Left ventricular systolic torsion correlates global cardiac performance during dyssynchrony and cardiac resynchronization therapy

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Lamia B, Tanabe M, Tanaka H, Kim HK, Gorcsan J 3rd, Pinsky MR. Left ventricular systolic torsion correlates global cardiac performance during dyssynchrony and cardiac resynchronization therapy. Am J Physiol Heart Circ Physiol 300: H853–H858, 2011. First published December 17, 2010; doi:10.1152/ajpheart.00177.2010.—Left ventricular (LV) systolic torsion is a primary mechanism contributing to stroke volume (SV). We hypothesized that change in LV torsion parallels changes in global systolic performance during dys-synchrony and cardiac resynchronization therapy (CRT). Seven anesthetized open chest dogs had LV pressure-volume relationship. Apical, basal, and mid-LV cross-sectional echocardiographic images were studied by speckle tracking analysis. Right atrial (RA) pacing served as control. Right ventricular (RV) pacing simulated left bundle branch block. Simultaneous RV-LV free wall and RV-LV apex pacing (CRTfw and CRTa, respectively) modeled CRT. Dyssynchrony was defined as the time difference in peak strain between earliest and latest segments. Torsion was calculated as the maximum difference between the apical and basal rotation. RA pacing had minimal dyssynchrony (52 ± 36 ms). RV pacing induced dyssynchrony (189 ± 61 ms, P < 0.05). CRTa decreased dyssynchrony (46 ± 36 ms, P < 0.05 vs. RV pacing), whereas CRTfw did not (110 ± 96 ms). Torsion during baseline RA was 6.6 ± 3.7°. RV pacing decreased torsion (5.1 ± 3.6°, P < 0.05 vs. control), and reduced SV, stroke work (SW), and dP/dmax compared with RA (21 ± 5 vs. 17 ± 5 ml, 252 ± 61 vs. 151 ± 64 ml, and 2,063 ± 456 vs. 1,603 ± 424 mmHg/s, respectively, P < 0.05). CRTa improved torsion, SV, SW, and dP/dmax compared with RV pacing (7.7 ± 4.7°, 23 ± 3 ml, 240 ± 50 ml, and 1,947 ± 647 mmHg/s, respectively, P < 0.05), whereas CRTfw did not (5.1 ± 3.6°, 18 ± 5 ml, 175 ± 48 ml, and 1,699 ± 432 mmHg/s, respectively, P < 0.05). LV torsion changes covaried across conditions with SW (r = 0.94±12.27, r = 0.81, P < 0.0001) and SV (r = 0.66±9.91, r = 0.81, P < 0.0001). LV dyssynchrony changes did not correlate with SW or SV (r = 0.12, P = 0.61 and r = 0.08, P = 0.73, respectively). Thus, we conclude that LV torsion is primarily altered by dyssynchrony, and CRT that restores LV performance also restores torsion.

cardiac resynchronization therapy

SEVERAL RECENT STUDIES HAVE shown that left ventricular (LV) torsion contributes directly to systolic LV function (12, 22, 24, 32) although previously some authors (6) had concluded that LV function was unaffected by the twisting phenomenon. LV torsion is created by shortening of myofibrils arranged in a helical orientation and is visualized as counterclockwise apical rotation and the clockwise basal rotation relative to a stationary midmyocardial reference point. There is a systolic twist (torsion) and an early diastolic untwist during the cardiac cycle (15, 16, 39). LV torsion has been measured noninvasively using tissue-tagging magnetic resonance imaging (MRI) (3, 7, 8, 25, 26, 33, 37, 40), two-dimensional (2-D) echocardiography (2, 23), and Doppler tissue imaging (30) in various cardiac diseases.

Recently, speckle tracking echocardiography has been validated as an accurate measurement of LV rotation and torsion by comparison with sonomicrometry in dogs and MRI tagging in humans (17, 29, 35, 42). LV contraction dyssynchrony is a common contraction abnormality and plays a major role in the pathophysiology of heart failure (1, 4, 5, 11, 13, 14, 19, 28, 38, 41, 43, 44, 45). Cardiac resynchronization therapy (CRT) can reverse dyssynchrony and improve global cardiac function in some but not all patients. The noninvasive measurement of LV torsion during dys-synchrony and CRT, and its relationship with global cardiac performance, has not been described. Considering the central role torsion plays in global LV performance, we hypothesized that LV torsion is impaired during LV contraction dyssynchrony and restored by CRT if global LV performance also improves.

