Hemodynamic improvement in cardiac resynchronization does not require improvement in left ventricular rotation mechanics: three-dimensional tagged MRI analysis.

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Hemodynamic Improvement in Cardiac Resynchronization Does Not Require Improvement in Left Ventricular Rotation Mechanics

Three-Dimensional Tagged MRI Analysis

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Background—Earlier studies have yielded conflicting evidence on whether or not cardiac resynchronization therapy (CRT) improves left ventricular (LV) rotation mechanics.

Methods and Results—In dogs with left bundle branch block and pacing-induced heart failure (n=7), we studied the effects of CRT on LV rotation mechanics in vivo by 3-dimensional tagged magnetic resonance imaging with a temporal resolution of 14 ms. CRT significantly improved hemodynamic parameters but did not significantly change the LV rotation or rotation rate. LV torsion, defined as LV rotation of each slice with respect to that of the most basal slice, was not significantly changed by CRT. CRT did not significantly change the LV torsion rate. There was no significant circumferential regional heterogeneity (anterior, lateral, inferior, and septal) in LV rotation mechanics in either left bundle branch block with pacing-induced heart failure or CRT, but there was significant apex-to-base regional heterogeneity.

Conclusions—CRT acutely improves hemodynamic parameters without improving LV rotation mechanics. There is no significant circumferential regional heterogeneity of LV rotation mechanics in the mechanically dyssynchronous heart. These results suggest that LV rotation mechanics is an index of global LV function, which requires coordination of all regions of the left ventricle, and improvement in LV rotation mechanics appears to be a specific but insensitive index of acute hemodynamic response to CRT. **(*Circ Cardiovasc Imaging*. 2010;3:456-463.)**

Key Words: MRI ■ tagging ■ ventricular function ■ mechanics ■ torsional deformation

Left ventricular (LV) rotation mechanics represents a critical link that converts 1-dimensional shortening of obliquely aligned myofibers into 3-dimensional (3D) ventricular contraction.[1] LV torsion is an important index of cardiac function,[2] which is known to decrease in heart failure.[3,4]

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Cardiac resynchronization therapy (CRT) improves hemodynamics and symptoms and decreases mortality in patients with moderate to severe heart failure associated with an intraventricular conduction delay, most commonly of a left bundle branch block (LBBB) type.[5] Some evidence suggests that CRT may acutely improve LV rotation mechanics and that improvement in LV rotation mechanics may be used to identify CRT responders.[3,6] However, another line of evidence reports that CRT does not improve LV rotation mechanics at all, even in responders.[7] This discrepancy may arise from technical and interpretative limitations of 2-dimensional (2D) echocardiography that was used in those studies. Correlation of LV rotation mechanics between 2D echocardiography and 2D tagged magnetic resonance imaging (MRI) has been well established,[2] but 2D imaging cannot assess the through-plane motion of the heart chambers that is a part of dynamic rotation mechanics during the cardiac cycle. In addition, a recent large, multicenter study demonstrated that no single echocardiographic parameter can accurately identify CRT responders, primarily because of high levels of both interobserver and intraobserver variability.[8]

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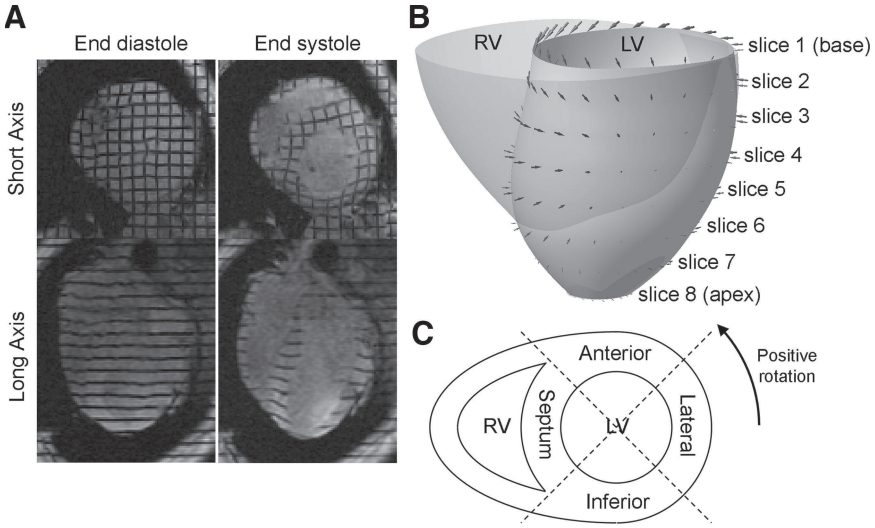

Figure 1. A, Tagged cine MR images acquired in 3 orthogonal directions (horizontal, vertical short-axis, and long-axis). B, 3D displacement map derived from tagged MRI. Each arrow (red) on the mesh represents a displacement vector at a total of 192 material points at the LV midwall (24 points on an LV short-axis slice×8 slices), which points from ED to ES. Systolic rotation is clockwise at the basal slice and counterclockwise at the apical slice, as viewed from the apex. C, LV regions. Anterior, lateral, inferior, and septal regions are shown as viewed from the apex. Both LV rotation and torsion were defined as zero at ED, and positive direction defined as counterclockwise as viewed from the apex.

In the present study, we sought to study the acute effects of CRT on LV rotation mechanics by 3D tagged MRI in dogs with LBBB and tachycardia-induced cardiomyopathy. Three-dimensional tagged MRI is the "gold standard" technique to measure myocardial motion in vivo, and it allows objective and extensive mapping of the 3D displacement field within the left ventricle. We also evaluated the regional heterogeneities of LV rotation mechanics in both circumferential and apex-to-base directions.

