Effects of mechanical limitation of apical rotation on left ventricular relaxation and end-diastolic pressure

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Iwasaki M, Masuda K, Asanuma T, Nakatani S. Effects of mechanical limitation of apical rotation on left ventricular relaxation and end-diastolic pressure. Am J Physiol Heart Circ Physiol 301: H1456–H1460, 2011. First published July 22, 2011; doi:10.1152/ajpheart.00316.2011.—Left ventricular (LV) twist is thought to play an important role in cardiac function. However, how twist affects systolic or diastolic function is not understood in detail. We acquired apical and basal short-axis images of dogs undergoing open-chest procedures (n = 15) using a GE Vivid 7 at baseline and during the use of an apical suction device (Starfish) to limit apical rotation. We measured LV pressure and stroke volume using a micromanometer-tipped catheter and an ultrasonic flow probe, respectively. Peak radial strain, peak rotation, peak twist, peak systolic twisting rate (TR), peak untwisting rate during isovolumic relaxation period (URIVR), and peak early diastolic untwisting rate after mitral valve opening (URe) were determined using speckle tracking echocardiography. Immobilizing the apex with gentle suction significantly decreased apical rotation (−50 ± 27%) and slightly increased basal rotation, resulting in a significant decrease in twist. The time constant of LV relaxation (τ) was prolonged, and LV end-diastolic pressure increased. TR and URIVR decreased. LV systolic pressure, peak positive and negative first derivative of LV pressure (±dP/dt), stroke volume, radial strain, and URe were not changed. The correlation between τ and URIVR (r = 0.63, P = 0.0006) was stronger than that between peak +dP/dt and TR (r = 0.46, P = 0.01). Diastolic function was impaired with reduced apical rotation and URIVR when the apex of the heart was immobilized using an apical suction device.

echocardiography; hemodynamics; speckle tracking

LEFT VENTRICULAR (LV) myocardial motion is generated by circumferential fibers in the midwall and longitudinal fibers in the endocardial and epicardial layers. The helical arrangement of LV myocardial fibers creates LV twist during systole (7, 29), defined as the difference between apical counterclockwise and basal clockwise rotation when viewed from the apex. Twist helps bring a more uniform distribution of the LV fiber stress and fiber shortening across the wall (2, 3). Untwisting begins before end systole and principally occurs during isovolumic relaxation (IVR) (5, 22, 28) as LV pressure rapidly decays (23, 24). The decline in LV pressure during IVR is caused by active myocardial relaxation and LV elastic recoil or untwisting that is associated with the release of potential energy stored during systole (15, 38). Untwisting generates intraventricular pressure gradients that in turn contribute to suction force for filling (8, 11, 20, 21). Thus the details of twisting and untwisting motions can provide unique insight into both myocardial systolic and diastolic function.

Changes in twist behavior have been demonstrated in various experimental and clinical settings (13, 17–19, 26, 30, 32, 34, 39, 41). Kim et al. (19) revealed a close correlation between LV twist and maximal positive first derivative of pressure (+dP/dt). Dong et al. (13) studied the physiological effect of loading conditions on twist measured by magnetic resonance imaging. A clinical research study (17) has shown that patients with myocardial infarction have reduced twist that correlated with the extent of an asynergic area. The timing and magnitude of the peak untwisting rate should be considered as an index of abnormal filling and diastolic dysfunction in hypertrophic obstructive cardiomyopathy (39), aortic stenosis (30), hypertension (32), and both systolic and diastolic heart failure (26, 34, 41). Although these studies have tried to reveal rotational differences depending on cardiac physiology and disease states, how twist affects systolic or diastolic function is not precisely understood. Therefore, we measured LV wall motion and hemodynamics before and after limiting twist using an apical suction device and then examined the effect of twist on cardiac function.

METHODS

Animal preparation and instrumentation. The Osaka University Research Ethics Committee for Animal Care approved the study protocol that included 20 dogs (weight, 14.6 ± 1.1 kg).

The dogs were anesthetized with a bolus of pentobarbital sodium (33–48 mg/kg), followed by a continuous infusion of pentobarbital sodium (6.2–8.2 mg kg⁻¹ h⁻¹) and lactate Ringer solution, intubated, and mechanically ventilated with room air using the external respirator SN-480-3 (Shimano Manufacturing, Tokyo, Japan). Electrocardiograms were monitored from limb leads. Pancuronium bromide (1 ml; 2 mg/ml) was administered intravenously as a muscle relaxant. A 5-Fr micromanometer-tipped catheter (Millar Instruments, Houston, TX) was advanced into the LV through the right femoral artery to continue into the LV through the right femoral artery to continuously measure LV pressure. After the left fifth or sixth intercostal thoracotomy in the right lateral decubitus position, the pericardium was opened and the heart was suspended in a pericardial cradle. An ultrasonic flow probe (diameter, 12–20 mm) was placed around the ascending aorta and connected to a flow meter (Transonic Systems, Ithaca, NY).

