ISSN 1936-878X/09/$36.00
PUBLISHED BY ELSEVIER INC.
DOI:10.1016/j.jcmg.2008.12.022

ORIGINAL RESEARCH

Opposing Wall Mechanics Are Significantly Influenced by Longitudinal Cardiac Rotation in the Assessment of Ventricular Dyssynchrony

Karen P. Phillips, MBBS, Zoran B. Popović, MD, PhD, Pascal Lim, MD, John E. Meulet, MBBS, Conor D. Barrett, MB, ChB, Luigi Di Biase, MD, Deborah Agler, RDCS, James D. Thomas, MD, Richard A. Grimm, DO

Cleveland, Ohio

OBJECTIVES This study sought to assess whether longitudinal rotation (LR) affects myocardial systolic velocity profiles and to compare velocity-based measures of dyssynchrony with LR for predicting cardiac resynchronization therapy (CRT) response.

BACKGROUND Longitudinal rotation, a rocking motion often seen when the dilated left ventricle (LV) is imaged in its horizontal long-axis plane, is a recently recognized phenomenon and a new predictor of response to CRT.

METHODS One hundred patients with CRT implants and suitable baseline echocardiograms were identified. Longitudinal rotation was assessed in the apical 4-chamber view by speckle-tracking techniques and myocardial systolic velocities for basal septum, and lateral LV were analyzed from tissue Doppler images. The quartiles of LR distribution were analyzed for differences in their systolic velocities. Correlation between measurements and reduction in LV end-systolic volume (ESV) at follow-up was performed.

RESULTS Quartile 1 had a mean LR of $-6.8 \pm 2.3°$; quartile 4 showed a mean LR of $2.3 \pm 1.6°$. A depressed peak velocity of lateral wall, when compared with the septum, was found for quartile 1 ($p = 0.01$), whereas the converse was noted in quartile 4 ($p = 0.0001$). The difference in amplitude of peak velocity between septal and lateral walls was found to correlate with the pattern of LR and with percentage reduction in LV ESV at follow-up in nonischemic patients. Septal–lateral delay was not correlated with the presence of LR, nor was it predictive of reduction in LV ESV.

CONCLUSIONS Patients with prominent clockwise LR have depressed long-axis systolic velocities of the lateral wall, whereas the patients with counterclockwise LR have depressed septal wall velocities. The difference in peak amplitude of basal septal and lateral systolic velocities is predictive of LR, and in the nonischemic subgroup correlates with quantitative LV reverse remodeling at follow-up. Velocity time-based measures, including septal–lateral delay were not predictive of CRT response. (J Am Coll Cardiol Img 2009;2:379–86) © 2009 by the American College of Cardiology Foundation

From the Department of Cardiovascular Medicine, Cleveland Clinic, Cleveland, Ohio. Supported by grants from the National Space Biomedical Research Institute through NASA NCC 9-58 (Houston, Texas), the Department of Defense (Ft. Dietrick, Maryland, USAMRMC grant no. 02360007), and the National Institutes of Health, National Center for Research Resources, General Clinical Research Center (grant MO1 RR-018390).

Manuscript received May 12, 2008; revised manuscript received November 25, 2008, accepted December 5, 2008.

JACC: CARDIOVASCULAR IMAGING, VOL. 2, NO. 4, 2009
APRIL 2009:379–86

Longitudinal cardiac rotation (LR) is a recently recognized reversible phenomenon occurring in patients with cardiomyopathy and dilated left ventricles that correlates with a response to cardiac resynchronization therapy (CRT) (Online Video) (1). In turn, clinical predictors of longitudinal rotation are etiology of cardiomyopathy, left ventricular (LV) dilation, and QRS duration, suggesting the importance of altered LV geometry and electrical activation (1). Abnormalities of regional strain distribution seem to underpin the observed patterns of LR.

See page 387

Because LR represents the motion of the whole heart, it can be expected that its presence affects myocardial velocity pattern. This may be relevant, because the most widely used methods for the assessment of mechanical dyssynchrony and response to CRT are based on timing of onset or peak myocardial systolic velocity (2,3). In this study, we hypothesized that the phenomenon of longitudinal cardiac rotation affects Doppler angle-dependent measures of longitudinal systolic velocity profiles. We also aimed to assess various velocity-based measures of dyssynchrony for predicting response to CRT.