Methods

All studies were performed according to the position of the American Heart Association on research animal use.[9] All protocols were approved by the animal care and use committee of the Johns Hopkins University School of Medicine and the National Heart, Lung, and Blood Institute. A subset of data included in this study has been presented previously in our reports,[10,11] which analyzed mechanical dyssynchrony.

Experimental Protocol

Experimental details have been described previously.[10] In brief, 7 adult mongrel dogs (20 to 30 kg) underwent radiofrequency ablation of the left bundle branch and 3 to 4 weeks of rapid ventricular pacing (210 to 250 beats/min) to create pacing-induced heart failure (HF). The animals with mechanical dyssynchrony and HF were anesthetized, and MRI-compatible pacing leads were positioned in the right atrium, epicardial mid-LV free wall (LV), and right ventricular anteroapex (RV) via median sternotomy. Chamber hemodynamics was measured with an MR-compatible micromanometer (Millar, SPC-350, 5F). Hearts were paced at the right atrium (LBBB+HF) or LV plus RV (CRT) at 20 beats/min above the intrinsic sinus rate and with atrioventricular delay selected to maximize dP/dt_{max} for each pacing configuration. Tagged cine MRI in 3 orthogonal directions (2 short-axis and 1 long-axis orientations) were acquired for each pacing protocol at a temporal resolution of 14.0 to 14.6 ms, which was used to derive 3D displacement field and finite strains (Figure 1A; supplemental movies 1 and 2 in the online-only Data Supplement).

Data Analysis

Cartesian 3D coordinates (x, y, z) of a total of 192 material points at the LV midwall (24 points on an LV short-axis slice×8 slices) at each time frame were derived from the 3D displacement field (Figure 1B). LV volume at each time frame was defined as the sum of multiple space-filling, tetrahedral volumes created by the LV midwall material points.[12] End diastole (ED) and end systole (ES) were defined as the time of the maximum and minimum LV volumes, respectively.

At each time frame, all marker coordinates were transformed into a moving cylindrical coordinate system (r, θ, z), with the origin at the centroid of the material points of the most basal LV short-axis slice and with the z axis passing through the centroid of the material points defining the most apical short-axis LV plane.[13] For each LV short-axis slice, overall rotation (in degrees) was defined at each time frame as the average angular displacement (θ) of the 24 material points on each LV short-axis slice, and the rotation of each LV region (anterior, lateral, inferior, and septal; Figure 1C) was calculated by averaging the corresponding 6 circumferential material points at those locations.[14] Torsion (in degrees) was defined as LV rotation of each region of each slice with respect to that of the corresponding region of the most basal short-axis slice.[2] Both rotation and torsion were defined as zero at ED, and positive rotation was defined as counterclockwise as viewed from the apex to base (Figure 1C). During systole in normal hearts, the apex has a positive (counterclockwise) rotation and the base, a negative (clockwise) rotation, resulting in a positive (counterclockwise) torsion.[15] The time course of rotation and torsion was linearly interpolated over time to yield the same number of data points during the cardiac cycle in each animal.[16]

Statistical Analysis

Values are mean±SD (n=7) unless otherwise specified. A Student t test was used to compare peak LV rotation, torsion, rotation rate, and torsion rate with and without CRT. Two-factor repeated-measures ANOVA was used to evaluate regional heterogeneity of the LV rotation mechanics with respect to circumferential (anterior, lateral, inferior, and septal) and apex-to-base (slices 1 through 8) directions. The results were also confirmed by mixed-effects models that treated the dogs as a random effect as opposed to a fixed effect. Statistics were performed with SigmaStat 3.0 (SPSS, Inc, Chicago, Ill) and JMP 6 (SAS Institute, Inc, Cary, NC) software.

Results

Hemodynamic parameters are summarized in Table 1. CRT significantly improved peak LV pressure ($P<0.001$), LV ED pressure ($P<0.002$), dP/dt_{max} ($P<0.0002$), dP/dt_{min} ($P<0.01$), LV ES volume ($P<0.001$), stroke volume (SV) ($P<0.04$), and ejection fraction (EF) ($P=0.02$).

Table 1. Hemodynamics

	LBBB+HF	CRT	*P* Value
Heart rate, beats/min	123±13	123±13	NS
AV delay, ms	144±10	69±18	0.0001
Peak LV pressure, mm Hg	86.8±7.7	97.4±12.6	<0.001
LV ED pressure, mm Hg	14.0±4.5	11±3.2	<0.002
dP/dt_{max}, mm Hg/s	1048±242	1392±413	<0.0002
dP/dt_{min}, mm Hg/s	−960±162.2	−1152±250	<0.01
LV ED volume, mL	62±26	60±26	0.07
LV ES volume, mL	49±27	46±28	<0.001
SV, mL	13±6	15±6	<0.04
EF, %	23±12.7	27.5±16.2	0.02

AV indicates atrioventricular; NS, not significant. Other abbreviations are as defined in text. Values are mean±SD.

LV Rotation Mechanics

Overall, CRT did not significantly change the maximum or minimum rotation (Table 2). However, CRT significantly shortened the time to the maximum rotation, which came immediately before ES. In addition, CRT significantly shortened the time to the minimum rotation. This indicates significant shortening of an initial large, brief, negative (clockwise) rotation, which peaked at ≈40 ms in the mechanically dyssynchronous (LBBB+HF) hearts (Figure 2).