LV pressure, its peak time derivative (dP/dt), and the time constant of LV relaxation (τ) calculated by a monoexponential model with (log transformation method) and without (nonlinear least squares method) the assumption of a zero asymptote were measured using a micromanometer-tipped catheter (12). Stroke volume was calculated using the integration of flow velocity with respect to systolic duration.

Echocardiography. Two-dimensional echocardiography was performed using a Vivid 7 (GE Vingmed Ultrasound AS, Horten, Norway). Short-axis images were acquired at basal, mid-, and apical levels at a high frame rate (88.5 frames/s) using an M3s transducer (GE Vingmed Ultrasound AS). Because the imaging plane affects the magnitude of apical rotation, the basal level was defined as that showing the tips of mitral valve leaflets, the midlevel was visible papillary muscle, and the apical level was just proximal to the level...
EFFECT OF LEFT VENTRICULAR TWIST ON CARDIAC FUNCTION

Table 1. Hemodynamic data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Suction</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate, beats/min</td>
<td>136 ± 23</td>
<td>137 ± 23</td>
<td>0.40</td>
</tr>
<tr>
<td>LVSBP, mmHg</td>
<td>103 ± 17</td>
<td>103 ± 20</td>
<td>0.46</td>
</tr>
<tr>
<td>LVEDP, mmHg</td>
<td>4.1 ± 3.2</td>
<td>5.7 ± 3.4</td>
<td>0.0003</td>
</tr>
<tr>
<td>+dP/dt, mmHg/s</td>
<td>1,620 ± 338</td>
<td>1,655 ± 394</td>
<td>0.42</td>
</tr>
<tr>
<td>−dP/dt, mmHg/s</td>
<td>−1,497 ± 416</td>
<td>−1,390 ± 410</td>
<td>0.14</td>
</tr>
<tr>
<td>τ, ms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With a zero asymptote</td>
<td>26.8 ± 6.9</td>
<td>31.7 ± 9.4</td>
<td>0.007</td>
</tr>
<tr>
<td>With a moving asymptote</td>
<td>46.8 ± 3.6</td>
<td>55.5 ± 7.2</td>
<td>0.003</td>
</tr>
<tr>
<td>SV (n = 9), ml</td>
<td>12.2 ± 3.7</td>
<td>12.3 ± 4.5</td>
<td>0.34</td>
</tr>
<tr>
<td>IRT/RR</td>
<td>0.129 ± 0.024</td>
<td>0.144 ± 0.023</td>
<td>0.026</td>
</tr>
</tbody>
</table>

Values are means ± SD; n, no. of animals. Stroke volume (SV) data of 6 dogs were excluded because of technical problems. LVSBP, left ventricular (LV) systolic blood pressure; LVEDP, LV end-diastolic pressure; dP/dt, first derivative of LV pressure; τ, time constant of LV relaxation; IRT, isovolumic relaxation time; RR, R-R interval.

Table 2. Radial strain, rotation, and twisting parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Suction</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apical radial strain, %</td>
<td>20.6 ± 5.2</td>
<td>17.6 ± 5.2</td>
<td>0.06</td>
</tr>
<tr>
<td>Basal radial strain, %</td>
<td>25.1 ± 6.2</td>
<td>26.0 ± 9.2</td>
<td>0.64</td>
</tr>
<tr>
<td>Global radial strain, %</td>
<td>25.5 ± 5.5</td>
<td>26.0 ± 6.3</td>
<td>0.68</td>
</tr>
<tr>
<td>Apical rotation, °</td>
<td>9.1 ± 2.4</td>
<td>4.2 ± 1.7</td>
<td>0.0001</td>
</tr>
<tr>
<td>Basal rotation, °</td>
<td>−4.5 ± 1.5</td>
<td>−5.8 ± 2.5</td>
<td>0.04</td>
</tr>
<tr>
<td>Twist, °</td>
<td>13.4 ± 2.9</td>
<td>9.7 ± 3.0</td>
<td>0.0006</td>
</tr>
<tr>
<td>TR, %</td>
<td>133 ± 34</td>
<td>95 ± 27</td>
<td>0.0002</td>
</tr>
<tr>
<td>URIVR, %</td>
<td>−98 ± 24</td>
<td>−65 ± 42</td>
<td>0.04</td>
</tr>
<tr>
<td>URd, %</td>
<td>−93 ± 38</td>
<td>−80 ± 31</td>
<td>0.18</td>
</tr>
</tbody>
</table>

Values are means ± SD. TR, peak systolic twisting rate; URIVR, peak untwisting rate during isovolumic relaxation; URd, peak diastolic untwisting rate.