ABBREVIATIONS AND ACRONYMS

ANOVA = analysis of variance
CRT = cardiac resynchronization therapy
ECG = electrocardiography/electrocardiogram
ESV = end-systolic volume
LR = longitudinal rotation
LV = left ventricle/ventricular
NYHA = New York Heart Association
RV = right ventricle/ventricular

METHODS

Study population. Patients were identified retrospectively by a search of our echocardiographic database for subjects who had undergone CRT and had a pre-implantation echocardiogram of satisfactory quality performed on a Vivid 7 ultrasound machine (Vingmed, GE Medical, Horten, Norway) during the period of March 2003 to December 2006. A total of 100 consecutive patients were identified, and they form the patient population of this study. Late post-CRT follow-up echocardiograms performed ≥6 weeks after the procedure were available for analysis for 76 of 100 patients. This sample size had a power of 90% to detect a correlation of ≥0.35 between end-systolic volume decrease and its predictor at a single-sided alpha level of 0.05. All patients met standard indications for CRT including New York Heart Association (NYHA) functional class III or IV symptoms despite optimal pharmacologic therapy with ejection fraction ≤35% and either electrocardiographic (ECG) evidence of QRS prolongation (>120 ms) or pre-existing right ventricular (RV) pacing. Additionally, we performed the analysis of Doppler tissue velocity data in 16 healthy control subjects in which LR values were already published (1). The Internal Review Board of the Cleveland Clinic approved the study, and subjects gave written informed consent to participate.

Database search and the definition of clinical terms. Patients were defined as having ischemic cardiomyopathy if coronary angiography showed coronary artery stenosis of at least 50% in any of the major of epicardial vessels, or if there was a documented history of prior myocardial infarction or coronary artery revascularization. Patients with LV enlargement and nonobstructive coronary anatomy at angiography were defined as having nonischemic cardiomyopathy. If ischemic cardiomyopathy was present, location and presence of the myocardial scars was identified by, in the order of precedence: magnetic resonance imaging, rubidium glucose positron emission tomography, stress–rest single-photon computerized emission tomography, or dobutamine stress echocardiography. The QRS duration complex was determined from the last ECG obtained before biventricular device implantation. To quantitate CRT-induced reverse LV remodeling, we assessed follow-up echocardiograms performed 40 days to 18 months after CRT start. If more than 1 echocardiogram was available, we used the one that was closest to 6 months after the start of CRT. Responders to CRT were defined by a decrease in LV end-systolic volume (ESV) of ≥15% at follow-up echocardiography.

Echocardiography methods. LV end-systolic and -diastolic volumes were assessed by Simpson biplane echocardiography. The timing of aortic valve closure was determined from the pulsed-wave Doppler tracings of the LV outflow tract.

Longitudinal cardiac rotation was analyzed in the apical 4-chamber view using speckle tracking software (EchoPac, GE Medical) as previously described (1). In brief, the region of interest is applied over the LV myocardium in an apical 4-chamber view. The software automatically tracks the down-rotational rate of myocardial motion with reference to the center of gravity of the region of interest. To obtain rotation, rotational rate is integrated over a single cardiac cycle, defined by the R waves of the ECG. Finally, end-systolic longitudinal rotation is defined as the rotation at the time of aortic valve closure. In accordance with engineering notation, the negative sign indicates clockwise rotation, and a

positive sign signifies counterclockwise rotation. Normal values for LR were published previously (1).

Tissue Doppler images of the apical 4-chamber view were analyzed to obtain myocardial velocities at basal septal and basal lateral LV segments as previously described (3). Traces of myocardial velocity profiles for 3 cardiac cycles were exported for each patient. From these profiles we obtained the timing and amplitudes of peak systolic velocities and calculated the following 3 parameters: 1) the difference in amplitude between the peak systolic velocities at basal septum and basal lateral wall, with the septal peak velocity as the reference; 2) the time difference between peak systolic velocity events at basal septum and basal lateral segments, again with reference to the septal peak velocity; and 3), because this timing difference was found to be a negative value in a proportion of patients, it was converted to an absolute value consistent with the previously described measure of septal–lateral delay (3).

Interobserver and intraobserver data variability and repeatability. To assess interobserver and intraobserver variability of LR (1) and myocardial systolic velocity measurements, 12 randomly selected clips were reviewed by a same observer >1 month apart after first measurement, and independently by a second observer. Variability in peak systolic velocity and time-to-peak systolic velocity randomly was assessed as mean absolute and mean relative difference ± 1 SD.

Absolute intraobserver and interobserver variability for longitudinal rotation was 0.8 ± 0.7° and 1.2 ± 1.1°. Absolute and relative intraobserver variability for peak systolic velocity was 0.10 ± 0.08 cm/s and 4 ± 3%, whereas it 8.7 ± 6.7 ms and 6.1 ± 4.0% for time-to-peak systolic velocity. Absolute and relative interobserver variability for peak systolic velocity was 0.11 ± 0.08 cm/s and 5 ± 4%, whereas it was 9.1 ± 7.0 ms and 6.3 ± 4.9% for time-to-peak systolic velocity.

Interobserver and intraobserver variability of LV ESVs was tested in an analogous manner in 10 randomly selected studies. Absolute and relative intraobserver variability was 24 ± 16 ml and 12 ± 8%, whereas absolute and relative interobserver variability was 30 ± 17 ml and 16 ± 9%.