CRT did not significantly change the maximum or minimum rotation rate (Table 3). However, CRT significantly shortened the time to the maximum rotation rate, which came immediately after the initial large, brief, negative (clockwise) rotation (Figure 2). CRT also significantly shortened the time to the minimum rotation rate in apical slices. This reflects a significant shift of the time of minimum rotation rate to immediately after ES, which is likely in the isovolumic relaxation phase.

CRT did not significantly change the maximum or minimum torsion or the time to the maximum or minimum torsion (Table 4). CRT did not significantly change the maximum or minimum torsion rate (Table 5). However, CRT significantly shortened the time to the maximum torsion rate, which came at the beginning of contraction (Figure 2).

Regional Assessment of LV Rotation Mechanics

Regional heterogeneity of LV rotation mechanics was evaluated in circumferential (anterior, lateral, inferior, and septal) and apex-to-base (slices 1 through 8) directions (online-only supplemental Figures 1 and 2). Overall, the mechanically dyssynchronous (LBBB+HF) hearts showed a similar time course in all 4 regions, characterized by an initial brief, negative (clockwise) rotation followed by a long systolic counterclockwise rotation, which peaked beyond ES at the base (slice 8).

In the mechanically dyssynchronous (LBBB+HF) hearts, there was no significant circumferential regional heterogeneity in any indices of LV rotation mechanics (online-only supplemental Table). However, as expected, there was significant apex-to-base regional heterogeneity in the maximum rotation, maximum torsion, and maximum and minimum torsion rate ($P<0.001$), reflecting an incremental nature of LV rotation as a function of the distance from the base. CRT did not significantly change the circumferential regional heterogeneity, and there was no significant circumferential regional heterogeneity in any indices of the LV rotation mechanics (supplemental Table).

In summary, there was no significant circumferential regional heterogeneity (anterior, lateral, inferior, and septal) in LV rotation mechanics in either LBBB+HF or CRT, but there was significant apex-to-base regional heterogeneity.

Discussion

The present study used 3D tagged cine MRI to examine the effects of CRT on LV rotation mechanics. Our results indicate that CRT clearly improves hemodynamics; however, CRT does not improve LV rotation mechanics. These results suggest that LV rotation mechanics may not be an essential component of LV function.

Table 2. LV Rotation

					Minimum			
	LBBB+HF		CRT		LBBB+HF		CRT	
	Value, °	Time, ms	Value, °	Time, ms	Value, °	Time, ms	Value, °	Time, ms
Slice 1 (base)	2.0±7.5	355±40	0.2±1.0	488±58*	−2.2±3.1	38±4	−1.2±2.0	25±3*
Slice 2	2.4±7.5	343±39	0.2±3.6	288±34*	−2.1±2.8	38±4	−1.1±1.9	25±3*
Slice 3	3.1±7.5	343±39	0.9±3.4	276±33*	−2.1±2.6	38±4	−0.9±1.8	25±3*
Slice 4	3.6±7.6	343±39	1.7±3.8	238±28*	−1.9±2.4	38±4	−0.8±1.7	25±3*
Slice 5	4.0±7.6	343±39	2.4±4.0	238±28*	−1.8±2.1	38±4	−0.6±1.6	25±3*
Slice 6	4.6±7.4	292±33	3.1±4.2	238±28*	−1.6±1.9	38±4	−0.6±1.0	451±54*
Slice 7	5.2±7.2	292±33	3.7±4.6	238±28*	−1.5±1.7	38±4	−0.6±0.9	463±55*
Slice 8 (apex)	5.6±7.5	292±33	4.0±4.8	263±31	−1.5±1.9	25±3	−0.6±1.3	463±55*

Abbreviations as defined in text. Values are mean±SD.
*$P<0.05$ vs LBBB+HF.

