JACC: CARDIOVASCULAR IMAGING
VOL. 3, NO. 2, 2010

ISSN 1936-878X/10/$36.00
PUBLISHED BY ELSEVIER INC.
DOI:10.1016/j.jcmg.2009.09.020

Usefulness of Echocardiographic Dyssynchrony in Patients With Borderline QRS Duration to Assist With Selection for Cardiac Resynchronization Therapy

Olusegun Oyenuga, MD, Hideyuki Hara, MD, Hidekazu Tanaka, MD, Han-Na Kim, MD, Evan C. Adelstein, MD, Samir Saba, MD, John Gorcsan III, MD
Pittsburgh, Pennsylvania

OBJECTIVES To test the hypothesis that echocardiographic dyssynchrony may assist in the selection of patients with borderline QRS duration for cardiac resynchronization therapy (CRT).

BACKGROUND Although echocardiographic dyssynchrony is currently not recommended to select patients with QRS duration widening for CRT, its utility in patients with borderline QRS widening is unclear.

METHODS Of 221 consecutive heart failure patients with an ejection fraction (EF) ≤35% referred for CRT, 86 had a borderline QRS duration of 100 to 130 ms (115 ± 8 ms) and 135 patients had wide QRS >130 ms (168 ± 26 ms). Dyssynchrony was assessed using interventricular mechanical delay, tissue Doppler imaging longitudinal velocity opposing wall delay, and speckle tracking radial strain for septal to posterior wall delay. Response to CRT was defined as ≥15% increase in EF, and reverse remodeling as ≥10% decrease in end-systolic volume.

RESULTS There were 201 patients with baseline quantitative echocardiographic data available, and 187 with follow-up data available 8 ± 5 months after CRT. A smaller proportion of borderline QRS duration patients (53%) were EF responders compared with 75% with widened QRS ($p < 0.05$). Interventricular mechanical delay ≥40 ms and opposing wall delay ≥65 ms were predictive of EF response in the wide QRS duration group, but not the borderline QRS duration group. Speckle tracking radial dyssynchrony ≥130 ms, however, was predictive of EF response in both wide QRS interval patients (88% sensitivity, 74% specificity) and borderline QRS interval patients (79% sensitivity, 82% specificity) and associated reverse remodeling with reduction in end-systolic volume ($p < 0.0005$).

CONCLUSIONS Radial dyssynchrony by speckle tracking strain was associated with EF and reverse remodeling response to CRT in patients with borderline QRS duration and has the potential to assist with patient selection. (J Am Coll Cardiol Img 2010;3:132–40) © 2010 by the American College of Cardiology Foundation

From The University of Pittsburgh, Pittsburgh, Pennsylvania. Dr. Gorcsan was supported in part by NIH award K24 HL04503-01 and receives research support in the form of donated equipment from the GE Corporation, and research grant support from Medtronic, St. Jude Medical, and Biotronik.

Manuscript received July 21, 2009; revised manuscript received September 3, 2009, accepted September 16, 2009.

Current clinical guidelines support cardiac resynchronization therapy (CRT) for symptomatic heart failure patients with a depressed ejection fraction (EF) and electrocardiographic widened QRS duration ≥120 ms (1). Although imaging measures of mechanical dyssynchrony have shown promise to improve patient response rate to CRT, they have not yet replaced widened QRS duration as a surrogate for mechanical dyssynchrony in current practice guidelines (2–8). Furthermore, the existing studies using dyssynchrony for selection of patients for CRT with narrow QRS interval have been inconclusive (9–11). Although this field continues to evolve, scenarios currently exist in clinical practice in which a patient may be considered a borderline candidate for CRT, and imaging markers of mechanical dyssynchrony may assist in patient selection. A recent consensus report by the American Society of Echocardiography and the Heart Rhythm Society advocated echocardiographic dyssynchrony as a possible adjunct to the selection criteria for CRT in patients with borderline QRS duration (12). Because data are limited in this specific patient group, our objective was to test the hypothesis that echocardiographic measures of mechanical dyssynchrony may assist in the selection of patients for CRT with borderline QRS duration.

See page 141

METHODS

The study included 221 consecutive patients in sinus rhythm with left ventricular (LV) ejection fraction (EF) ≤35% and New York Heart Association functional class III or IV heart failure despite optimal pharmacological therapy referred for CRT. The protocol was approved by the Institutional Review Board on Biomedical Research, and all patients gave informed consent consistent with protocol. Patients with borderline QRS duration were prospectively defined as those with QRS interval width between 100 ms and 130 ms inclusive. The borderline group consisted of 86 patients. The mean age was 60 ± 11 years, 24 (28%) patients were female, the mean EF was 24 ± 5%, the mean QRS duration was 115 ± 8 ms, and 55% had ischemic cardiomyopathy. The remaining 135 CRT patients with widened QRS duration >130 ms had similar demographic data: mean age 64 ± 12 years, 43 female (32%), mean EF 24 ± 6%, 58% ischemic cardiomyopathy, but greater mean QRS duration of 168 ± 26 ms, by definition. A biventricular pacing system was implanted with a standard right ventricular apical lead and left ventricular lead positioned in a posterior or lateral epicardial vein through the coronary sinus. All patients were receiving optimal pharmacological therapy, including angiotensin-converting enzyme inhibitors, β-blockers, and spironolactone, if tolerated.