In patients with at least 2 echocardiographic studies performed between 6 weeks and 18 months of follow-up, we assessed time-related variability (i.e., repeatability) of ESVs by standard deviation. We identified 28 patients who satisfied this criterion, with a total of 76 studies. ESV variability during follow-up was 20 ± 15 ml (11 ± 8%).

Statistical analysis. Results are expressed as mean ± SD, unless otherwise stated. Between-group and within-group comparisons were performed by unpaired and paired *t* test, respectively, except for NYHA functional class, for which the Mann-Whitney *U* test was used. The Fisher exact test was used for comparison of frequencies for noncontinuous variables. An F ratio was used to compare difference in variances (i.e., dispersion) between 2 groups.

To characterize the impact of LR on myocardial velocities, the entire distribution of mean LR values for the CRT population was divided into quartiles. A 1-way analysis of variance (ANOVA) was performed to test for differences in the measures of septal and lateral velocities among the quartiles, followed by Tukey Honestly Significant Difference post-hoc tests, if appropriate. Additionally, the first and fourth quartiles were selected to construct the average profiles of their myocardial velocities. The velocity profiles were scaled to percent systole duration, with systole duration defined from the onset of the R-wave to aortic valve closure determined from the pulsed wave of the LV outflow tract (4).

Correlation between measurements was performed by calculating the Pearson correlation coefficient. Because the estimate of the correlation coefficient between the septal–lateral velocity difference and the LV ESV decrease during follow-up may be unstable due to a wide range of follow-up times, we performed an estimation of correlation coefficient median with corresponding 95% confidence intervals using bootstrapping. A total of 2,000 iterations were performed by random sampling with replacement of the original dataset. A value of $p < 0.05$ was considered significant.

RESULTS

Baseline clinical and demographic variables are given in Table 1 for ischemic and nonischemic subgroups, along with response rates and follow-up echocardiographic data. In the ischemic cardiomyopathy group, 19 patients had lateral scar, 27 patients had a scar in nonlateral locations, whereas in 7 patients data were not available. Late post-CRT follow-up echocardiograms performed 6 weeks to 18 months (median: 194 days, first and third quartile: 111 and 274 days) after the procedure were available for analysis for 79 of the 100 patients. In the remaining 21 patients, a coronary sinus lead was not implanted because of technical reasons in 7 cases, whereas 1 patient at the 6-month follow-up was in atrial fibrillation with only 66% of cycles paced. Of the remaining 13 patients, 3 patients died (1.5 months, 7 months, and 3 years after pacemaker implantation), whereas 2 underwent

Table 1. Baseline Patient Characteristics and Echocardiographic Follow-Up Data

	Nonischemic Patients (n = 47)	Ischemic Patients (n = 53)	p Value
Age (yrs)	57 ± 13	69 ± 10	<0.001
Male (n)	28	48	<0.001
NYHA functional class	3.1 ± 0.5	3.0 ± 0.4	0.40
QRS (ms)	155 ± 29	151 ± 33	0.53
EDV at baseline (ml)	251 ± 92	234 ± 87	0.57
ESV at baseline (ml)	194 ± 87	172 ± 61	0.14
EF at baseline (%)	25 ± 10	27 ± 9	0.22
Follow-up rate (n)	36/47	40/53	1.0
Response rate (n)	20/38	19/41	0.5
EDV post-CRT implantation (ml)	241 ± 103*	219 ± 81*	0.85
ESV post-CRT implantation (ml)	166 ± 90†	157 ± 76‡	0.68
EF post-CRT implantation (%)	32 ± 12†	31 ± 13‡	0.72

*p < 0.01 versus baseline. †p < 0.0005 versus baseline. ‡p < 0.05 versus baseline.
CRT = cardiac resynchronization therapy; EDV = end-diastolic volume; EF = ejection fraction; ESV = end-systolic volume; NYHA = New York Heart Association.

heart transplantation (2 weeks, 2 years, and 6 months after pacemaker implantation).

In 16 healthy control subjects, peak septal and lateral systolic velocity amplitudes were 5.2 ± 0.9 cm/s and 5.9 ± 1.7 cm/s (p = 0.027), mean septal-to-lateral peak velocity time difference was 4.5 ± 23.0 ms (p = 0.45), whereas the mean septal–lateral delay was 13.6 ± 18.6 ms (p = 0.51).

Longitudinal rotation pattern and amplitude of peak myocardial systolic velocity. Septal and lateral systolic velocity profiles for quartile 1 and quartile 4 patients are depicted in Figures 1A and 1B. Quartile 1 patients showed prominent clockwise LR (mean rotation of −6.8 ± 2.3°) and more often had a nonischemic etiology of heart failure (22 of 25 patients). In this quartile, peak systolic velocity was higher in septal than in lateral wall (3.2 ± 1 cm/s and 2.4 ± 0.9 cm/s, p = 0.01), the mean septal–lateral delay was 65 ± 37 ms and the mean septal-to-lateral peak velocity time difference was 56 ± 50 ms.