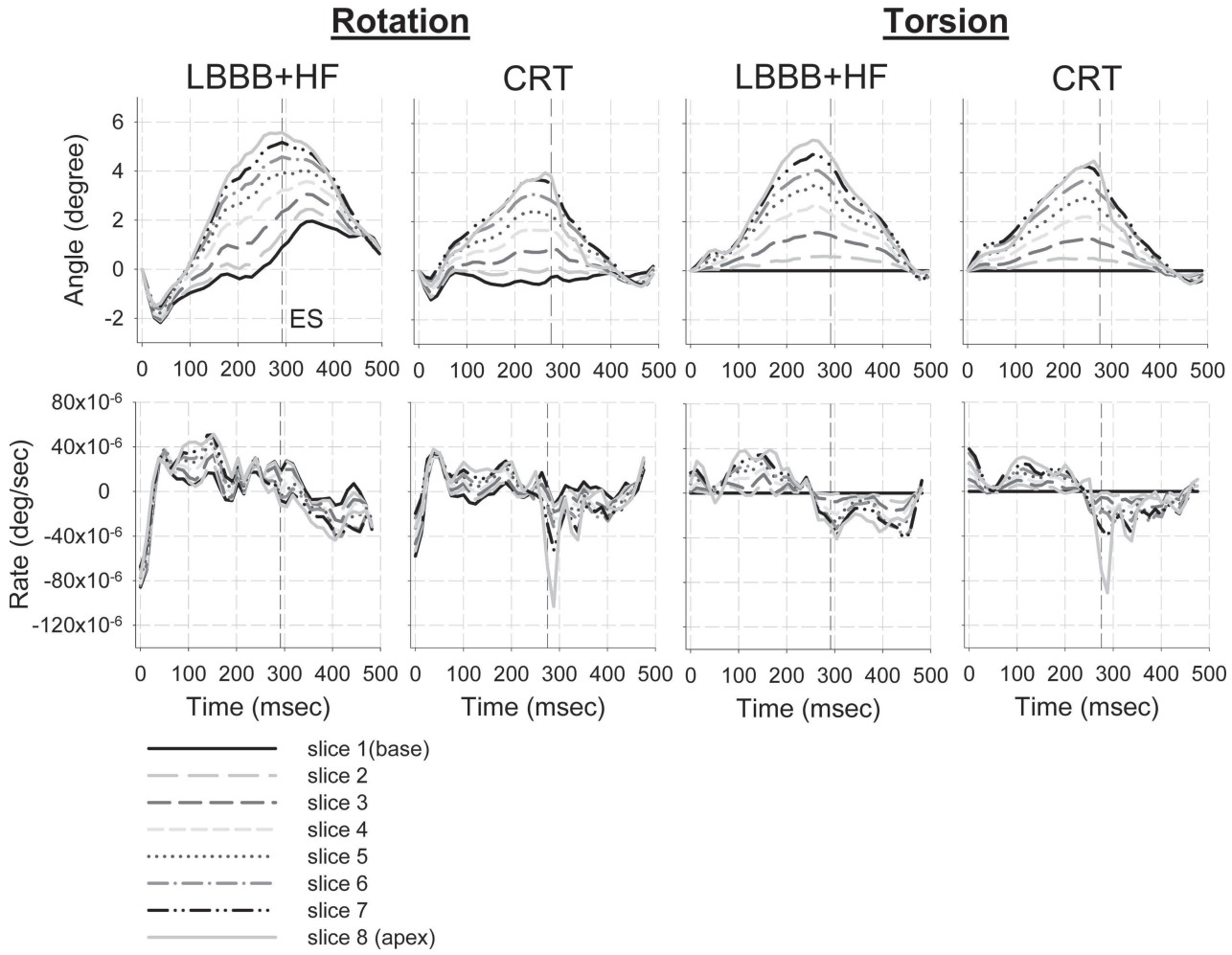

Figure 2. LV rotational mechanics with and without CRT on each slice. Values are mean (n=7). Abbreviations are as defined in text.

Effects of CRT on LV Rotation Mechanics in the Mechanically Dyssynchronous Heart

Normal LV torsional deformation begins with a brief, clockwise torsion (untwisting or pretwisting) during the isovolumic contraction phase, resulting from basal counterclockwise rotation and apical clockwise rotation, because endocardially located Purkinje fibers activate endocardial myofibers first.[15] Our results show that this brief, clockwise torsion is absent in the mechanically (LBBB+HF) dyssynchronous heart because the normal Purkinje conduction or the normal endocardial-to-epicardial activation sequence is disrupted. Instead, all slices make a relatively large and simultaneous clockwise rotation (Figure 2), which likely results from early activa-

Table 3. LV Rotation Rate

	Maximum				Minimum			
	LBBB+HF		CRT		LBBB+HF		CRT	
Rotation Rate, Value $\times 10^{-5}$	Value, °/s	Time, ms	Value, °/s	Time, ms	Value, °/s	Time, ms	Value, °/s	Time, ms
Slice 1 (base)	3.3±9.5	51±6	3.3±9.7	38±4*	−8.6±14	0±0	−5.8±8.8	0±0
Slice 2	3.3±9.2	51±6	3.1±9.4	38±4*	−8.3±13	0±0	−5.3±8.2	0±0
Slice 3	3.6±8.9	51±6	3.1±9.1	38±4*	−8.4±13	0±0	−4.7±7.8	0±0
Slice 4	3.8±8.9	51±6	3.4±9.0	50±6	−8.2±12	0±0	−4.0±7.5	0±0
Slice 5	4.4±8.2	152±17	3.6±9.0	50±6*	−7.7±12	0±0	−3.2±7.3	0±0
Slice 6	4.8±8.2	152±17	3.6±9.3	38±4*	−7.0±11	0±0	−3.3±4.9	301±36*
Slice 7	5.1±7.8	152±17	3.5±9.6	38±4*	−6.8±11	0±0	−5.2±9.7	288±34*
Slice 8 (apex)	5.1±7.9	152±17	3.8±9.8	38±4*	−7.6±11	0±0	−10±17	288±34*

Abbreviations as defined in text. Values are mean±SD.
*$P<0.05$ vs LBBB+HF.

Table 4. LV Torsion

	Maximum				Minimum			
	LBBB+HF		CRT		LBBB+HF		CRT	
Torsion	Value, °	Time, ms	Value, °	Time, ms	Value, °	Time, ms	Value, °	Time, ms
Slice 1 (base)	0.0±0.0	0±0	0.0±0.0	0±0	0.0±0.0	482±54	0.0±0.0	0±0
Slice 2	0.6±0.7	266±30	0.5±0.8	250±30	−0.1±0.3	482±54	−0.2±0.5	451±54
Slice 3	1.6±1.1	266±30	1.3±1.2	250±30	−0.1±0.4	482±54	−0.3±0.7	451±54
Slice 4	2.6±1.2	266±30	2.2±1.3	250±30	−0.2±0.5	482±54	−0.3±0.7	463±55
Slice 5	3.5±1.4	254±29	2.9±1.5	250±30	−0.3±0.8	482±54	−0.4±0.9	463±55
Slice 6	4.1±1.5	266±30	3.6±1.8	250±30	−0.4±1.1	482±54	−0.4±1.1	463±55
Slice 7	4.7±1.6	254±29	4.3±2.2	250±30	−0.4±1.3	482±54	−0.5±1.0	476±57
Slice 8 (apex)	5.3±1.9	254±29	4.5±2.4	263±31	−0.1±1.0	482±54	−0.5±1.3	463±55

Abbreviations as defined in text. Values are mean±SD.
*$P<0.05$ vs LBBB+HF.

tion of the inferoseptal LV, which is the site of LBBB in this model. All slices then made a long, counterclockwise rotation during systole, which peaked beyond ES at the base (slice 1). This systolic counterclockwise rotation at the basal slice diminished the magnitude of peak instantaneous torsion.

