Relation of Left Ventricular Lead Placement in Cardiac Resynchronization Therapy to Left Ventricular Reverse Remodeling and to Diastolic Dyssynchrony

Aleksandr Rovner, MD[a,b], Lisa de las Fuentes, MD[a,b], Mitchell N. Faddis, MD, PhD[b], Marye J. Gleva, MD[b], Victor G. Dávila-Román, MD[a,b], and Alan D. Waggoner, MHS[a,b,*]

The effects of left ventricular (LV) lead placement for cardiac resynchronization therapy (CRT) on LV remodeling and dyssynchrony are not well defined. Sixty-one patients (age 60 ± 11 years, 76% men) were evaluated by echocardiography before and 4 ± 2 months after CRT and grouped by the LV lead placement (lateral, posterolateral, or anterolateral). Echocardiographic measurements included LV volumes and LV ejection fraction. Tissue Doppler imaging was used to assess for inter- and intraventricular systolic and diastolic dyssynchrony. Analysis of variance was used to determine the effect of the LV lead placement on echocardiographic variables after CRT. The LV lead was placed in a lateral cardiac vein in 33 patients (54%), posterolateral in 15 (25%), and anterior in 13 (21%). Lateral LV lead placement was associated with significantly smaller LV volumes compared with the posterolateral lead placement ($p < 0.01$). Diastolic dyssynchrony improved significantly with lateral lead placement compared with the anterior lead location ($p < 0.05$). Improvement in LV ejection fraction and inter- and intraventricular systolic dyssynchrony was similar among the 3 groups. In conclusion, in patients undergoing CRT, a lateral lead location resulted in greater reverse LV remodeling and improved diastolic dyssynchrony compared with other lead placement locations. **(Am J Cardiol 2007;99:239–241)**

Cardiac resynchronization therapy (CRT) by transvenous placement of the left ventricular (LV) pacing lead improves LV systolic and diastolic function and clinical outcomes in patients with heart failure refractory to medical therapy.[1–4] The effects of LV lead placement on interventricular mechanical delay or tissue Doppler imaging measurements of systolic and diastolic intraventricular dyssynchrony have not been extensively evaluated. The hypothesis of this study was that LV lead location would have different effects on systolic and diastolic LV dyssynchrony at short-term follow-up.

Methods and Results

This was a single-blinded longitudinal study of consecutive patients who received a CRT device and were evaluated at the Cardiovascular Imaging and Clinical Research Core Laboratory, Washington University School of Medicine, St. Louis, Missouri, before and 4 ± 2 months after CRT. The Human Research Protection Office of Washington University approved the study, and all patients provided written informed consent.

Patients received a CRT device only or a CRT/defibrillator device as determined by the implanting physician. The right atrial and right ventricular leads were positioned in the appendage and the apex or septum, respectively. The LV lead position was targeted to the lateral coronary vein; if unavailable, the posterolateral coronary vein or anterior vein was used. Placement of the LV lead was confirmed by fluoroscopy at the time of device implantation.

A commercial ultrasound system (Acuson Sequoia C256, Siemens Medical Systems, Mountain View, California) was used for the echocardiographic examination. Two-dimensional measurements included LV volumes and LV ejection fraction (LVEF).[5] M-mode echocardiography was used to measure the times from QRS onset to peak contraction of the septum and to the posterior wall; the difference between the 2 intervals was calculated to determine the intraventricular dyssynchrony.[6] Continuous-wave Doppler was used to determine interventricular dyssynchrony as the difference in time from QRS onset to the onset of pulmonary artery flow and QRS onset to the onset of aortic flow (QRS to pulmonic flow–QRS to aortic flow difference).[3]

Assessment of LV diastolic function included pulse-wave Doppler measurements of mitral inflow velocities (E-wave and A-wave), E/A ratio, and deceleration time.[7] Tissue Doppler imaging was performed in the apical 4- and 2-chamber views to determine the peak systolic and diastolic velocities at the 4 sites (i.e., lateral, septal, anterior, and inferior) of the mitral valve annulus. The intervals from the QRS onset to peak systolic contraction and to the onset of peak diastolic relaxation were measured at each site. The maximal delays among the 4 sites (i.e., QRS onset to peak

[a]Cardiovascular Imaging and Clinical Research Core Laboratory and [b]Cardiovascular Division, Washington University School of Medicine, St. Louis, Missouri. Manuscript received May 12, 2006; revised manuscript received and accepted July 21, 2006.