In contrast, quartile 4 patients showed modest counterclockwise LR (mean rotation of 2.3 ± 1.6°) with a nonischemic etiology present in the minority of subjects (7 of 27 patients, p < 0.0001 compared with quartile 1), and had a peak systolic velocity lower in septal than in lateral wall (1.9 ± 1.3 cm/s and 3.1 ± 1.3 cm/s, p = 0.001). The mean septal–lateral delay was 48 ± 40 ms, and the mean septal–lateral peak velocity time difference was 2 ± 63 ms. Additionally, 1-way ANOVA showed that the quartiles predicted septal and lateral velocity amplitude with respective p values of 0.0009 and 0.03 (Table 2).

The difference in amplitude of peak systolic velocity between septal and lateral walls was found to correlate strongly with the presence and the pattern of LR (r = −0.58, p < 0.0001) as shown in Figure 2.

Septal–lateral delay was not significantly correlated with LR (r = −0.19, p = 0.07), whereas the septal–lateral peak velocity time difference showed only a weak correlation (r = −0.29, p = 0.004).

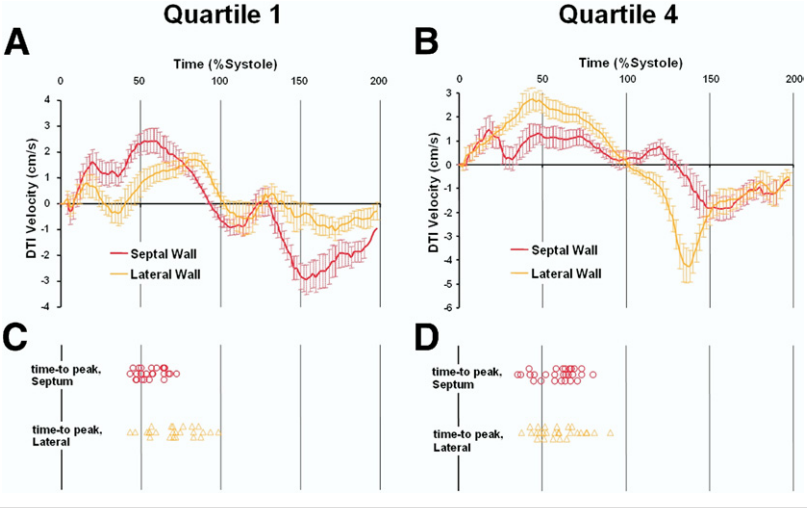

Figure 1. Direction of Longitudinal Rotation and the Shape of Doppler Myocardial Velocity Curves

(Top) Mean tissue Doppler myocardial velocity curves are depicted over 1 cardiac cycle for basal septal and lateral walls for all patients in quartile 1 of longitudinal rotation **(A)** and for all patients in quartile 4 **(B)**. **Bars** indicate standard errors. **(Bottom)** Plots of the distribution of individual time-to-peak velocity measures of septal and lateral walls, corrected for percentage of systole, for patients in quartile 1 **(C)** and quartile 4 **(D)**. DTI = Doppler tissue imaging.

Longitudinal rotation and the shape of systolic myocardial velocity profile. We further hypothesized that presence of LR alters the shape and skew of already depressed myocardial velocity curves, thus introducing error into interpretation of the timing of their peak values. To test this, we compared the timing of peak systolic velocities in quartiles 1 and 4 of LR. The time from R-wave onset to peak systolic velocity in quartile 1 was 216 ± 45 ms for septum and 272 ± 64 ms for lateral wall ($p < 0.0001$). Importantly, the dispersion of peak velocity values of the lateral wall was significantly larger than for the septum ($p = 0.005$) (Fig. 1C). The time to peak systolic velocity in quartile 4 was 228 ± 57 ms for septum and 230 ± 56 ms for lateral wall, with no difference in the timing ($p = 0.96$) or dispersion ($p = 0.62$) (Fig. 1D).

As expected, in healthy control subjects, time to peak systolic velocity in both septal and lateral walls was shorter than in corresponding walls of quartiles 1 and 4 (146 ± 30 ms for the septal and 150 ± 23 ms for the lateral wall, $p < 0.0001$ for all comparisons). Furthermore, dispersion measures for the septal wall were greater in quartile 4 when compared with healthy control subjects ($p = 0.03$), whereas dispersion of timing for the lateral wall was greater in both quartiles 1 and 4 when compared with the control group ($p < 0.004$ for both).