CRT diminished the duration of the initial simultaneous clockwise rotation by synchronizing RV and LV activation (Figure 2). However, CRT did not recover the brief clockwise torsion during isovolumic contraction that is seen in the normal heart due to endocardial activation.[15] This is because both the RV and LV leads in CRT electrically stimulate the LV from the epicardium or from the outer surface. Epicardial pacing reverses the normal endocardial-to-epicardial activation sequence, and mechanical activation indeed begins in the epicardium.[16] Mechanical activation of the epicardium causes counterclockwise LV torsion because the epicardial fibers are directed to approximately −60 degrees with reference to the circumferential direction.[17]

CRT also recovered basal systolic clockwise rotation, as seen in the normal heart. The combination of basal clockwise and apical counterclockwise rotation during systole appears to contribute to maximizing peak instantaneous torsion. However, CRT did not significantly change the maximum or minimum rotation in any slice (Table 2). The net effect is that CRT did not significantly change the maximum torsion (Table 4).

Although CRT did not significantly change the maximum or minimum rotation rate, CRT did significantly shift the time of the minimum rotation rate and the minimum torsion rate to the isovolumic relaxation phase in apical slices ($P<0.001$, Table 3). This could represent improvement of LV diastolic suction,[18] but because the minimum torsion rate is not significantly different (Table 5), its mechanical effect is unclear.

Regional Assessment of LV Rotation Mechanics With and Without CRT

In the mechanically dyssynchronous heart, regional heterogeneity of LV wall motion with the presence of early- (septal) and late- (lateral) activated regions is easily recognized by clinical imaging modalities, such as echocardiography and MRI. In addition, regional mechanics derived from wall motion is significantly different between early- and late-activated regions.[19] However, our results indicate that there is no significant circumferential (anterior, lateral, inferior, and

Table 5. LV Torsion Rate

	Maximum				Minimum			
	LBBB+HF		CRT		LBBB+HF		CRT	
Torsion Rate, Value $\times 10^{-5}$	Value, °/s	Time, ms	Value, °/s	Time, ms	Value, °/s	Time, ms	Value, °/s	Time, ms
Slice 1 (base)	0.0±0.0	0±0	0.0±0.0	0±0*	0.0±0.0	0±0	0.0±0.0	0±0
Slice 2	0.90±1.4	152±17	0.60±4.6	100±12*	−0.82±0.77	444±50	−0.71±0.61	401±48
Slice 3	1.7±1.6	152±17	1.1±1.9	0±0*	−1.7±1.6	419±47	−1.4±1.5	388±46
Slice 4	2.2±1.5	152±17	1.8±1.8	0±0*	−2.5±2.0	419±47	−2.0±1.7	376±45
Slice 5	2.7±1.7	152±17	2.5±2.2	0±0*	−2.9±2.4	419±47	−2.4±1.6	376±45
Slice 6	3.2±1.9	152±17	3.4±2.9	0±0*	−3.9±2.1	444±50	−2.8±1.6	376±45*
Slice 7	3.5±1.4	152±17	3.8±3.3	0±0*	−4.1±2.3	444±50	−4.0±5.0	288±34*
Slice 8 (apex)	3.9±1.5	165±19	3.1±1.9	113±13*	−4.1±3.0	304±34	−9.1±13	288±34

Abbreviations as defined in text. Values are mean±SD.
*$P<0.05$ vs LBBB+HF.

septal) regional heterogeneity in LV rotation mechanics of the mechanically dyssynchronous heart, even though LV rotation is also derived from wall motion.

Our results may simply reflect the fact that LV rotation is a global motion that results from coordination of all regions of the LV. This concept is supported by the fact that rotation mechanics is well correlated with indices of global LV function rather than regional function.[20] In fact, our finding is consistent with a 3D tagged MRI study by Sorger et al,[14] who found no significant regional heterogeneity of LV rotation mechanics in normal dog hearts with mechanical dyssynchrony by RV pacing.

Effects of CRT on Hemodynamics and LV Rotation Mechanics

Our results demonstrate that CRT significantly improves hemodynamics without improving LV rotation mechanics. This suggests that hemodynamic improvement in CRT does not require improvement of LV rotation mechanics.

To understand the relationship between hemodynamics and LV rotation mechanics, we need to consider what the primary hemodynamic effect of CRT is. By re-coordinating contraction timing, CRT shifts the end-systolic pressure-volume point (and relationship) leftward.[21] This results from a decline in late systolic stretch of one side of the wall (typically septum), and does not imply a contractility increase. LVESV declines, and as end-diastolic volume (LVEDV) is little altered, both SV and EF increase.[21,22] The fall in LVESV is often used to identify CRT responders.[23] Greater ejected SV increases systolic pressure as systemic vascular properties are not acutely changed.[21] CRT also significantly increases dP/dt_{max}, but this occurs before ejection, and is caused by the loss of internal chamber unloading (contraction of one wall stretching the other). Pressure can rise faster if muscle activation is synchronized. In summary, the primary effect of CRT is mechanical resynchronization, and all other changes can be easily explained by this.