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*Corresponding author: Tel: 314-362-6934; fax: 314-747-8170.

E-mail address: waggonera@msnotes.wustl.edu (A.D. Waggoner).

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Table 1
Baseline characteristics of patients by left ventricular lead location (n = 61)

Characteristic	Lateral (n = 33)	Anterior (n = 13)	Posterolateral (n = 15)
Age (yrs)	62 ± 10	63 ± 11	55 ± 13
Men (%)	24 (73%)	12 (92%)	11 (73%)
Coronary artery disease (%)	7 (21%)	6 (46%)	7 (47%)
Diabetes mellitus (%)	5 (15%)	2 (15%)	5 (33%)
QRS duration (ms)	180 ± 23	179 ± 22	176 ± 37
Heart rate (beats/min)	75 ± 13	72 ± 12	76 ± 12
Systolic blood pressure (mm Hg)	111 ± 17	116 ± 13	110 ± 20
Echocardiographic data			
Ejection fraction (%)	25 ± 5	25 ± 5	25 ± 7
LV end-diastolic volume (ml)	253 ± 96	206 ± 72	204 ± 77
LV end-systolic volume (ml)	193 ± 83	158 ± 62	154 ± 63
E/A ratio	1.3 ± 1.1	1.5 ± 1.2	1.8 ± 1.2
Deceleration time (ms)	186 ± 53	200 ± 106	173 ± 49
Dyssynchrony data			
Septal–posterior wall difference (ms)	113 ± 87	126 ± 57	117 ± 42
QRS–Sm difference (ms)	59 ± 24	69 ± 27	71 ± 27
QRS to pulmonic flow–QRS to aortic flow difference (ms)	60 ± 37	45 ± 15	46 ± 24
QRS–Em difference (ms)	60 ± 32	64 ± 36	54 ± 36

Em = peak diastolic velocity; Sm = peak systolic velocity.

Table 2
Absolute improvement in echocardiographic and dyssynchrony measurements at four months' follow-up by left ventricular lead location (n = 61)

Variable	Lateral (n = 33)	Anterior (n = 13)	Posterolateral (n = 15)
Heart rate (beats/min)	7 ± 2	4 ± 4	4 ± 3
LV end-diastolic volume (ml)	47 ± 26	20 ± 36	4 ± 12*
LV end-systolic volume (ml)	49 ± 22	32 ± 28	15 ± 30†
Ejection fraction (%)	9 ± 8	10 ± 6	7 ± 7
Septal–posterior wall motion difference (ms)	63 ± 18	55 ± 27	54 ± 25
QRS–Sm difference (ms)	15 ± 7	20 ± 10	14 ± 9
QRS to pulmonic flow–QRS to aortic flow difference (ms)	17 ± 5	17 ± 7	19 ± 7
QRS–Em difference (ms)	19 ± 7	5 ± 12‡	9 ± 10

* $p < 0.001$ versus lateral; † $p < 0.01$ versus lateral; ‡ $p < 0.05$ versus lateral.
Abbreviations as in Table 1.

systolic contraction difference and the onset of peak diastolic relaxation difference) were calculated to determine the intraventricular LV systolic and diastolic dyssynchrony, respectively (Figure 1).

Variables are expressed as means ± SDs. Student's *t* test was used to analyze the differences between the pre- and post-CRT groups. The Mann-Whitney U and chi-square tests were used to compare nonparametric and categorical variables. Analysis of variance with Tukey-Kramer adjustment for multiple comparisons determined the effect of the LV lead position on the echocardiographic variables. A p value <0.05 was determined as statistically significant. All statistical analyses were performed using Statistical Package for Social Sciences, version 12.0 (SPSS, Chicago, Illinois).