All echocardiographic studies and off-line analyses were performed using standard imaging systems (VIVID 7; GE-Vingmed, Horton, Norway, or Siemens Medical Solutions, Mountain View, California). Briefly, routine digital gray-scale 2-dimensional and tissue Doppler imaging cine loops were obtained, including mid-LV short axis views at the level of the papillary muscle, routine apical views, and pulsed Doppler interrogation of the right ventricular and LV outflow tract as well as mitral inflow. EF was calculated by biplane Simpson's rule (13). Routine pulsed Doppler was used as previously described (7,12). Left ventricular pre-ejection delay (PED) was determined as the interval from the onset of the electrocardiographic QRS complex to the onset of LV ejection velocity in the outflow tract (Fig. 1). Interventricular mechanical delay (IVMD) was determined as the time difference in onset of right ventricular ejection velocity to PED. The filling time ratio (FT/RR) was calculated from the mitral inflow velocity duration from the onset of E wave to the end of A wave divided by the R-R interval and expressed as a percentage. Pre-defined cutoff values considered consistent with significant dyssynchrony were ≥140 ms for PED, ≥40 ms for IVMD, and ≤40% for FT/RR (12,14).

ABBREVIATIONS AND ACRONYMS

CRT = cardiac resynchronization therapy
EF = ejection fraction
FT/RR = filling time ratio
IVMD = interventricular mechanical delay
LV = left ventricular
PED = pre-ejection delay

Intraventricular dyssynchrony was determined using tissue Doppler imaging and/or speckle tracking as previously described in detail (6,12,15,16). For tissue Doppler imaging, regions of interest (7 × 15 mm) were placed in the basal and midventricular segments for each of the 3 standard views for 12-site time to peak velocity analysis. Manual adjustments were made so that the regions of interest had the most reproducible peak velocities (Fig. 2). Segmental time to peak systolic wave velocity was calculated from the onset of the QRS complex. For longitudinal speckle tracking by velocity vector imaging, endocardial to mid-wall tracing of routine digital cineloops was performed. Velocity was determined toward a point of reference placed at the LV apex for generation of time-velocity curves from all 3 apical views. Longitudinal dyssynchrony was defined as the maximal

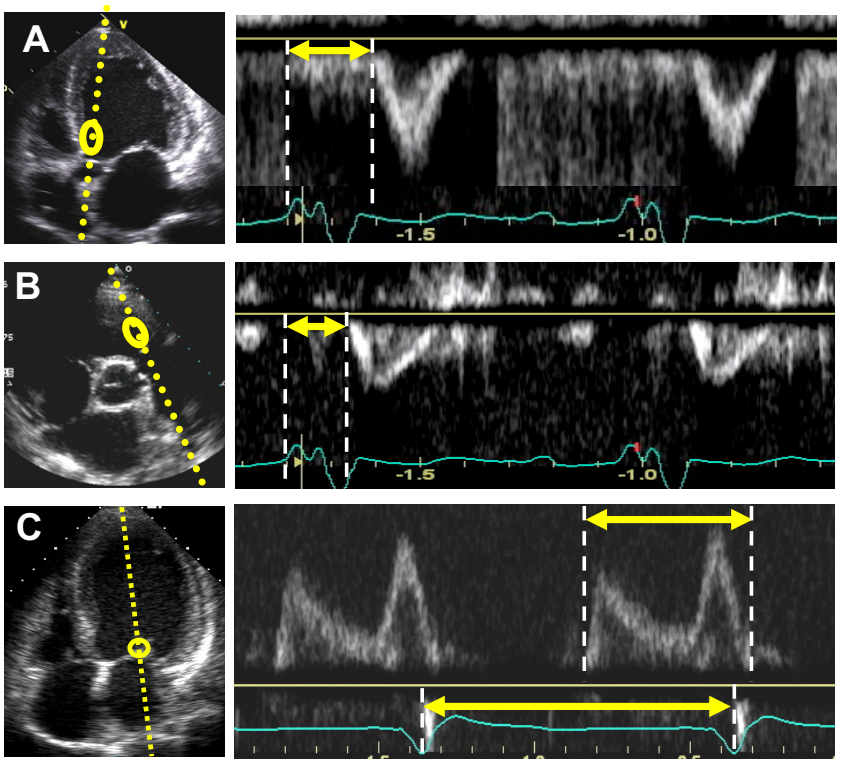

Figure 1. Dyssynchrony by Pulsed Doppler

(A) Pulsed Doppler sample volume in the left ventricular outflow tract with pre-ejection delay as time from onset of QRS complex to onset of flow **(arrow)**. **(B)** Pulsed Doppler sample volume in the right ventricular outflow track with time from onset of QRS complex to onset of flow **(arrow)**. Interventricular mechanical delay was the difference in this time from pre-ejection delay shown in panel **A**. **(C)** Pulsed Doppler sample volume in mitral inflow. Filling time **(top arrow)** was divided by R-R interval **(bottom arrow)**.