Because LV rotation results from shortening of obliquely oriented myofibers, a change in LV chamber size, or SV when EDV is constant, should uniquely determine the extent of LV rotation.[24] Earlier studies have shown that an increase in SV increases LV rotation and torsion when contractility is constant.[25] Thus, the present findings are surprising and challenge this notion.

An additional factor to consider is that CRT essentially uses epicardial pacing to stimulate the LV from both the septum and the lateral walls. As described earlier, epicardial pacing alters the normal transmural activation sequence, and the reverse transmural mechanical activation sequence[16] alone appears to reduce LV rotation and torsion. In a 3D tagged MRI study, Sorger et al[14] found that biventricular pacing in the normal dog heart disrupts normal transmural gradient in rotation and significantly reduces peak LV rotation and torsion without significant changes in hemodynamics compared with atrial pacing. This finding indicates that the normal endocardial-to-epicardial electrical activation sequence is critical in generating normal LV rotation mechanics. However, in the studies by Sorger et al,[14] biventricular pacing was performed without any atrioventricular delay. This likely abolished atrial kick and decreased preload, which may have contributed to a decrease in LV rotation and torsion compared with those of normal atrioventricular conduction.[25]

In our data, these positive and negative effects of CRT on LV rotation mechanics appear to cancel each other; therefore, the net result is that CRT did not significantly change LV rotation mechanics. The positive effect of CRT on LV rotation mechanics is likely dependent on the magnitude of improvement in SV.[25] This concept is demonstrated by the fact that LV torsion was unchanged in CRT responders (defined as a reduction of ES volume $>15\%$[8]) and worsened in nonresponders.[7] The negative effect of CRT on LV rotation mechanics by altering the normal transmural mechanical activation sequence may be relatively constant, owing to the local nature of electrical pacing effects. It may be possible to minimize or abolish the negative effect and improve LV rotation mechanics by pacing the LV endocardium in CRT, ie, septal endocardium and lateral endocardium. In fact, a recent report by Mills et al[26] suggests that LV endocardial pacing tends to maintain regional and global cardiac mechanics. In summary, the presence of both positive and negative effects can explain the apparently conflicting effects of CRT on LV rotation mechanics despite consistent hemodynamic improvements.[3,7]

Clinical Implications

Improvement in LV rotation mechanics would identify CRT responders, because it appears to be associated with improvement in SV. However, because CRT inherently has a negative effect on LV rotation mechanics by epicardial pacing, LV rotation mechanics could only be marginally improved or not changed at all in some subsets of patients. Therefore, CRT responders could have no improvement in LV rotation mechanics, as in our data set. In summary, LV rotation mechanics is a specific but insensitive index of identifying CRT responders.

Limitations

Because the animals in our study were not known to have coronary artery disease, by definition, this is a model of nonischemic cardiomyopathy. There is a possibility that effects of CRT on LV rotation mechanics may be different between ischemic and nonischemic cardiomyopathy. However, recent reports[6,7] suggest that the effects of CRT on LV rotation mechanics are not significantly different between ischemic and nonischemic cardiomyopathy.

Because congestive heart failure in this model is reversible in 24 to 48 hours once pacing is discontinued,[27] this animal model may not be suitable for evaluating the chronic effects of CRT on hemodynamic parameters and LV rotation mechanics. However, this is an excellent model to evaluate the acute effects of CRT on hemodynamic parameters and LV rotation mechanics. In addition, this model recapitulates many biochemical, molecular, and structural features relevant to human HF, and its mechanical response to CRT is analogous to that in patients with dilated cardiomyopathy and conduction delay.[10]

The 3D displacement that we measured in open-chest, anesthetized dogs may not accurately reflect that of closed-chest, conscious animals. Some of the LV rotation mechanics that we observed may be specific to this model. For example, LV rotation mechanics may be different at a different level of block of LBBB. This study examined LV rotation mechanics only acutely, and long-term effects of CRT on LV rotation mechanics were not assessed in this study.

In addition, acute hemodynamic improvement with CRT may not be a surrogate for long-term outcomes, such as reverse remodeling and improvement in mortality. However, a recent report by Steendijk et al[28] demonstrates that hemodynamic improvements in acute settings are maintained chronically, which suggests that hemodynamic improvements may contribute to the long-term clinical outcomes.

In conclusion, CRT significantly improves hemodynamics without improving LV rotation mechanics. There is no significant circumferential regional heterogeneity of LV rotation mechanics in the mechanically dyssynchronous heart. Therefore, LV rotation mechanics is an index of global LV function, which requires coordination of all regions of the LV, and improvement in LV rotation mechanics appears to be a specific but insensitive index of acute hemodynamic response.

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Disclosures

Dr McVeigh serves as a consultant for Surgivision, Inc.

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CLINICAL PERSPECTIVE

Left ventricular (LV) rotation mechanics provides important indices of cardiac function. Earlier studies have yielded conflicting evidence on whether or not cardiac resynchronization therapy (CRT) improves LV rotation mechanics. This discrepancy may arise from technical and interpretative limitations of the 2-dimensional echocardiography that was used in those studies. In the present study, we sought to study the acute effects of CRT on LV rotation mechanics by 3D tagged magnetic resonance imaging in dogs with left bundle branch bloc and tachycardia-induced cardiomyopathy. Three-dimensional tagged magnetic resonance imaging is the gold standard technique to measure myocardial motion in vivo, and it allows objective and extensive mapping of the 3D displacement field within the left ventricle. The results of our study indicate that CRT acutely improves hemodynamic parameters without improving LV rotation mechanics. This suggests that improvement in LV rotation mechanics appears to be a specific but insensitive index of an acute hemodynamic response to CRT.