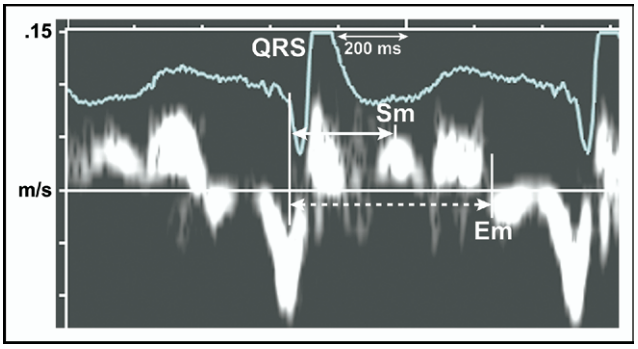

Figure 1. Measurements of tissue Doppler intervals. *Solid line,* time from QRS to peak systolic myocardial velocity (Sm); *dashed line,* time to onset of early diastolic myocardial velocity (Em).

The 61 patients were grouped by LV lead position at CRT device implantation as lateral (n = 33), posterolateral (n = 15), and anterior (n = 13). No differences were found among the groups in demographic, 2-dimensional and Doppler echocardiographic, or tissue Doppler imaging-derived measurements at baseline (Table 1). A trend of a greater prevalence ($p = 0.07$) of an ischemic etiology of heart failure was noted in the anterior and posterolateral groups.

The absolute values of improvement in echocardiographic measurements are shown in Table 2. LV volumes decreased significantly after CRT in the lateral group compared with the posterolateral group, and also compared with the anterior group, although these were not statistically significant. There were no differences in the LVEF response by lead location.

Inter- and intraventricular systolic dyssynchrony also improved in the 3 groups, regardless of the LV lead location. Diastolic dyssynchrony improved significantly only in the lateral lead group compared with the anterior lead group ($p < 0.05$). LV diastolic filling indexes (i.e., E/A ratio and deceleration time) improved to a similar extent regardless of the LV lead location.

Discussion

The results of this study have demonstrated that a lateral LV lead location resulted in significant decreases in LV volumes compared with posterolateral lead placement. Furthermore, diastolic dyssynchrony significantly improved with a lateral LV lead position compared with anterior lead placement. Systolic LV dyssynchrony improved to a similar extent regardless of the LV pacing site.

Previous investigations have reported conflicting results in the effects of LV lead location on hemodynamic and clinical outcomes after CRT.[1,8–11] When the LV lead placement was targeted to the site with the longest electromechanical delay, significant reductions in LV volumes and improvement in LVEF resulted at short-term follow-up after CRT.[12,13] The results of the present study are in general agreement with those of previous investigations. Decreases in LV volumes in patients with a LV lead located in a lateral coronary vein were greater compared with those with pos-

terolateral lead locations. However, the improvement in LVEF was similar regardless of the LV lead location.

The LV lead position and the effects on ventricular dyssynchrony have not been extensively studied and may be of importance to provide additional insights regarding the response in LVEF and LV remodeling after CRT.[14] In addition, the effects of LV lead position on diastolic function after CRT have not been previously reported. Studies from this laboratory have demonstrated that LV diastolic function after CRT improves in patients and is coupled to the response in systolic function and the etiology of heart failure.[4,15,16] The results of the present study have demonstrated that diastolic dyssynchrony (i.e., QRS onset to the onset of diastolic relaxation difference among mitral annular sites) improves with a lateral LV lead location compared with an anterior lead location with a trend also evident compared with a posterolateral lead location. This may be a result of the higher prevalence of ischemic heart failure etiology in the anterior and posterolateral lead groups. Thus, the LV lead placement location may potentially have an effect on diastolic resynchronization after CRT, independent of the effects on LV systolic performance.

The number of patients in this study was small and the position of the LV lead and heart failure etiology were not equally distributed in the study groups, which could potentially influence the widespread applicability of the findings. The results of this study, however, are consistent with previous reports regarding the effects of LV lead position on LV systolic function and clinical outcomes.