difference in peak velocity at basal and mid segments in opposing walls per view. Significant longitudinal dyssynchrony was defined as the maximal time difference between opposing walls in one view ≥65 ms, or the 12-site time to peak SD (Yu Index) of ≥33 ms. For uniformity, the same cutoffs were used for either software approach (3,4).

Speckle tracking of routine grayscale mid-LV short-axis images was also performed as previously described to assess radial dyssynchrony (6,16,17). Briefly, an end-diastolic circular region of interest was traced slightly within the endocardial cavity, using a point-and-click approach with special care taken to adjust tracking of all endocardial segments. A second larger concentric circle was then automatically generated and manually adjusted near the epicardium. Time to peak segmental radial strain was determined from the highest peak positive strain value throughout the cardiac cycle, beginning slightly before the onset of the QRS complex to include very early mechanical activation (17) (Fig. 3). Radial dyssynchrony was then determined by measuring the time difference between the anteroseptal and posterior wall with ≥130 ms pre-defined as significant (6,16).

Group data were presented as means ± SD and were compared using the Student *t* test for paired and unpaired data. Proportional differences were evaluated using the Fisher exact test, and the chi-square test was used for noncontinuous variables. Receiver-operator characteristic (ROC) curves were constructed for dyssynchrony variables to determine the sensitivity, specificity, and areas under the curves at pre-defined cutoffs. Least-squares linear regression analysis was used to determine potential associations between IVMD with longitudinal and radial opposing wall delays. Response to CRT was prospectively defined as a relative increase in EF of ≥15% from baseline to 6-month follow-up, and reverse remodeling was defined as a decrease in end-systolic volume ≥10%, as used in previous studies (6,15,16). All follow-up EF and volume data were acquired by investigators who were blind to baseline data.

Table 1. Prevalence of Dyssynchrony in Borderline QRS Duration and Wide QRS Duration Patients

Dyssynchrony Index	Cutoff	Wide QRS Duration (n = 123)	Borderline QRS Duration (n =78)	Significance
Pre-ejection delay	≥140 ms	73/106 (69%)	16/70 (23%)	<0.0001
IVMD	≥40 ms	53/98 (54%)	11/61 (18%)	<0.001
FT/RR	≤40%	29/90 (32%)	7/60 (12%)	<0.005
Longitudinal opposing wall delay	≥65 ms	78/110 (70%)	38/67 (58%)	NS
Yu Index	≥33 ms	76/118 (64%)	35/67 (52%)	NS
Radial septal to posterior wall delay	≥130 ms	80/104 (71%)	36/76 (47%)	<0.05

IVMD = interventricular mechanical delay; FT/RR = filling time ratio; NS = not significant.

RESULTS

Of the 221 consecutive patients referred for CRT, 20 (9%) had poor echocardiographic windows with technically inadequate images and were prospectively excluded from all subsequent analyses. Accordingly, the study group consisted of 201 patients: 78 patients with borderline QRS duration between 100 and 130 ms and 123 patients with wide QRS duration >130 ms. All baseline demographic data were similar between groups, except for QRS duration by definition. Follow-up echocardiographic data were available on 187 of these patients 8 ± 5 months after CRT; 72 in the borderline QRS duration group and 115 in the wide QRS duration group.

With the exception of longitudinal opposing wall delay by tissue Doppler imaging, there was significantly less prevalent dyssynchrony using pre-defined cutoff values in the borderline QRS duration patients compared with the wide QRS duration patients (Table 1). PED, IVMD, and FF/RR occurred infrequently in the borderline QRS duration patients. In the borderline QRS duration group, IVMD was weakly associated with longitudinal velocity opposing wall delay ($r = 0.25$, $p < 0.01$), but more closely associated with radial strain dyssynchrony ($r = 0.56$, $p < 0.0001$). Among the 187 patients with follow-up LV volume and EF data, a significantly smaller proportion of patients in the borderline QRS duration group were CRT responders (38 [53%] compared with 86 [75%] patients). The association of dyssynchrony indices with EF response is shown in Table 2, and the individual ROC curves are shown in Fig. 4. Among the pulsed Doppler dyssynchrony markers, only IVMD seemed to be significantly predictive of EF response in the wide QRS duration group. Neither IVMD, PED, nor FT/RR was found to be predictive of EF response in the borderline QRS duration group. Although these pulsed Doppler indexes at the pre-determined cutoff values were found to have high specificities, their low sensitivities resulted in relatively modest area under the ROC curve values. Longitudinal dyssynchrony by either opposing wall delay or Yu Index was predictive of EF response in the wide QRS duration group, but not in the borderline QRS duration group.

