td>
<td>5.2±1.5</td>
<td>6.4±2.8</td>
<td>6.4±3.3</td>
</tr>
<tr>
<td><strong>Basal rotation (degree)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endo</td>
<td>2.6±1.9</td>
<td>4.2±2.3</td>
<td>5.7±2.9 *</td>
</tr>
<tr>
<td>Epi</td>
<td>2.4±1.4</td>
<td>3.1±1.3</td>
<td>5.0±2.6 *</td>
</tr>
<tr>
<td><strong>LV torsion (degree)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endo</td>
<td>9.5±2.8 *</td>
<td>16.0±3.5 *</td>
<td>19.3±4.8 *</td>
</tr>
<tr>
<td>Epi</td>
<td>7.2±1.8</td>
<td>9.1±3.5</td>
<td>10.8±3.1 *</td>
</tr>
<tr>
<td><strong>Radial strain (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Apex</td>
<td>39.0±9.3</td>
<td>49.5±9.0</td>
<td>61.9±15.5 *</td>
</tr>
<tr>
<td>Base</td>
<td>38.5±7.1</td>
<td>52.8±11.1 *</td>
<td>55.4±10.1 *</td>
</tr>
</tbody>
</table>

LV, left ventricular; Endo, endocardium; Epi, epicardium.

*p<0.05 vs baseline, †p<0.05 vs 5 μg·kg⁻¹·min⁻¹, *p<0.05 vs epicardium.
Assessment of LV Rotation and Radial Strain

LV Torsion by 2DTT vs Tagged MRI

The LV torsion in both the Endo and Epi as measured by 2DTT significantly correlated with that by tagged MRI (Endo: r=0.95, Epi: r=0.85, p<0.05). The LV torsion evaluated by 2DTT was smaller than that by tagged MRI (Fig 8).

Observer Variabilities

Inter- and intra-observer variabilities for LV torsion were 5.6% (Endo), 9.2% (Epi), and 6.4% (Endo), 9.0% (Epi).
Fig 6. Segmental rotation angles in the left ventricular apex (A) and base (B). There are regional differences in basal rotation but few in apical rotation. ANT, anterior; LAT, lateral; POST, posterior; IVS, intraventricular septum. Solid bars, endocardium; Open bars, epicardium. *p<0.05.

Fig 7. Segmental left ventricular (LV) torsion. Few regional differences can be seen. ANT, anterior; LAT, lateral; POST, posterior; IVS, intraventricular septum. Solid bars, endocardium; Open bars, epicardium.

Fig 8. Validation of left ventricular (LV) torsion against tagged magnetic resonance imaging (MRI). The LV torsion in both the endocardium and epicardium as measured by 2-dimensional echocardiographic tissue tracking system (2DTT) significantly correlated with that by tagged MRI.
LV Radial Strain

The apical RS increased at 5 g·kg⁻¹·min⁻¹ (NS), and increased with 10 g·kg⁻¹·min⁻¹ Dob (39.0±9.3 to 49.5±9.9% (5 g·kg⁻¹·min⁻¹) to 61.9±15.5% (10 g·kg⁻¹·min⁻¹), \( p<0.01 \)). The basal RS initially increased at 5 g·kg⁻¹·min⁻¹, but showed no further increase with 10 g·kg⁻¹·min⁻¹ Dob (Table 2). The apical RS significantly correlated with LV torsion in the Endo \((r=0.42, p<0.05)\), not in the Epi. The basal RS did not correlate with LV torsion in either the Endo or the Epi.

Discussion

We separately assessed the basal and apical rotations in the LV Endo and Epi using a newly developed 2D echocardiographic tissue tracking technique (2DTT), and demonstrated that the effect of an inotropic agent on these rotations differed between the LV base and apex. Namely, Dob augmented the apical rotation angle in the Endo to a greater degree than in the Epi, although little difference was observed between the Endo and Epi for basal rotation. Consequently, LV Endo torsion was greater than Epi torsion during Dob infusion.