1. Rossillo A, Verma A, Saad EB, Corrado A, Gasparini G, Marrouche NF, Golshayan AR, McCurdy R, Bhargava M, Khaykin Y, et al. Impact of coronary sinus lead position on biventricular pacing: mortality and echocardiographic evaluation during long-term follow-up. *J Cardiovasc Electrophysiol* 2004;15:1120–1125.
2. Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L, Tavazzi L. The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med* 2005;352:1539–1549.
3. St. John Sutton MG, Plappert T, Abraham WT, Smith AL, DeLurgio DB, Leon AR, Loh E, Kocovic DZ, Fisher WG, Ellestad M, et al. Effect of cardiac resynchronization therapy on left ventricular size and function in chronic heart failure. *Circulation* 2003;107:1985–990.
4. Waggoner AD, Faddis MN, Gleva MJ, de las Fuentes L, Dávila-Román VG. Improvements in left ventricular diastolic dysfunction after cardiac resynchronization therapy are coupled to response in systolic performance. *J Am Coll Cardiol* 2005;46:2244–2249.
5. Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, Gutgesell H, Reichek N, Sahn D, Schnittger I, for the American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. *J Am Soc Echocardiogr* 1989;2:358–367.
6. Pitzalis MV, Iacoviello M, Romito R, Massari F, Rizzon B, Luzzi G, Guida P, Andriani A, Mastropasqua F, Rizzon P. Cardiac resynchronization therapy tailored by echocardiographic evaluation of ventricular asynchrony. *J Am Coll Cardiol* 2002;40:1615–1622.
7. Quinones MA, Otto CM, Stoddard M, Waggoner A, Zoghbi WA. Recommendations for quantification of Doppler echocardiography: a report from the Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. *J Am Soc Echocardiogr* 2002;15:167–184.
8. Butter C, Auricchio A, Stellbrink C, Fleck E, Ding J, Yu Y, Huvelle E, Spinelli J. Effect of resynchronization therapy stimulation site on the systolic function of heart failure patients. *Circulation* 2001;104:3026–3029.
9. Gold MR, Auricchio A, Hummel JD, Giudici MC, Ding J, Tockman B, Spinelli J. Comparison of stimulation sites within left ventricular veins on the acute hemodynamic effects of cardiac resynchronization therapy. *Heart Rhythm* 2005;2:376–381.
10. Gasparini M, Mantica M, Galimberti P, Bocciolone M, Genovese L, Mangiavacchi M, Marchesina UL, Faletra F, Klersy C, Coates R, Gronda E. Is the left ventricular lateral wall the best lead implantation site for cardiac resynchronization therapy? *Pacing Clin Electrophysiol* 2003;26:162–168.
11. Arzola-Castaner D, Taub C, Heist EK, Fan D, Haelewyn K, Mela T, Picard MH, Ruskin JN, Singh JP. Left ventricular lead proximity to an akinetic segment and impact on outcome of cardiac resynchronization therapy. *J Cardiovasc Electrophysiol* 2006;17:1–5.
12. Ansalone G, Giannantoni P, Ricci R, Trambaiolo P, Fedele F, Santini M. Doppler myocardial imaging to evaluate the effectiveness of pacing sites in patients receiving biventricular pacing. *J Am Coll Cardiol* 2002;39:489–499.
13. Murphy RT, Sigurdsson G, Mulamalla S, Agler D, Popovic ZB, Starling RC, Wilkoff BL, Thomas JD, Grimm RA. Tissue synchronization imaging and optimal LV pacing site in cardiac resynchronization therapy. *Am J Cardiol* 2006;97:1615–1621.
14. Bleeker GB, Kaandorp TAM, Lamb HJ, Boersma E, Steendijk P, de Roos A, van der Wall EE, Schalij M, Bax JJ. Effect of posterolateral scar tissue on clinical and echocardiographic improvement after cardiac resynchronization therapy. *Circulation* 2006;113:969–976.
15. Waggoner AD, Faddis MN, Gleva MJ, de las Fuentes L, Osborn J, Heuerman S, Dávila-Román VG. Cardiac resynchronization therapy acutely improves diastolic function. *J Am Soc Echocardiogr* 2005;18:216–220.
16. Waggoner AD, Rovner A, de las Fuentes L, Faddis MN, Gleva MJ, Sawhney N, Dávila-Román VG. Clinical outcomes after cardiac resynchronization therapy: importance of left ventricular diastolic function and origin of heart failure. *J Am Soc Echocardiogr* 2006;19:307–313.