The presence of radial dyssynchrony by speckle tracking was the most predictive of EF response in both wide QRS duration and borderline QRS duration patient groups (Fig. 5). Speckle tracking radial dyssynchrony ≥130 ms was predictive of EF response in the wide QRS duration patients (88%

Table 2. Association of Dyssynchrony Indexes With Ejection Fraction Response to Resynchronization Therapy in Wide QRS Duration and Borderline QRS Duration Patients

		Wide QRS Duration (n = 115)		Borderline QRS Duration (n = 72)	
Dyssynchrony Index	Cutoff	Sensitivity	Specificity	Sensitivity	Specificity
Pre-ejection delay	≥140 ms	76%	50%	31%	83%
IVMD	≥40 ms	66%	85%	23%	92%
FT/RR	≤40%	31%	67%	15%	96%
Longitudinal opposing wall delay	≥65 ms	78%	76%	64%	54%
Yu Index	≥33 ms	72%	64%	55%	57%
Radial septal to posterior wall delay	≥130 ms	88%	74%	79%	82%

Abbreviations as in Table 1.

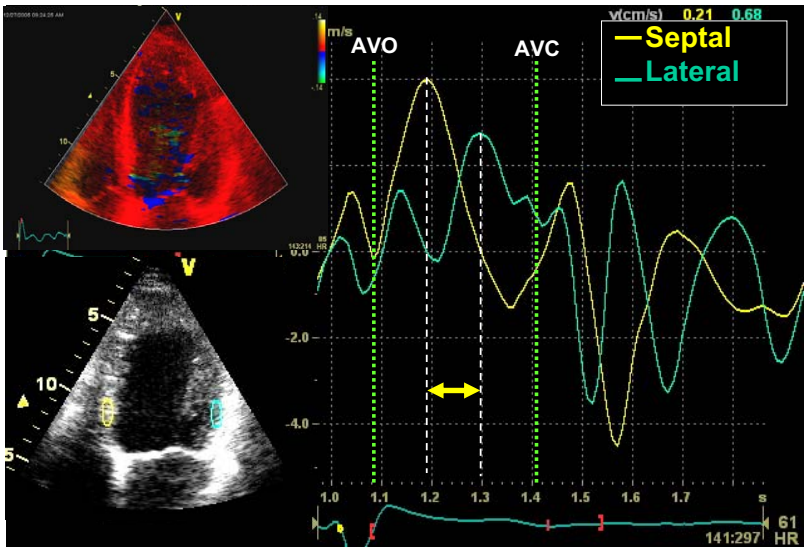

Figure 2. Tissue Doppler Velocity Opposing Wall Delay

Time-velocity plots from septum **(yellow line)** and lateral wall **(blue line)** using the apical 4-chamber view and demonstrating the opposing wall delay in peak velocities **(arrow)** during the ejection interval. AVC = aortic valve closure; AVO = aortic valve opening.

sensitivity, 74% specificity). Although less sensitive, radial dyssynchrony was a relatively specific predictor of EF response in the borderline QRS duration patients (79% sensitivity, 82% specificity). Radial dyssynchrony was also associated with significant reverse remodeling demonstrated by reductions in end-systolic volume from 155 ± 72 ml to 119 ± 71 ml in the wide QRS duration group and 155 ± 56 ml to 119 ± 57 ml in the borderline QRS duration group (both $p < 0.0005$). Borderline QRS duration patients who lacked radial dyssynchrony did not have a significant reverse remodeling response to CRT (Fig. 6).

Intraobserver variability for determining routine pulsed Doppler dyssynchrony measures was 3 ± 4% and interobserver variability was 4 ± 5%. Intraob-