SUPPLEMENTAL MATERIAL

Supplemental Table

Variable	LBBB+HF				CRT			
	RMANOVA		Mixed Effects		RMANOVA		Mixed Effects	
	Circumferential	Apex-Base	Circumferential	Apex-Base	Circumferential	Apex-Base	Circumferential	Apex-Base
Max Rotation	0.15	<0.001	0.55	<0.001	0.31	<0.001	0.63	<0.001
Max Rotation Rate	0.98	0.48	0.98	0.46	0.67	0.92	0.88	0.99
Min Rotation	0.66	0.51	0.49	0.25	0.98	0.84	0.98	0.46
Min Rotation Rate	0.92	0.92	0.97	0.88	0.96	0.87	0.98	0.18
Max Torsion	0.06	<0.001	0.06	<0.001	0.18	<0.001	0.07	<0.001
Max Torsion Rate	0.69	<0.001	0.25	<0.001	0.28	<0.001	0.06	<0.001
Min Torsion	0.93	0.79	0.70	0.70	0.99	0.42	0.95	0.44
Min Torsion Rate	0.27	<0.001	0.18	<0.001	0.76	0.06	0.85	<0.001

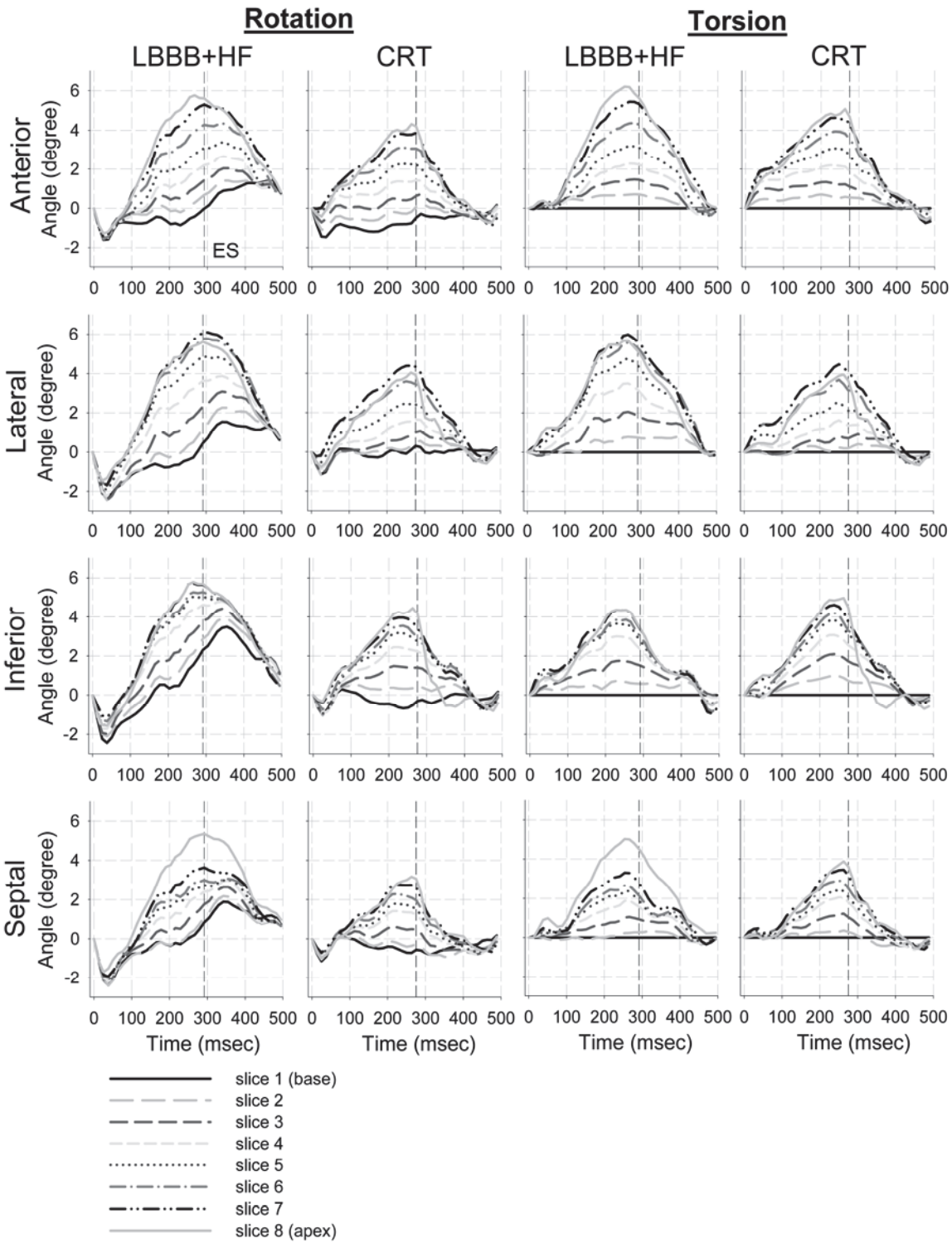
Regional heterogeneity analysis. P values of regional heterogeneity analysis of indices of LV rotation mechanics with respect to circumferential (anterior, lateral, inferior and septal) and apex-base (slice 1 through 8) directions obtained from RMANOVA and a mixed effects model are shown.