METHODS

Preparation. Seven mongrel male dogs, weighing 20.6 ± 1.5 kg, were studied after an overnight fast. The protocol was approved by the institutional animal care and use committee and conformed to the position of the American Heart Association on research animal use. All dogs were anesthetized with pentobarbital sodium (30 mg/kg induction; 1.0 mg/kg/h with intermittent boluses, as needed) and mechanically ventilated. A 6-Fr 11-pole multielectrode conductance catheter (Webster Laboratories, Irvine, CA) and a LV micromanometer catheter (MPC-500; Millar, Houston, TX) were placed for LV pressure-volume analysis by the right internal carotid artery and the left common carotid artery, as previously described (11). After a median sternotomy, a snare occluder was placed around the inferior vena cava to transiently alter preload. The pericardium was opened and temporary epicardial pacing wires (A & E Medical, Farmingdale, NJ) were placed on the right atrium (RA), right ventricular (RV) free wall near the anterior infundibulum, LV midfree wall near the midposterior lateral wall, and LV apex for multisite stimulation. The pericardium was reopposed with multiple interrupted sutures, and positive end-expiratory air was placed in the right atrium (RA), right ventricular (RV) free wall near the anterior infundibulum, LV midfree wall near the midposterior lateral wall, and LV apex for multisite stimulation. The pericardium was reopposed with multiple interrupted sutures, and positive end-expiratory pressure (PEEP) was applied to reexpand the lungs. Afterward, 5 cm H2O PEEP was applied to maintain end-expiratory lung volume for the remainder of the experiment. Fluid resuscitation was performed before starting the protocol to restore apneic LV end-diastolic volume to values similar to where they were before sternotomy.

Hemodynamic data analysis. LV pressure, volume, and electrocardiogram signals were digitized at 250 Hz and stored on disk for off-line analysis. The following hemodynamic parameters were assessed for global LV performance: LV peak systolic pressure, stroke volume (SV), and stroke work (SW) as the integral of the LV pressure-volume loop.
Echocardiography. An echocardiographic system (Aplio SSA-770A; Toshiba Medical Systems, Tokyo, Japan) was used to obtain images with a 3.0 MHz transducer directly applied to the heart. Digital routine grayscale 2-D and tissue Doppler cine loops from three consecutive beats were obtained at end-expiratory apnea from basal LV short-axis view and apical LV short-axis view at depths of 8 cm using a fixed transducer position. Gray scale images were collected at frame rates of 49 Hz with a pulse repetition frequency of 4.5 kHz. Gain settings were adjusted to optimize endocardial definition. We defined the proper short-axis levels as follows (30): at the basal level, the mitral valve, and, at the apical level, LV cavity alone with no visible papillary muscles. Mid-LV short-axis views were selected with the papillary muscle as a consistent anatomic landmark. The LV cross section was made as circular as possible. We used customized software within a personal computer workstation (AplioQ; Toshiba) for off-line analysis of speckle tracking imaging. Off-line analysis of apical and basal rotation was then performed on digitally stored images (AplioQ; Toshiba). LV torsion was defined as a net difference of LV rotation between apical and basal short-axis planes. Normally, the apex rotates counterclockwise, whereas the base rotates clockwise when viewed from apex. Counterclockwise LV rotation as viewed from the apex was expressed as a positive value, and clockwise LV rotation was expressed as a negative value (Fig. 1).

**LV rotation by speckle tracking imaging.** The speckle tracking analysis was used to generate regional LV strain from routine B-mode grayscale echocardiographic images. The best-quality digital 2-D cardiac cycle was selected. A circular region of interest was traced on the endocardial and epicardial border of the short-axis view using a point-and-click approach. Speckles within the region of interest were tracked in subsequent frames by the imaging software. The location shift of these speckles from frame to frame, representing tissue movement, provided the spatial and temporal data. The workstation computes LV rotation of each short-axis image. Averaged LV rotation data on the midmyocardial contour were used for the calculation of LV torsion. The basal and apical LV rotation speckle tracking imaging data were exported to a spreadsheet program (Excel 2000; Microsoft, Seattle, WA) to calculate LV torsion.

Counter-clockwise rotation was represented as a positive value, color-coded as blue, and clockwise rotation was represented as negative value, color-coded as red. The software divided the short-axis image into six equal segments.