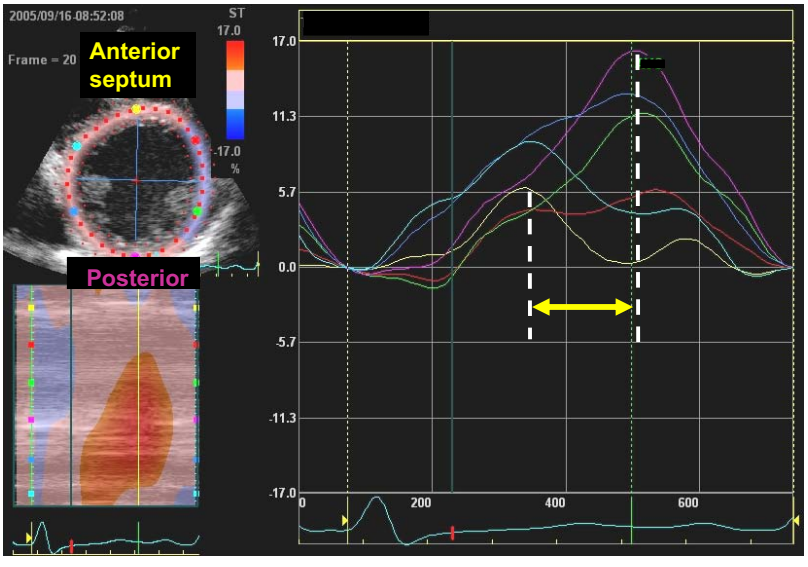

Figure 3. Speckle Tracking Radial Strain

Time strain plots from the mid-ventricular short-axis view demonstrating anteroseptal **(yellow line)** to posterior wall **(purple line)** delay in peak strain **(arrow)**.

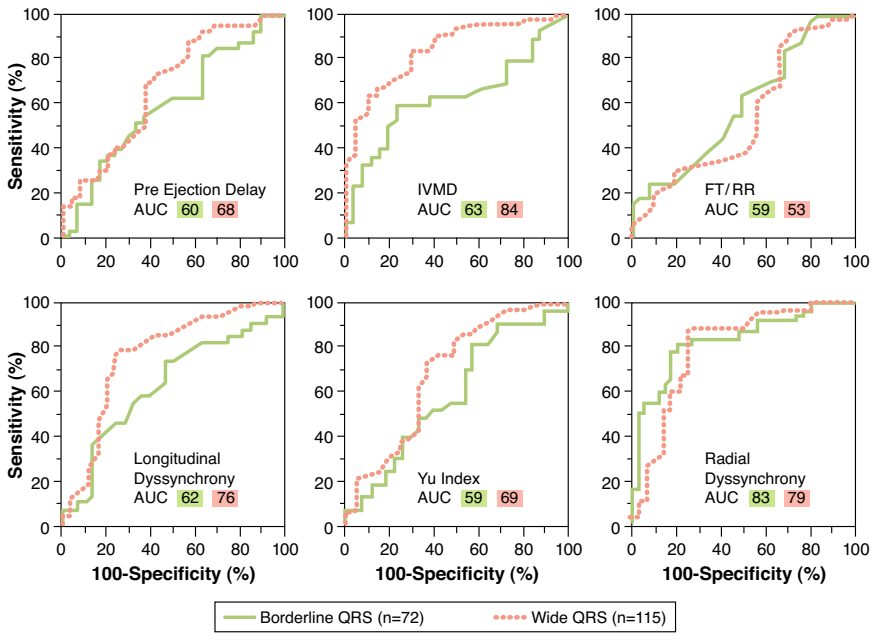

Figure 4. Receiver-Operator Characteristic Curves

Analysis of 6 dyssynchrony indexes and their association with ejection fraction response to cardiac resynchronization therapy in borderline QRS duration patients **(solid green lines)** and wide QRS duration patients **(dashed pink lines)**. Area under the curve (AUC) values appear in each plot. FT/RR = filling time ratio; IVMD = interventricular mechanical delay.

server variability for determining tissue Doppler imaging longitudinal dyssynchrony was 6 ± 7% and interobserver variability was 8 ± 7%. Intraobserver variability for determining speckle tracking strain data from the identical digital cineloops used for dyssynchrony was 8 ± 7% and interobserver variability was 9 ± 7%.

DISCUSSION

This study of a large series of consecutive patients referred for CRT demonstrates that differences in mechanical dyssynchrony and response to CRT in patients with borderline QRS duration of 100 to 130 ms compared with those with widened QRS

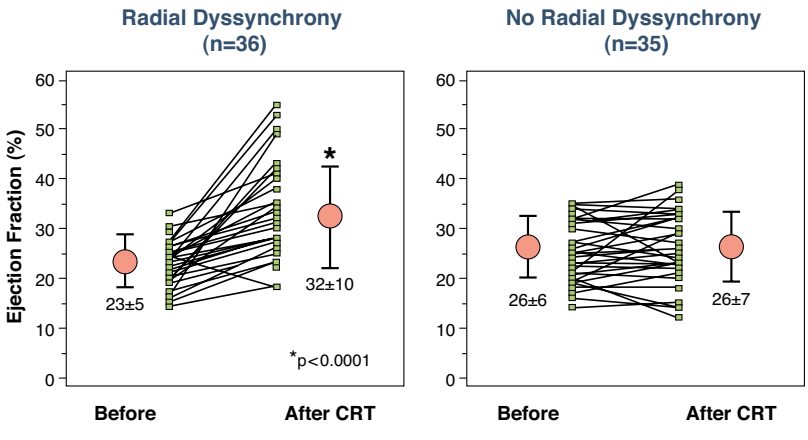

Figure 5. Ejection Fraction Response to Resynchronization Therapy

Line plots of ejection fraction values before and 8 ± 5 months after cardiac resynchronization therapy (CRT) in patients with borderline QRS duration with and without significant radial dyssynchrony.