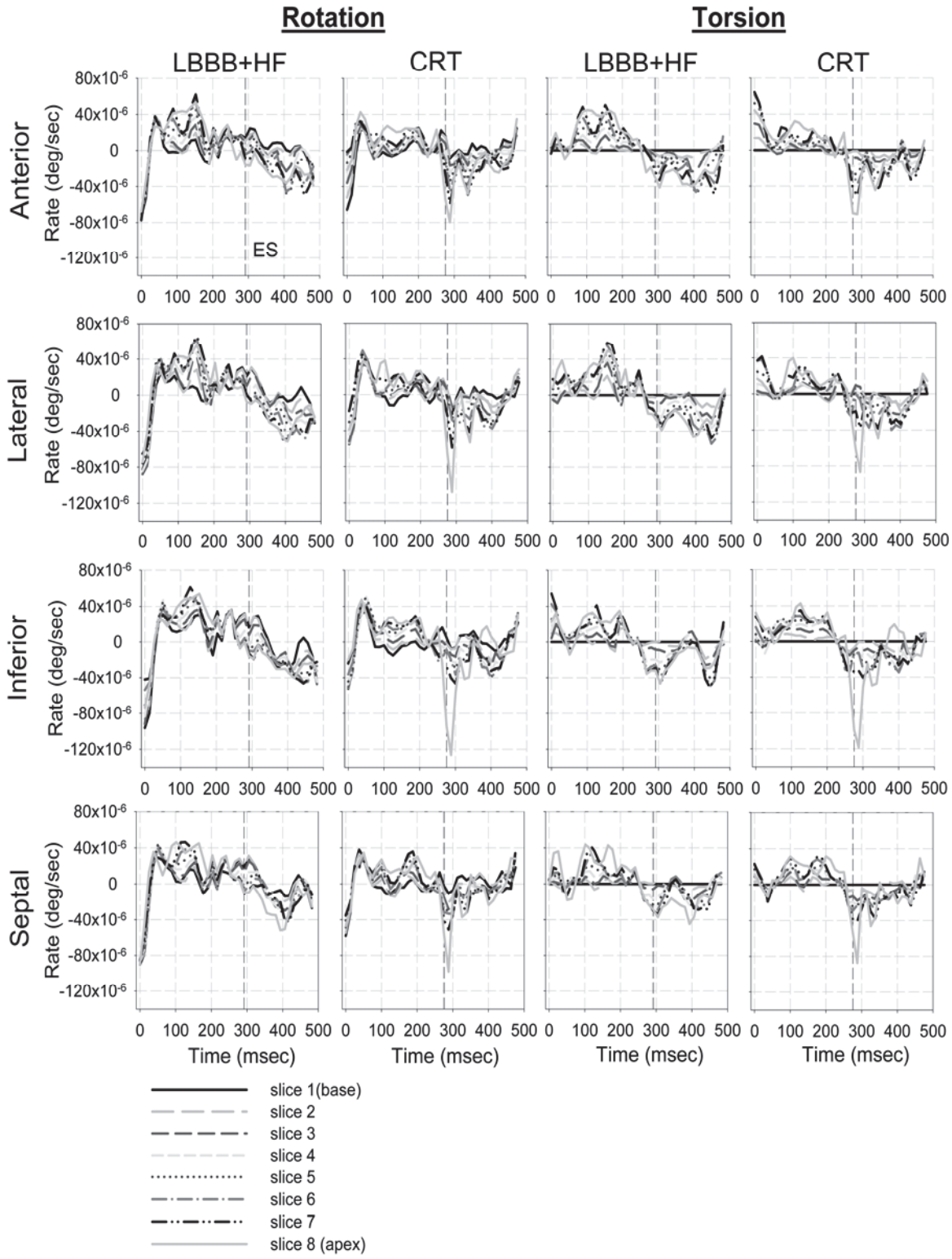
Supplemental Figure 1. *LV rotation and torsion with and without CRT in each region.* Values are mean (n=7). Abbreviations as in Figure 2.

Supplemental Figure 2. *LV rotation rate and torsion rate with and without CRT in each region.* Values are mean (n=7). Abbreviations as in Figure 2.

Supplemental Movie 1. *Sample tagged cine MRI for short-axis (left panel) and long-axis (right panel) slices during right atrial pacing in dogs with left bundle branch block and pacing-induced heart failure (LBBB+HF)* (Courtesy of Dr. Owen P. Faris).

Supplemental Movie 2. *Sample tagged cine MRI for short-axis (left panel) and long-axis (right panel) slices during biventricular pacing in dogs with left bundle branch block and pacing-induced heart failure (CRT)* (Courtesy of Dr. Owen P. Faris).


Rotation
Torsion
LBBB+HF
CRT
LBBB+HF
CRT
Anterior
Lateral
Inferior
Septal
Angle (degree)
ES
Time (msec)
slice 1 (base)
slice 2
slice 3
slice 4
slice 5
slice 6
slice 7
slice 8 (apex)


Rotation
Torsion
LBBB+HF
CRT
LBBB+HF
CRT
Anterior
Lateral
Inferior
Septal
Rate (deg/sec)
80x10-6
40x10-6
0
-40x10-6
-80x10-6
-120x10-6
ES
0 100 200 300 400 500
Time (msec)
slice 1(base)
slice 2
slice 3
slice 4
slice 5
slice 6
slice 7
slice 8 (apex)