An additional observation noted during velocity curve analysis is the frequent appearance of 2 or more peaks during the ejection interval, often of similar magnitude (Fig. 3). This phenomenon was observed most frequently in curves with more severe depression of peak amplitude. A modest inverse correlation could be shown between the peak amplitude of septal wall and the presence of numerous systolic peaks ($r = -0.37$, $p < 0.01$), but no consistent relationship was observed for the lateral wall ($r = -0.18$, $p = 0.26$). Interpretation of a single peak timing event was significantly more subjective in this setting, and analysis of multiple cardiac cycles across at least 2 different clipped images was required to achieve a consensus for measurement.

Predictive value for CRT response. LV ESV decreased by 24 ± 29% in quartile 1 ($n = 16$, $p < 0.001$ vs. baseline), and by 13 ± 25% in quartile 4 ($n = 19$, $p < 0.02$ vs. baseline). There was no difference in time to echocardiography follow-up between ischemic and nonischemic patients ($p = 0.76$). An inverse correlation emerged for the difference in amplitude of peak systolic velocity between septal and lateral walls with subsequent percentage reduction in LV ESV at follow-up in the nonischemic subgroup ($r = -0.45$, $p = 0.004$) as shown in Figure 4A, but was not present for ischemic cardiomyopathy ($r = -0.19$, $p = 0.24$), however, with only a trend toward difference between r values ($p = 0.20$). By bootstrapping, the median value for the coefficient of correlation between the septal–lateral velocity difference and the LV end-systolic volume decrease in nonischemic cardiomyopathy patients was −0.47 (95% confidence interval [CI]: −0.216 to −0.67), whereas it was −0.15 (95% CI: −0.477 to 0.216) in ischemic cardiomyopathy, indicating that standard estimates of correlation coefficient were stable.

Neither septal–lateral delay nor the septal–lateral peak velocity time difference were predictive of quantitative reduction in LV ESV at follow-up in either subgroup of etiology ($p = NS$ for both) (Figs. 4B and 4C).

Table 2. Septal and Lateral Velocities According to Quartiles of Longitudinal Rotation

	Quartile			
	1	2	3	4
Septal velocity (cm/s)	3.3 ± 1.1	2.5 ± 1.2	2.0 ± 0.9*	1.9 ± 1.3*
Lateral velocity (cm/s)	2.4 ± 0.9	2.6 ± 1.2	2.6 ± 0.8	3.1 ± 1.3*
Velocity diff (cm/s)	0.9 ± 1.4	−0.2 ± 1.1*	−0.6 ± 1*	−1.2 ± 1.3*†

*$p < 0.01$ versus quartile 1. †$p < 0.05$ versus quartile 2.
Velocity diff = difference of peak systolic velocity amplitude between basal septal and lateral walls.

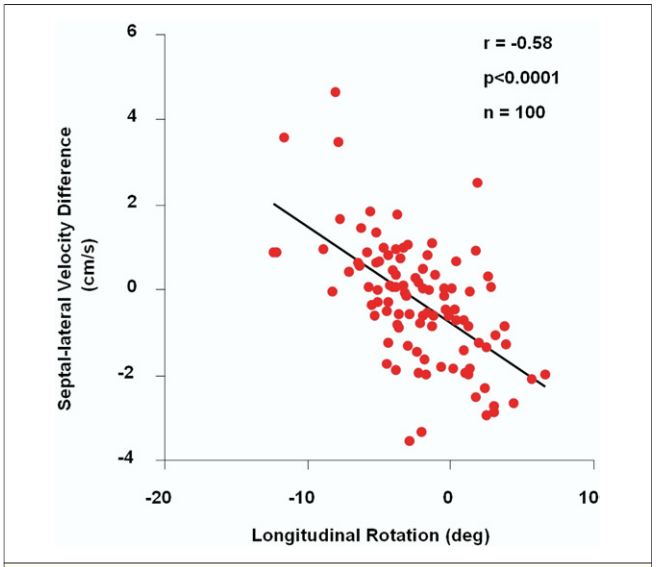

Figure 2. Relationship Between Longitudinal Rotation and a Septal–Lateral Difference in Amplitudes of Peak Systolic Velocity

A correlation between longitudinal rotation (x axis) and a difference in amplitudes of peak systolic velocity recorded at the base of septal and lateral walls (septal–lateral velocity difference; y axis). Data were obtained from 100 patients who were cardiac resynchronization therapy candidates. A moderately strong (−0.58) but highly significant ($p < 0.0001$) inverse correlation was observed.