The LV torsion was calculated during RA pacing, as heart rate control, and compared with RV pacing, RA-RV-LV free wall pacing, and RA-RV-LV apex pacing to reflect LV free wall CRT (CRTfw) and apical CRT (CRTa), respectively. Time-to-peak strain for each of the six regional (9) time-strain curves for each cross-sectional LV study was determined. Dyssynchrony was defined as the time difference in peak strain between the earliest and latest segments, as previously described (20).

**Protocol.** All measurements were made during apnea with 5 cmH2O positive end-expiration pressure. To avoid retrograde conduction for all pacing steps of the protocol, RA pacing was performed at frequencies 5–10/min above the intrinsic rhythm. To control for any heart rate-specific changes in global and regional function, RA pacing was defined as normal ventricular contraction for subsequent comparisons. All succeeding ventricular pacing studies were then done with sequential pacing at an arteriovenous delay of 20 ms. This pacing delay prevented atrial fusion beats from contaminating the ventricular pacing effects of CRT but also eliminated atrial contraction from augmenting LV filling. High RV free wall pacing was used to induce a left bundle branch block-like contraction pattern (20). We then compared the impact of CRTfw and CRTa on regional and global LV performance. The order of CRTfw and CRTa was alternated among sequential animals to eliminate any sequencing effects. Pacing was maintained for >30 s before measurements were made for each step so that hemodynamic equilibrium could be established. In practice, hemodynamic stability usually took <15s to occur. Between each ventricular-paced rhythm interval, the animals were returned to RA pacing, and all hemodynamic variables were stabilized to baseline levels before the next step in the protocol was initiated.

**Statistical analysis.** Data are expressed as means ± SD. ANOVA for repeated measures was used for comparisons among different pacing modalities. One-way ANOVA with repeated measures and post hoc testing was used to evaluate the effects of different pacing.
LV TORSION PREDICTS GLOBAL CARDIAC PERFORMANCE

Table 1. LV hemodynamic characteristics and LV torsion during RA and RA-RV pacing and simulated CRTa and CRTfw

<table>
<thead>
<tr>
<th>Parameter</th>
<th>RA Pacing</th>
<th>RV Pacing</th>
<th>CRTa</th>
<th>CRTfw</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR, beats/min</td>
<td>139 ± 8</td>
<td>139 ± 8</td>
<td>139 ± 8</td>
<td>139 ± 8</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>96 ± 11</td>
<td>78 ± 13*</td>
<td>83 ± 11</td>
<td>83 ± 11</td>
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<tr>
<td>LV ESP, mmHg</td>
<td>109 ± 8</td>
<td>92 ± 13*</td>
<td>94 ± 5</td>
<td>95 ± 8</td>
</tr>
<tr>
<td>LV EDP, mmHg</td>
<td>12 ± 5</td>
<td>11 ± 5*</td>
<td>9 ± 5†</td>
<td>10 ± 5†</td>
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<tr>
<td>EDV, ml</td>
<td>40 ± 3</td>
<td>34 ± 5*</td>
<td>34 ± 5</td>
<td>34 ± 5</td>
</tr>
<tr>
<td>SV, ml</td>
<td>21 ± 5</td>
<td>17 ± 5*</td>
<td>23 ± 3†</td>
<td>18 ± 5</td>
</tr>
<tr>
<td>CO, l/min</td>
<td>2.9 ± 0.8</td>
<td>2.3 ± 0.5*</td>
<td>3.2 ± 0.5†</td>
<td>2.5 ± 0.5</td>
</tr>
<tr>
<td>SW, ml</td>
<td>252 ± 61</td>
<td>151 ± 64*</td>
<td>240 ± 50†</td>
<td>175 ± 48</td>
</tr>
<tr>
<td>dP/dtmax, mmHg/s</td>
<td>2,063 ± 456</td>
<td>1,603 ± 424*</td>
<td>1,946 ± 547†</td>
<td>1,699 ± 432</td>
</tr>
<tr>
<td>dP/dtmin, mmHg/s</td>
<td>-2,325 ± 464</td>
<td>-1,684 ± 482*</td>
<td>-2,061 ± 440†</td>
<td>-1,973 ± 472†</td>
</tr>
<tr>
<td>Ees, mmHg/ml</td>
<td>2.7 ± 1.3</td>
<td>5.1 ± 2.1*</td>
<td>2.9 ± 1.6†</td>
<td>4.1 ± 1.9</td>
</tr>
<tr>
<td>LV torsion, degrees</td>
<td>6.6 ± 3.7</td>
<td>5.1 ± 3.6*</td>
<td>7.7 ± 4.7†</td>
<td>5.1 ± 3.6</td>
</tr>
<tr>
<td>Dyssynchrony, ms</td>
<td>52 ± 36</td>
<td>189 ± 61</td>
<td>46 ± 36†</td>
<td>110 ± 96</td>
</tr>
</tbody>
</table>