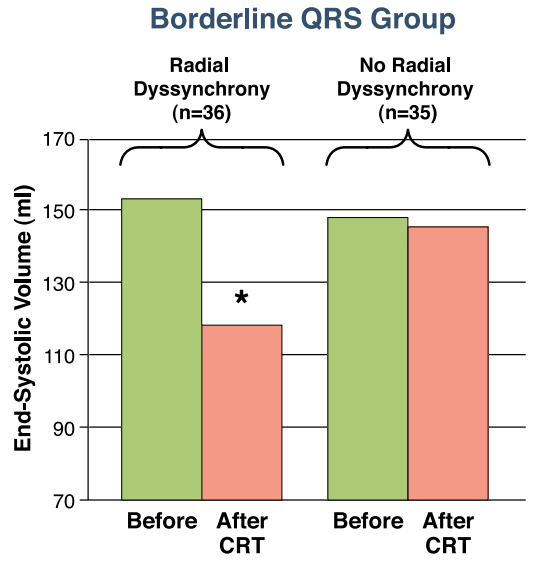

Figure 6. Reverse Remodeling Response to Resynchronization Therapy

*$p < 0.0001$. Bar graphs of mean end-systolic volume values before and 8 ± 5 months after cardiac resynchronization therapy (CRT) in patients with borderline QRS duration with and without significant radial dyssynchrony.

duration >130 ms. Specifically, the prevalence of dyssynchrony by PED, IVMD, FT/RR, or radial septal to posterior wall delay was less in the borderline QRS duration patients compared with the wide QRS duration patients and the overall EF response rate to CRT was less in the borderline QRS duration patients. The markers of IVMD and longitudinal dyssynchrony were comparatively more predictive of response in the wide QRS duration patients. However, radial strain dyssynchrony by speckle tracking echocardiography was associated with response to CRT in both borderline QRS and wide QRS duration patients, with significant improvements observed in EF and end-systolic volume. These observations have the potential to extend the use of echocardiographic dyssynchrony assessment, in particular by speckle tracking radial strain, to patients with borderline QRS duration who are being considered as potential candidates for CRT.

Several clinical trials have previously confirmed that the majority of patients with heart failure, reduced EF, and widened QRS duration benefit from CRT (18–22). However, it has been shown that approximately 25% to 30% of patients with wide QRS duration do not seem to benefit from CRT, and several echocardiography studies have associated lack of mechanical dyssynchrony with nonresponse to CRT (2–6,16,23). A recent multicenter study of the predictors of responders to CRT, known as the PROSPECT (Predictors of Response to Cardiac Resynchronization Therapy) study, failed to show conclusively that a single echocardiographic dyssynchrony measure can be highly predictive of response (8). Although problems with technical acquisition and variability interfered with precise interpretation of the results of the PROSPECT study, the conclusion was that routine clinical selection criteria for CRT, including QRS duration, have not yet been replaced (12,24,25). Because the benefits of CRT have been of great clinical significance, it is desirable to provide this therapy to individuals who may possibly benefit from CRT. Accordingly, clinicians have used dyssynchrony information to assist in patient selection for CRT in patients with borderline QRS duration for compassionate use, recognizing that the 120-ms cutoff may be somewhat arbitrary. A potential mechanistic explanation for why radial dyssynchrony was more predictive of response than longitudinal dyssynchrony in the borderline QRS duration patients is that the radial pattern of dyssynchrony is more pronounced than in the longitudinal dimension, as shown by Helm et al. (26) in an elegant tagged cine magnetic resonance study. They observed that circumferential strain in the short-axis plane was much more sensitive to detect dyssynchrony than longitudinal strain. Because the degree of dyssynchrony may be more subtle in patients with narrow QRS duration, it is possible that radial dyssynchrony was more predictive than longitudinal dyssynchrony, although the precise reason was uncertain.