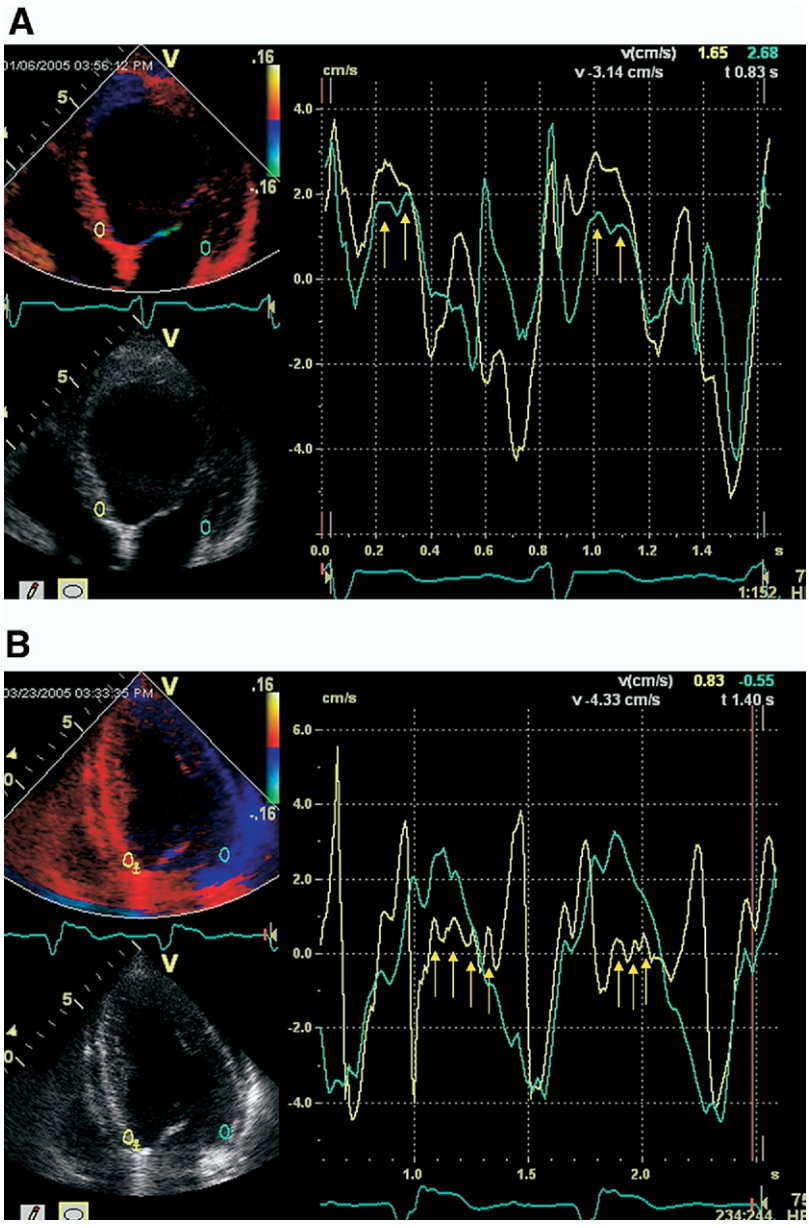

Figure 3. Longitudinal Rotation and Its Impact on Myocardial Velocity Profiles

(A) Myocardial velocity traces of a patient with clockwise longitudinal rotation belonging to quartile 1. Lateral wall velocities **(green)** have lower amplitudes than septal velocities **(yellow)**, and show 2 distinct systolic peaks of alternating amplitudes **(arrows)**. **(B)** In contrast, myocardial velocity traces from a patient with counterclockwise longitudinal rotation belonging to quartile 4 show relatively depressed septal wall velocities with 3 distinct systolic peaks **(arrows)**. In these settings, subjective interpretation is often required to select a single peak systolic velocity for timing event. Please see the accompanying Online Video.

DISCUSSION

A major finding of this study is that longitudinal cardiac rotation alters the profile and amplitude of basal septal and lateral systolic myocardial velocities. Moreover, the difference in amplitude between peak septal and lateral systolic velocities at baseline, which is correlated with LR, predicts the magnitude of reduction in LV end-systolic volume at follow-up in the nonischemic subgroup, whereas time difference and septal–lateral delay do not.

Myocardial velocity curves in the CRT population. Healthy subjects show heterogeneity in the amplitude of peak systolic regional basal velocities, but

have highly synchronized timing (5). In contrast, patients with heart failure and bundle branch block timing synchrony is disturbed (6), although little is known of the effect of these conditions on the shape of the systolic velocity curve. Here we show that LR affects timing, amplitude, and shape of regional velocities, with blunting of the velocity of the wall in the direction of LR. Candidates for CRT who have pronounced clockwise or counterclockwise LR also have greater differences between basal regional velocities than normal subjects despite a lower average amplitude. The blunting of velocities results in a flattened shape of the curve, with multiple oscillation replacing the distinct peak of the normal systolic velocity profile.