RESULTS

Among 20 dogs, five were excluded from the analysis because of apparent myocardial dysfunction before the experiment (n = 2), poor image quality due to an attached apical suction device (n = 2), or suction device failure (n = 1). Accordingly, data from 15 dogs (weight, 14.9 ± 1.2 kg) are presented. Mean intraobserver difference for peak twist was 0.00 ± 0.50° (range, −0.82 to +0.94°) and 0.91 ± 5.2°/s (range, −8.5 to +7.1°/s) for URIVR. Mean interobserver difference for peak twist was 0.12 ± 0.65° (range, −0.78 to +0.92°) and 1.1 ± 3.5°/s (range, −3.9 to +5.5°/s) for URIVR.

Hemodynamics. Table 1 shows hemodynamics before and during apical immobilization with gentle suction. Both τ with a zero asymptote and that with a moving asymptote and the relative duration of IVR were prolonged, and LV end-diastolic pressure (LVEDP) increased during suction. Other indexes, including +dP/dt and stroke volume, remained unchanged. Since beat-by-beat variation of τ with a moving asymptote in each run (mean of the SD = 3.5 ms; range, 0.8 – 6.2) was larger than that of τ with a zero asymptote (mean of the SD = 0.9 ms; range, 0.3-2.6), we used the latter τ for further analysis.

Speckle tracking echocardiography. Table 2 shows changes in radial strain, rotation, and twisting parameters during suction. After suction, apical radial strain tended to decrease, but it was not statistically significant. Basal radial strain and global radial strain did not change. These indicated that the apical suction device did not significantly affect wall thickening. Peak apical rotation significantly decreased, whereas peak basal rotation slightly increased, resulting in a significant decrease in peak twist during suction. TR and URIVR were also decreased, but URd remained unchanged. The representative rotational profiles at baseline and during suction in Fig. 1 clearly show decreases in twist and URIVR.

Correlation between twisting parameters and cardiac function. Figure 2 shows relationships between twist parameters and systolic or diastolic parameters. TR was significantly correlated with +dP/dt (r = 0.46, P = 0.01), whereas URIVR was more closely correlated with τ (r = 0.63, P = 0.0006) and −dP/dt (r = 0.61, P = 0.001). Furthermore, URIVR tended to correlate with LVEDP, although this did not reach statistical significance (r = 0.36, P = 0.07).

DISCUSSION

In the present study, we used an apical suction device to limit rotation without interfering with wall thickening of the

Mechanical limitation of apical rotation and experimental protocol. We applied mechanical immobilization using the apical suction device Starfish (Medtronic, Minneapolis, MN), which was designed for off-pump coronary artery bypass surgery. The Starfish was placed at the apex and connected to a suction pump (SP40, MARKOS-MEFAR, Bovezzo, Italy). Apical rotation was limited by transient suction (<3 min) with gentle power maintained at −40 kPa not to affect wall thickening. We confirmed that the apex remained in its anatomical position without additional displacement or distortion of the heart by two-dimensional echocardiography.

We simultaneously measured LV short-axis images and hemodynamics at baseline and during the use of the suction device. Transducer position is important because apical rotation obtained from a more caudal position is overestimated (36). We carefully acquired short-axis images at the apical level that were as similar as possible to those at baseline.

Data analysis. Data were analyzed off-line using EchoPac software (GE Vingmed Ultrasound AS). During the analysis, the LV endocardium was traced at end systole and the width of a region of interest was adjusted to include the entire myocardial wall. The software automatically tracked the speckle pattern frame by frame as described (27). Radial strain and the rotation of each image plane were calculated throughout one cardiac cycle. Peak radial strain and peak rotation at the apex and the base were measured as the maximum amplitude of their profiles throughout one cardiac cycle. Peak global radial strain was defined as the maximum value of the averaged apical, mid-, and basal radial strain profiles. Twist was calculated as the difference between apical and basal rotation profiles, and peak twist was measured. Twisting rate was calculated as the first derivative of twist. We also measured peak systolic twisting rate (TR), peak untwisting rate during IVR (URIVR), and peak early diastolic untwisting rate (URd), defined as the peak negative value after mitral valve opening. All speckle tracking data were averaged over three consecutive beats.

Statistical analysis. Data are presented as means ± SD. Baseline and immobilized conditions were statistically compared using paired t-tests. The Pearson product-moment correlation coefficient was used to identify relationships between selected variables, and the reproducibility of deformational parameters was evaluated using the Bland-Altman analysis. Intraobserver and interobserver variabilities were assessed for peak twist and URIVR values in 10 randomly selected studies. A P value of <0.05 was considered statistically significant.
We found that limiting apical rotation significantly impaired diastolic function (prolongation of \( \tau \) and elevation of LVEDP).