Only 1 randomized CRT trial, known as RethinQ (Resynchronization Therapy in Patients with Narrow QRS), was performed to date in heart failure patients with narrow QRS duration <130 ms and dyssynchrony, primarily measured by tissue Doppler imaging (9). This study failed to reach statistical significance for the primary end point of peak myocardial oxygen consumption; however, CRT seemed to benefit patients in terms of New York Heart Association functional class and 6-min walk distance in the nonischemic subgroup. The authors concluded that CRT did not benefit patients with narrow QRS duration; however, the subgroup of patients with borderline QRS duration of 120 to 130 ms showed significant benefit with CRT in the primary end point. Accordingly, the interaction of QRS duration, the presence of me-

chanical dyssynchrony, and the response to CRT is not entirely clear in patients with borderline QRS duration. The results of this study are in agreement with RethinQ results in that the response to CRT seems to be less prevalent in patients with narrower QRS duration compared with clearly widened QRS duration and adds the marker of radial dyssynchrony as a potential predictor of response to CRT in the borderline QRS duration patients.

Study limitations. An important limitation of this study is that the decision for CRT implantation was made by clinicians caring for these patients, and this was not a randomized clinical trial. Accordingly, the echocardiographic dyssynchrony results may have influenced the decision for CRT implantation in the borderline QRS duration patients. However, because we studied several measures of interventricular and intraventricular dyssynchrony as part of our baseline assessment, it is unlikely that an individual measure would selectively influence the decision for implantation. The true value of echocardiographic measures of dyssynchrony in assisting patient selection for CRT among patients who are viewed as borderline candidates because of borderline QRS duration must be tested further in a clinical trial in a larger series. Another limitation of this study is that change in EF and end-systolic volumes were used to define response to CRT and clinical outcome measures such as 6-min walk distance and quality-of-life questionnaires were not systematically performed as part of this study. Measures of reverse LV remodeling have been shown to be objective measures of response to CRT and associated with patient survival, so these measures seem to be clinically relevant (16,27). There are several possible technical limitations with variability in both tissue Doppler imaging and speckle tracking analysis (8,16). These data were derived from a single laboratory with a small group of investigators who perform off-line analysis with a very similar approach. A possible limitation is that the dyssynchrony analysis was performed using software from 2 different vendors; however, we recently demonstrated that they produce similar results (17). Another important limitation is that factors other than dyssynchrony affect LV functional and reverse remodeling response, including contractile reserve, arrhythmias, scar burden, and lead location in relation to scar and area with latest activation (28–32). An analysis of all these factors in comparison with radial dyssynchrony in these patients was beyond the scope of the present investigation, but is warranted for future studies. Technological advances in echocardiography hardware and software continue, but training and experience continue to be important to achieve reproducible results.

CONCLUSIONS

This study demonstrated that echocardiographic dyssynchrony was less prevalent in patients with borderline QRS duration as compared with those with wide QRS duration using routine pulsed Doppler measures or speckle tracking radial septal-to-posterior wall delay. Although IVMD and longitudinal dyssynchrony were comparatively more predictive of CRT response in patients with wide QRS duration, radial dyssynchrony by speckle tracking was associated with CRT response in both borderline QRS and wide QRS duration patients. These observations have the potential to extend the use of echocardiographic dyssynchrony assessment, in particular by speckle tracking radial strain, to patients with borderline QRS duration to assist with selection for CRT.

Acknowledgments

The authors are grateful to the entire University of Pittsburgh Medical Center, Presbyterian University Hospital electrophysiology laboratory, and echocardiography laboratory staff for facilitating this study.

Reprint requests and correspondence: Dr. John Gorcsan III, University of Pittsburgh, Scaife 564, 200 Lothrop Street, Pittsburgh, Pennsylvania 15213-2582. *E-mail: gorcsanj@upmc.edu.*

REFERENCES

1. Hunt SA, Abraham WT, Chin MH, et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). J Am Coll Cardiol 2005;46:e1–82.
2. Bax JJ, Abraham T, Barold SS, et al. Cardiac resynchronization therapy: part 1—issues before device implantation. J Am Coll Cardiol 2005;46:2153–67.
3. 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.
4. Gorcsan J 3rd, Kanzaki H, Bazaz R, Dohi K, Schwartzman D. Usefulness of echocardiographic tissue synchronization imaging to predict acute response to cardiac resynchronization therapy. Am J Cardiol 2004;93:1178–81.