There is a paucity of data regarding the effect of specific cardiac pathophysiology on myocardial velocity curves. However, we have previously shown that the pattern of LR (clockwise or counterclockwise) depends on the distribution of longitudinal and radial strains. Thus, it seems that a specific pattern of nonuniform strain distribution determines LR pattern, which in turn impacts the shape of myocardial velocity profiles. The possibility of RV systolic interaction impacting the timing of multiple peaks in the systolic velocity profile of the LV free wall in the heart failure state has also been raised (7).

Clinical implication for current prediction models of CRT. Two factors make our findings clinically relevant. First, LR is not a rare phenomenon and seems frequent in patients who are good CRT candidates. Secondly, the findings from 2 recent prospective, randomized trials (8,9) that assessed septal–lateral myocardial velocity delay by tissue Doppler imaging as a tool in selecting potential candidates for CRT were largely underwhelming. Although the PROSPECT (Predictors of Response to CRT) trial was a head-to-head comparison of several different dyssynchrony parameters (including septal–lateral opposing wall delay) to predict CRT response in a standard population of heart failure patients with QRS duration >130 ms, the RethinQ (Cardiac Resynchronization Therapy in Patients with Heart Failure and Narrow QRS) study assessed response to CRT in patients with a QRS duration <130 ms and mechanical dyssynchrony (defined by either septal–lateral delay or anteroseptal–posterior opposing wall delay of >65 ms). The studies were concordant in their findings that septal–lateral delay had marginal predictive power in the populations tested. In light of our findings, these results might have been anticipated as the LR influences on myocardial velocity profiles rendering them difficult to interpret by time-to-peak measures alone. This can

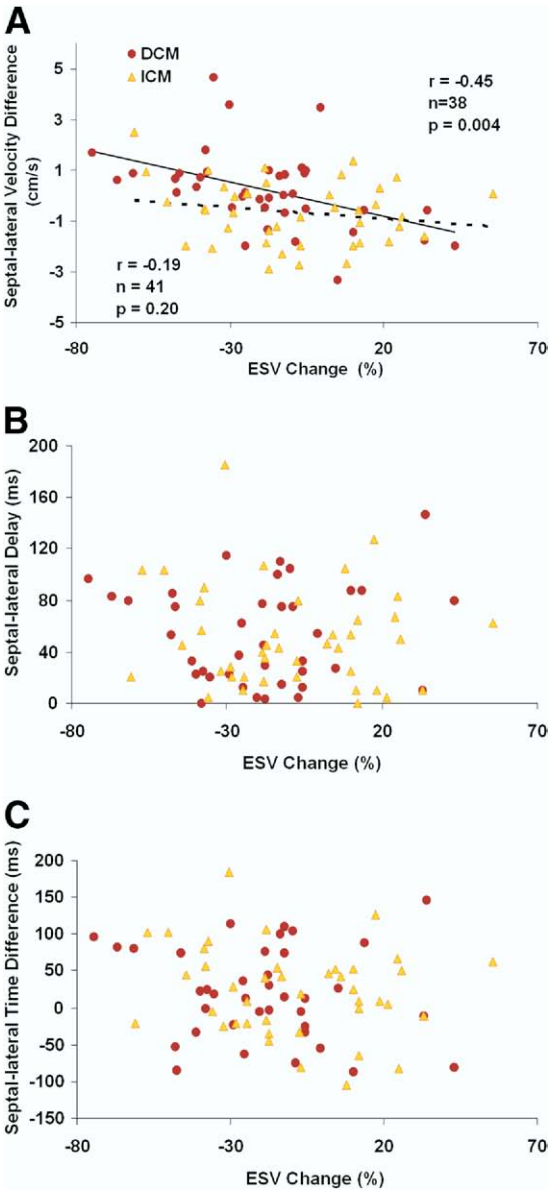

Figure 4. Predictors of Relative End-Systolic Volume Change During Cardiac Resynchronization Therapy

(A) Relationship between the difference in peak systolic velocity amplitude between basal septal and lateral walls at baseline and subsequent reduction in left ventricular end-systolic volume at follow-up for the nonischemic **(red circles)** and ischemic **(yellow triangles)** subgroup. Whereas nonischemic subjects show a significant correlation with end-systolic volume reduction, ischemic subjects do not. **(B)** Relationship between septal–lateral delay at baseline and **(C)** septal–lateral time difference in peak systolic velocity at baseline, and subsequent reduction in left ventricular end-systolic volume at follow-up for the nonischemic **(red circles)** and ischemic **(yellow triangles)** subgroup. Neither measure in ischemic or nonischemic subjects shows a correlation with reduction in end-systolic volume. DCM = nonischemic cardiomyopathy; ESV = end-systolic volume; ICM = ischemic cardiomyopathy.

probably be generalized to other time-to-peak (2,10) or time-to-onset velocity measures of dyssynchrony (6), because they are based on similar fundamental concepts. Although recent results of the PROSPECT and the RethinQ trials will lead to a greater scrutiny of any new dyssynchrony measure, we believe that septal–lateral basal velocity difference can be used in conjunction with other relevant clinical and dyssynchrony parameters to predict CRT outcome (11,12).