**Effect of an apical suction device on myocardial motion.** An apical suction device is used to immobilize part of the heart during off-pump coronary artery bypass grafting to facilitate coronary artery exposure while minimizing hemodynamic instability. Here we used the device to reduce apical rotation without affecting wall thickening. We applied gentle suction to the apex for a short period, which allowed us to significantly reduce apical rotation and twist without decreasing radial strain. Previous investigations have shown a dependence of twist on myocardial contraction (5, 6, 18), but we achieved a state where twist and radial thickening responded independently. Radial strain is mainly dominated by subendocardial shortening (16), whereas twist is mainly determined by subepicardial shortening (31). If a suction device at the apex limits only subepicardial motion, twist can decrease with preserved radial strain.

Some studies have demonstrated a relationship between twist and systolic function (13, 18, 19, 23, 25). Considering these findings, we initially postulated that a twist limitation would decrease systolic function and stroke volume. However, we found limiting apical rotation significantly impaired early diastolic relaxation.

**Diastolic function is impaired by apical immobilization.** Several studies have suggested that untwisting might be a good index of early diastolic relaxation (9, 14, 23, 26, 31, 41, 42).

![Representative example of rotational profiles at baseline and during suction. Top: rotation and twist. Bottom: rotation rate and twisting rate. Dotted and dashed-dotted lines represent apical and basal profiles, respectively. Solid lines show twist and twisting rates.](image)

**Fig. 1.**

![Relationships between twist and systolic or diastolic parameters. Correlation between time constant of left ventricular (LV) relaxation (\( \tau \); a zero asymptote model) and peak untwisting rate during isovolumic relaxation period (UR\(_{IVR}\)) was closest. TR, peak systolic twisting rate; LVEDP, LV end-diastolic pressure; dP/dt, first derivative of LV pressure.](image)

**Fig. 2.**
However, these studies showed only a close relationship between relaxation and untwisting. No reports have demonstrated that untwisting motion directly facilitates ventricular relaxation. Moreover, because twisting and untwisting are interactive, twist is also closely related to systolic function parameters such as radial strain (1, 33) and ejection fraction (4, 13, 17, 19). Thus we limited only apical rotation to understand the role of twisting/untwisting on systolic and diastolic function. We found that twisting/untwisting is closely related to diastolic function.

The untwisting rate in this study comprised one wave form that peaked during IVR (n = 11) and another that peaked after mitral valve opening (n = 4). We observed that the maximum untwisting rate (i.e., the most negative twisting rate) occurred during IVR under baseline conditions in some dogs and after mitral valve opening during suction in others. Although the reason why the untwisting rate comprised two peaks remains obscure, we consider that the peak untwisting rate during IVR reflects active myocardial relaxation and that subsequent untwisting after mitral valve opening reflects passive myocardial expansion by filling. Thus we reported the peak untwisting rate during IVR separately from the peak untwisting rate after mitral valve opening.

Untwisting mainly occurs during the IVR that precedes diastolic filling (22, 28). Notomi et al. (23) and others (14, 40, 41) have reported that the peak untwisting rate closely correlates with τ. They also showed that it is an independent predictor of intraventricular pressure gradients (23), which is the suction force that facilitates early filling (15). In the present study, the decrease in the untwisting rate resulting from reduced apical rotation impaired relaxation and elevated LVEDP. This was probably because the potential energy required for myocardial recoil was not sufficiently stored within the extracellular collagen matrix during systole. As a result, LV minimum pressure did not decrease and LVEDP increased.

Study limitations. Our observations were limited to the short-axis planes. We could not acquire apical long-axis images and measure LV length because of the suction device attached at the apex. Thus we did not correct twisting and untwisting parameters by LV length. We have to recognize that our open-chest and open-pericardium experiments are different from the clinical situation.

It has been suggested that the pericardium significantly affects rotation (10, 35). However, to effectively limit the apical rotation, we had to open the pericardium and place the device directly to the apex. Although our study does not exemplify the clinical situation, we believe our findings provided some important physiological understanding because we focused on the changes of the parameters induced by apical immobilization. The apical suction device itself might damage the LV myocardium. However, the suction device used here is constructed of flexible materials, and low suction power was applied for only a short period. Furthermore, post-systolic shortening, which is a sign of myocardial ischemia (37), did not occur during suction at radial strain profiles. We confirmed that LV pressure, radial strain, and rotation returned to the baseline levels after 5 min of detaching the suction device from some dogs. Thus the suction device probably did not cause myocardial damage. Moreover, because the suction device arm (4.5 cm) is larger than the apical diameter (about 4 cm), the device itself might not mechanically limit ventricular expansion during diastole.

Conclusions. Limiting apical rotation using an apical suction device decreased the untwisting rate during IVR and impaired diastolic function (prolongation of τ and elevation of LVEDP).

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

REFERENCES