Data are means ± SD; n = 7 dogs in each group. RA, right atrial; RV, right ventricular; CRTa, cardiac synchronization therapy (CRT) at left ventricular (LV) apex; CRTfw, CRT at LV free wall; HR, heart rate; MAP, mean arterial pressure; LV EDP, LV end-diastolic pressure; LV ESP, LV end-systolic pressure; LV EDV, LV end-diastolic volume; SV, stroke volume; CO, cardiac output; dP/dtmax, maximum rate of change of LV pressure; dP/dtmin, minimum rate of change of LV pressure; SW, LV stroke work; Ees, end-systolic elastance. *P < 0.05, RA vs. RV. †P < 0.05 vs. RV.

modes on torsion and indexes of global LV performance. Significance was determined as P < 0.05. Linear regression analysis was used to compare changes in LV torsion and changes in SW and SV. Interobserver variability was assessed in 10 randomly selected studies for torsion and was calculated as a ratio (expressed as a percentage) of the difference between the values obtained by each observer (expressed as an absolute value) divided by the mean of the two values. Intraobserver variability was calculated by a similar approach.

RESULTS

Baseline radial strain dyssynchrony and changes in LV dyssynchrony during different pacing modes. The maximum time difference from the earliest to latest peak strain among six segments, as a measure of contraction synchrony, was minimal with RA pacing (52 ± 36 ms) but increased during RV pacing (189 ± 61 ms, P < 0.05 vs. RA pacing) (Table 1). CRTa reduced the maximal time difference in peak strain compared with RV pacing (46 ± 36 ms, P < 0.05 vs. RV pacing), whereas CRTfw did not alter it compared with RV pacing (110 ± 96 ms). Changes in LV dyssynchrony from baseline did not correlate with changes in SW (r = 0.61) or SV (r = 0.12, P = 0.61) or SV (r = 0.08, P = 0.73).

Baseline LV torsion and changes in LV torsion during different pacing modes. Figure 2 and Supplemental Fig. E. 1 (video) (Supplemental data for this article may be found on the American Journal of Physiology: Heart and Circulatory Physiology website) shows a typical case of counterclockwise apical rotation, clockwise basal rotation, and torsion during RA pacing, RV pacing, CRTa, and CRTfw.

Torsion analysis without pacing but from a lower heart rate was done, and all torsion values were similar to that of the RA baseline values (6.6 ± 3.7° vs. 6.6 ± 3.7°; sinus rhythm vs. RA).

![Fig. 2. An example of basal rotation (green), apical rotation (blue), and torsion (red) for one animal during control [right atrial (RA) pacing], right ventricular (RV) pacing, and both apical cardiac resynchronization therapy (CRTa (CRTapex)) and free wall cardiac resynchronization therapy (CRTfw). Maximum (Max.) torsion is the maximal difference between apical and basal rotation in degrees.](http://ajpheart.physiology.org/)

Downloaded from http://ajpheart.physiology.org/ by 10.220.33.6 on October 15, 2017.
LV torsion was reduced during RV pacing compared with RA pacing (5.1 ± 3.6° vs. 6.6 ± 3.7°, \(P < 0.05\)). CRTa improved LV torsion compared with RV pacing (7.7 ± 4.7° vs. 5.1 ± 3.6°, \(P < 0.05\)), whereas CRTfw had no effect on LV torsion compared with RV pacing (5.1 ± 3.6° vs. 5.1 ± 3.6°) (Table 1 and Fig. 3). Changes in LV torsion from baseline correlated significantly with changes in SW (\(r = 0.81, P < 0.0001\)) (Fig. 4) and SV (\(r = 0.81, P < 0.0001\) and \(y = 0.66x + 0.91\)). Although the absolute change in torsion, in degrees, was small, with a mean decrement in torsion from RA to RV of only −1.5°, decrements in LV SW of >20% were universally associated with a decrease in LV torsion. Changes in LV torsion did not correlate with changes in LV dyssynchrony (\(y = −0.001x −6.68, r = −0.23, P = 0.30\)).

**Effects of pacing on global LV function.** RV pacing decreased LV SV and SW compared with RA, whereas CRTa significantly improved LV SV and SW compared with RV pacing, and CRTfw did not alter either LV SV or SW (Table 1).