Study limitations. The current study was retrospective, which has impacted follow-up rates and variability in follow-up time. Furthermore, our finding that the difference in amplitude of septal and lateral velocities correlated with reverse remodeling only in dilated cardiomyopathy patients may be attributable to nonphysiological factors, such as a relatively more rare occurrence of positive septal–lateral velocity difference in ischemic subjects. Also, it might be argued that the predictive capacity of the septal–lateral peak velocity amplitude difference as an echocardiographic measure for quantitative response to CRT in the nonischemic population is modest. Our definition of ischemic heart disease may be imperfect, because coronary artery stenosis of >50% may occur also in patients with nonischemic etiology of dilated cardiomyopathy. The number of patients was too small to accurately define specific cutoff points that would separate responders from nonresponders. Additionally, our method seems inefficient in patients with ischemic cardiomyopathy, who often do not show reverse remodeling during CRT. Finally, no adjustment was made for comparisons of multiple variables.

CONCLUSIONS

Significant alterations in the profile and amplitude of myocardial systolic velocity curves are observed in association with different patterns of LR. The difference in peak amplitude of basal septal and lateral systolic velocities is predictive of LR, and in the nonischemic subgroup it correlated with quantitative left ventricular reverse remodeling at follow-up. Time-to-peak velocity-based measures were not predictive of CRT response.

Acknowledgement

The authors thank Dr. Deborah Kwon for her thoughtful comments on the manuscript.

Reprint requests and correspondence: Dr. Richard A. Grimm, Heart and Vascular Institute, Cleveland Clinic, 9500 Euclid Avenue, Cleveland, Ohio 44195. *E-mail: grimmr@ccf.org.*

REFERENCES

1. Popovic ZB, Grimm RA, Ahmad A, et al. Longitudinal rotation: an unrecognised motion pattern in patients with dilated cardiomyopathy. Heart 2008;94:e11.
2. Yu CM, Chau E, Sanderson JE, et al. Tissue Doppler echocardiographic evidence of reverse remodeling and improved synchronicity by simultaneously delaying regional contraction after biventricular pacing therapy in heart failure. Circulation 2002;105:438–45.
3. Bax JJ, Molhoek SG, van Erven L, et al. Usefulness of myocardial tissue Doppler echocardiography to evaluate left ventricular dyssynchrony before and after biventricular pacing in patients with idiopathic dilated cardiomyopathy. Am J Cardiol 2003;91:94–7.
4. Notomi Y, Popovic ZB, Yamada H, et al. Ventricular untwisting: a temporal link between left ventricular relaxation and suction. Am J Physiol Heart Circ Physiol 2008;294:H505–13.
5. Yu CM, Lin H, Ho PC, Yang H. Assessment of left and right ventricular systolic and diastolic synchronicity in normal subjects by tissue Doppler echocardiography and the effects of age and heart rate. Echocardiography 2003;20:19–27.
6. Bader H, Garrigue S, Lafitte S, et al. Intra-left ventricular electromechanical asynchrony. A new independent predictor of severe cardiac events in heart failure patients. J Am Coll Cardiol 2004;43:248–56.
7. Marciniak M, Bijnens B, Baltabaeva A, et al. Inter-ventricular interaction as a possible mechanism for the presence of a bi-phasic systolic velocity profile in normal left ventricular free walls. Heart 2008;94:1058–64.
8. Beshai JF, Grimm RA, Nagueh SF, et al. Cardiac-resynchronization therapy in heart failure with narrow QRS complexes. N Engl J Med 2007;357:2461–71.
9. Chung ES, Leon AR, Tavazzi L, et al. Results of the Predictors of Response to CRT (PROSPECT) trial. Circulation 2008;117:2608–16.
10. Bax JJ, Bleeker GB, Marwick TH, et al. Left ventricular dyssynchrony predicts response and prognosis after cardiac resynchronization therapy. J Am Coll Cardiol 2004;44:1834–40.
11. Bleeker GB, Kaandorp TA, Lamb HJ, et al. Effect of posterolateral scar tissue on clinical and echocardiographic improvement after cardiac resynchronization therapy. Circulation 2006;113:969–76.
12. Lim P, Buakhamsri A, Popovic ZB, et al. Longitudinal strain delay index by speckle tracking imaging. A new marker of response to cardiac resynchronization therapy. Circulation 2008;118:1130–7.

Key Words: biventricular pacing ■ dyssynchrony ■ echocardiography ■ myocardial tissue velocities ■ ventricular function.

APPENDIX

For an accompanying video and legend, please see the online version of this article.