Evaluation of LV Torsion

LV torsion has been assessed by biplane cinefluoroscopic marker images obtained from cardiac transplant recipients with implanted radioopaque LV myocardial markers. Tagged MRI has also been introduced to noninvasively assess LV torsion in various cardiac diseases by measuring LV myocardial deformation using labeling of specific ventricular regions. However, implantation of myocardial markers occurs in a limited number of patients undergoing cardiac surgery or in experimental models, and the influence of the surgery should not be ignored. Both fluoroscopic and MRI analyses require special equipment for image acquisition, the frame rates are also limited, and these methods are time-consuming.

Recently, Notomi et al evaluated LV torsion using a 2D strain analysis based on a speckle tracking technique, and demonstrated that LV torsion evaluated by this new method was consistent with the values obtained by tagged MRI, with acceptable variability. In the present study, we introduced our novel 2D tissue tracking system, based on a pattern-matching algorithm described previously, for measuring LV myocardial strain, without any limitations of Doppler angle dependency. In the present study, the LV torsion measured by 2DTT significantly correlated with that by tagged MRI, although the value was smaller than that for tagged MRI. This difference may be related to basal and apical positioning about LV long axis. Compared with the method of Notomi et al, we can place a small region of interest (ROI) on both the Endo and Epi, thereby quantifying the LV circumferential rotation and RS simultaneously.

To our knowledge, this is the first study to evaluate endo- and epi-torsion separately in humans during Dob infusion. Buchalter et al also reported both subepicardial and subendocardial torsion by tagged MRI in anesthetized dogs and that endo-torsion was greater than epi-torsion by approximately 2-fold. Our results show that LV endo-torsion was slightly greater than epi-torsion at rest, and became greater than epi-torsion by approximately 2-fold during Dob infusion, which suggests that circumferential radial shear based on different fiber orientations exists between the LV Endo and Epi and that it increased with inotropic stimulation.

LV Radial Strain

In this study, we could evaluate the change in myocardial thickening and in LV circumferential rotation simultaneously by placing a small ROI on both the Endo and Epi. Toyoda et al reported that myocardial strain by 2DTT closely correlated with the myocardial RS obtained by sonomicrometry. It has been previously reported that the RS of the LV base initially increases with inotropic stimulation, but there is no further increase because of tachycardia. However, the alteration in RS in the LV apex with inotropism remains unknown. In this study, 2DTT demonstrated that the response to Dob at the LV base differed from that at the apex. In the LV apex, RS increased as the Dob dose increased, whereas in the LV base, RS initially increased at 5 g·kg⁻¹·min⁻¹, but there was no further increase with 10 g·kg⁻¹·min⁻¹, similar to the results of previous reports. Our results suggest that the contractile reserve for Dob stress in the LV apex might be greater than that in the LV base. This strain change against Dob was similar to that of the LV torsional change, and the apical RS significantly correlated with the LV torsion in the Endo. Furthermore, as previously described for the results of LV torsion, the results suggested that circumferential-radial shear based on the different fiber orientation exists between the LV Endo and Epi, and might increase RS with inotropic stimulation. Therefore, these results suggest that LV Endo-torsion may be related to LV wall thickening. A previous report shows different behavior of the Endo and Epi with increasing LV wall thickening (ie, the fractional contribution of the Endo was greater than that of the Epi). Therefore, the increased apical Endo-rotation that contributed to the augmentation of LV torsion and apical RS played an important role in increasing the LV systolic contractile function under inotropic stimulation.

Study Limitations

First, similar to other automated imaging tracking modalities, the quality of our tracking algorithm is dependent on the 2D echocardiographic images. We carefully obtained images that clearly visualized the myocardium during the whole cardiac cycle. Second, because image tracking is performed frame by frame by our algorithm,
once a frame has an error, then such an error may become even larger in the next frame. Third, the tracking points with 2DTT in the LV short-axis images move in and out of the imaging plane because of the longitudinal motion of the LV. Therefore, we used low-dose Dob infusion to minimize such motion.

**Conclusion**

A greater augmentation of the apical LV rotation was observed in the LV endocardium than in the epicardium with inotropic stimulation, thus suggesting that circumferential-radial shear based on different fiber orientation exists between the endo- and epicardium. This may contribute to the greater augmentation of LV torsion in the endocardium and the increase in apical RS with inotropic stimulation.

**References**