JACC: CARDIOVASCULAR IMAGING, VOL. 3, NO. 2, 2010
FEBRUARY 2010:132–40

5. Sogaard P, Egeblad H, Kim WY, et al. Tissue Doppler imaging predicts improved systolic performance and reversed left ventricular remodeling during long-term cardiac resynchronization therapy. J Am Coll Cardiol 2002;40: 723–30.
6. Suffoletto MS, Dohi K, Cannesson M, Saba S, Gorcsan J 3rd. Novel speckle-tracking radial strain from routine black-and-white echocardiographic images to quantify dyssynchrony and predict response to cardiac resynchronization therapy. Circulation 2006;113:960–8.
7. Yu CM, Fung WH, Lin H, Zhang Q, Sanderson JE, Lau CP. Predictors of left ventricular reverse remodeling after cardiac resynchronization therapy for heart failure secondary to idiopathic dilated or ischemic cardiomyopathy. Am J Cardiol 2003;91:684–8.
8. Chung ES, Leon AR, Tavazzi L, et al. Results of the Predictors of Response to CRT (PROSPECT) trial. Circulation 2008;117:2608–16.
9. 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.
10. Bleeker GB, Holman ER, Steendijk P, et al. Cardiac resynchronization therapy in patients with a narrow QRS complex. J Am Coll Cardiol 2006;48:2243–50.
11. Yu CM, Chan YS, Zhang Q, et al. Benefits of cardiac resynchronization therapy for heart failure patients with narrow QRS complexes and coexisting systolic asynchrony by echocardiography. J Am Coll Cardiol 2006;48: 2251–7.
12. Gorcsan J 3rd, Abraham T, Agler DA, et al. Echocardiography for cardiac resynchronization therapy: recommendations for performance and reporting—a report from the American Society of Echocardiography Dyssynchrony Writing Group endorsed by the Heart Rhythm Society. J Am Soc Echocardiogr 2008;21:191–213.
13. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18:1440–63.
14. Yu CM, Abraham WT, Bax J, et al. Predictors of response to cardiac resynchronization therapy (PROS PECT)—study design. Am Heart J 2005;149:600–5.
15. Cannesson M, Tanabe M, Suffoletto MS, Schwartzman D, Gorcsan J 3rd. Velocity vector imaging to quantify ventricular dyssynchrony and predict response to cardiac resynchronization therapy. Am J Cardiol 2006;98: 949–53.
16. Gorcsan J 3rd, Tanabe M, Bleeker GB, et al. Combined longitudinal and radial dyssynchrony predicts ventricular response after resynchronization therapy. J Am Coll Cardiol 2007;50: 1476–83.
17. Tanaka H, Hara H, Saba S, Gorcsan J 3rd. Prediction of response to cardiac resynchronization therapy by speckle tracking echocardiography using different software approaches. J Am Soc Echocardiogr 2009;22:677–84.
18. Abraham WT, Fisher WG, Smith AL, et al. Cardiac resynchronization in chronic heart failure. N Engl J Med 2002;346:1845–53.
19. Blanc JJ, Etienne Y, Gilard M, et al. Evaluation of different ventricular pacing sites in patients with severe heart failure: results of an acute hemodynamic study. Circulation 1997;96: 3273–7.
20. Bristow MR, Saxon LA, Boehmer J, et al. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med 2004;350: 2140–50.
21. Cleland JG, Daubert JC, Erdmann E, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med 2005;352: 1539–49.
22. Foster AH, Gold MR, McLaughlin JS. Acute hemodynamic effects of atrio-biventricular pacing in humans. Ann Thorac Surg 1995;59:294–300.
23. Dohi K, Suffoletto MS, Schwartzman D, Ganz L, Pinsky MR, Gorcsan J 3rd. Utility of echocardiographic radial strain imaging to quantify left ventricular dyssynchrony and predict acute response to cardiac resynchronization therapy. Am J Cardiol 2005;96: 112–6.
24. Bax JJ, Gorcsan J 3rd. Echocardiography and noninvasive imaging in cardiac resynchronization therapy: results of the PROSPECT (Predictors of Response to Cardiac Resynchronization Therapy) study in perspective. J Am Coll Cardiol 2009;53:1933–43.
25. Yu CM, Bax JJ, Gorcsan J 3rd. Critical appraisal of methods to assess mechanical dyssynchrony. Curr Opin Cardiol 2009;24:18–28.
26. Helm RH, Leclercq C, Faris OP, et al. Cardiac dyssynchrony analysis using circumferential versus longitudinal strain: implications for assessing cardiac resynchronization. Circulation 2005;111:2760–7.
27. 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.
28. Adelstein EC, Saba S. Scar burden by myocardial perfusion imaging predicts echocardiographic response to cardiac resynchronization therapy in ischemic cardiomyopathy. Am Heart J 2007; 153:105–12.
29. Bilchick KC, Dimaano V, Wu KC, et al. Cardiac magnetic resonance assessment of dyssynchrony and myocardial scar predicts function class improvement following cardiac resynchronization therapy. J Am Coll Cardiol Img 2008;1:561–8.
30. 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.
31. Lancellotti P, Senechal M, Moonen M, et al. Myocardial contractile reserve during exercise predicts left ventricular reverse remodelling after cardiac resynchronization therapy. Eur J Echocardiogr 2009;10:663–8.
32. Ypenburg C, Sieders A, Bleeker GB, et al. Myocardial contractile reserve predicts improvement in left ventricular function after cardiac resynchronization therapy. Am Heart J 2007; 154:1160–5.

Key Words: echocardiography ■ Doppler ultrasound ■ heart failure ■ pacing therapy.