**Reproducibility.** Intra- and interobserver variability was analyzed in eight randomly selected studies for torsion values by speckle tracking analysis using six standard segments. Intra- and interobserver variability for torsion expressed as the mean percent error (absolute difference/mean) was 7 ± 7 and 8 ± 9%, respectively.

**DISCUSSION**

Our study has two primary findings. First, LV torsion, quantified by speckle tracking, is impaired by dyssynchronous contraction and improved by CRT only if CRT also improves cardiac performance. Second, the degree of change in torsion parallels the degree of change in LV SW across all pacing modes, with the greatest sensitivity coming from decrements in LV SW of >20% always associated with a decrease in LV torsion compared with baseline. The implication of these data is that torsion, a primary cardiac contraction variable, is not only affected by dyssynchrony and CRT but can be used to track CRT effectiveness. Changes in dyssynchrony do not parallel the degree of change in LV SW.

LV torsion has been studied using cardiac magnetic resonance (CMR) in previous studies (26, 27, 46). However, CMR data acquisition is cumbersome and its postacquisition data analysis laborious. 2-D speckle tracking echocardiography imaging when collected at apical and basal planes enables the noninvasive measurement of apical and basal rotation and then calculation of LV torsion. This speckle tracking technique has been validated against CMR (17, 30, 35). These findings should not be surprising because LV torsion is a sensitive marker of global LV function (10, 24, 26, 27, 42). LV torsion correlates with the percentage change in LV area (20) in humans and to SV and ejection fraction in animals (10). Furthermore, we previously showed in this canine model that LV contraction dyssynchrony can be quantified as regional differences in radial strain wherein the principal segment displaying maximal dyssynchrony defined most of the impaired ejection effectiveness (20).

We and others have previously shown that, in the setting of dyssynchrony contraction, the slope of the end-systolic pressure-volume relationship (Ees) may vary independent of SW (18, 20). In the present study, we showed that Ees does not correlate with changes in strain (\(r = 0.1464\) and \(P = 0.5622\)). Not surprisingly, in the present study, the relationship between Ees and torsion is also poor (\(r = −0.3035\) and \(P = 0.2207\)). Although torsion does not correlate with Ees, it does with both SW and SV (\(r = 0.81\) and 0.81, \(P < 0.0001\), respectively).

**Limitations.** There are some limitations of our study. First, we studied an intact canine model without intrinsic conduction defects or impaired contractility in which dyssynchrony was created by ventricular pacing. Extrapolation to clinical studies regarding site selection for optimal CRT cannot be made. For example, we (18, 20), and others (31), have documented that LV CRTa is superior to LV CRTfw in terms of global LV performance and resynchronization in animal models of pacing-induced dyssynchrony. However, similar apical pacing...
superiority has not been reported in human CRT studies. The apex may be better than free wall in otherwise healthy animals because apical pacing can activate the His Purkinje system more centrally than occurs with free wall pacing. Second, torsion changes induced by pacing in an acute open chest animal may not be the same as under conditions of chronic heart failure induced by arrhythmias in humans. However, we (20, 36) recently showed similar regional strain activity in an intact chronic heart failure model as that seen in our acute open chest animal model. It is unlikely that torsion would be qualitatively different from regional strain in chronic heart failure. Third, we manually placed the echo probe at specific points along the long axis to get the apical and basal rotation needed to calculate torsion. Small variations to probe distance between animals may be responsible for the variation in absolute torsion seen across animals. Putting markers on the heart to define apical and basal sites would have increased the consistency of measurement within animals across pacing modes but would not address the issue of longitudinal differences in positioning across animals. Because we used an external fixed device to hold the echo probe at the same point and orientation across pacing modes, all within-animal measures were constant across pacing modes. Longitudinal probe-sensing differences may exist between animals and may explain why in one of our animals the degree of torsion was higher than in others. However, even in this example, the qualitative changes in torsion with pacing were similar across all animals.

Finally, speckle tracking echocardiography is dependent on frame rates, as well as image resolution. Low-acquisition frame rates degrade assessment of regional myocardial motion and its subsequent strain rate analysis. In contrast, increasing frame rate reduces scan-line density, which reduces image resolution (21, 34). Suffoletto et al. (41) found frame rates in the range of 30–90 Hz with a mean of 65 Hz suitable for speckle tracking analysis. Thus, in our study, we used a mean frame rate of 49 Hz suitable for speckle tracking analysis.

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DISCLOSURES

No conflicts of interest are declared by the authors.

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