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Invasive Acute Hemodynamic Response to Guide Left Ventricular Lead Implantation Predicts Chronic Remodeling in Patients Undergoing Cardiac Resynchronization Therapy

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Objectives We evaluated the relationship between acute hemodynamic response (AHR) and reverse remodeling (RR) in cardiac resynchronization therapy (CRT).

Background CRT reduces mortality and morbidity in heart failure patients; however, up to 30% of patients do not derive symptomatic benefit. Higher proportions do not remodel. Multicenter trials have shown echocardiographic techniques are poor at improving response rates. We hypothesized the degree of AHR at implant can predict which patients remodel.

Methods Thirty-three patients undergoing CRT (21 dilated and 12 ischemic cardiomyopathy) were studied. Left ventricular (LV) volumes were assessed before and after CRT. The AHR (maximum rate of left ventricular pressure [LV-dP/dt_{max}]) was assessed at implant with a pressure wire in the LV cavity. Largest percentage rise in LV-dP/dt_{max} from baseline (atrial antibradycardia pacing or right ventricular pacing with atrial fibrillation) to dual-chamber pacing (DDD)-LV was used to determine optimal coronary sinus LV lead position. Reverse remodeling was defined as reduction in LV end systolic volume ≥15% at 6 months.

Results The LV-dP/dt_{max} increased significantly from baseline (801 ± 194 mm Hg/s to 924 ± 203 mm Hg/s, $p < 0.001$) with DDD-LV pacing for the optimal LV lead position. The LV end systolic volume decreased from 186 ± 68 ml to 157 ± 68 ml ($p < 0.001$). Eighteen (56%) patients exhibited RR. There was a significant relationship between percentage rise in LV-dP/dt_{max} and RR for DDD-LV pacing ($p < 0.001$). A similar relationship for AHR and RR in dilated cardiomyopathy and ischemic cardiomyopathy ($p = 0.01$ and $p = 0.006$) was seen.

Conclusions Acute hemodynamic response to LV pacing is useful for predicting which patients are likely to remodel in response to CRT both for dilated cardiomyopathy and ischemic cardiomyopathy. Using AHR has the potential to guide LV lead positioning and improve response rates. (J Am Coll Cardiol 2011;58:1128–36) © 2011 by the American College of Cardiology Foundation

Cardiac resynchronization therapy (CRT) is a well-established treatment for patients with severe heart failure. Cardiac resynchronization therapy improves quality of life (1,2), prognosis (3), and in the long-term is associated with left ventricular (LV) reverse remodeling (RR) (4). However a significant number of patients do not derive clinical benefit. This has led to various strategies particularly with echocardiographic imaging techniques to improve patient selection. Nevertheless, recent findings have not supported the use of echocardiographic-derived dyssynchrony indexes to guide CRT (5,6).

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Maximum rate of left ventricular pressure (LV-dP/dt_{max}) is a reproducible marker of LV contractility. Several studies

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have used acute hemodynamic response (AHR) to determine lead position (7–9) as well as optimize pacing settings (10,11). Studies have evaluated the effect of LV pacing in the context of CRT with LV-dP/dt_{max} as an endpoint (8,11–13). The implication is that acute improvement in contractility translates into beneficial effects from CRT in the longer term. Although it is logical that energy, which is wasted as a result of LV dyssynchrony, might be "harnessed" by LV pacing to improve cardiac function, it is likely there are more complex mechanisms involved in remodeling. Echocardiographic-based assessments of AHR to CRT have shown it is a useful predictor of long-term clinical outcome (14,15). However, echocardiographic-derived LV-dP/dt_{max} is confined to patients with enough mitral regurgitation to obtain a clear signal and is difficult to measure during CRT implant. Although it has been shown that invasive measurement of AHR improves with CRT (13), it remains unclear whether an AHR at the time of CRT equates to RR and improvement in quality of life.

The current consensus is to position the LV lead in a lateral or posterolateral branch of the coronary sinus (CS) (16,17). A recent study found a marked variation in hemodynamic response, depending on LV pacing position (8). We hypothesized that AHR at the time of CRT implant could help guide lead placement and predict chronic response. We used invasive LV-dP/dt_{max} to guide conventional coronary sinus LV lead placement in an unselected group of heart failure patients during CRT implant. We investigated how this related to chronic response by determining LV remodeling and clinical response at 6 months.

Methods

Patients. Patients fulfilling standard criteria for CRT (New York Heart Association [NYHA] functional class III to IV drug refractory heart failure, left ventricular ejection fraction [LVEF] ≤35%, LV end-diastolic diameter ≥55 mm, and prolonged QRS >120 ms) were recruited. The study complied with the local ethics committees, and informed consent was obtained from each patient. Clinical characteristics are presented in Table 1.

Echocardiographic assessment. Before CRT, patients underwent echocardiography with a GE Vivid 7 scanner (General Electric-Vingmed, Milwaukee, Wisconsin). Analysis was performed with EchoPac (version 6.0.1, General Electric-Vingmed). Ejection fractions and LV dimensions and volumes were measured with 2-dimensional biplane Simpson's modified method.

The interventricular mechanical delay (IVMD) was calculated as the difference between the LV and right ventricular (RV) pre-ejection periods measured from the QRS to onset of pulmonary and aortic flows, respectively (18,19). Intraventricular dyssynchrony was assessed with tissue Doppler imaging (TDI) by measuring the difference between septal to lateral peak velocity within the aortic valve opening and closing times (20). Systolic dyssynchrony index (SDI) was measured (21) with TomTec 4D LV-Analysis software (TomTec Imaging Systems, Inc., Munich, Germany).

Implant and acute hemodynamic measurements. During CRT implant hemodynamic evaluation was performed with a 0.014-inch-diameter high-fidelity Certus PressureWire and PhysioMon software (Radi Medical Systems, Uppsala, Sweden) with a 500-Hz frequency response introduced into the LV through a 5-F multipurpose catheter from either a femoral or radial arterial access site (22). The multi-purpose catheter was removed or withdrawn into the aorta, leaving the pressure wire in a stable position within the LV cavity. Once venous access was acquired for pacing lead implants, 2,500 U of heparin were given, followed by saline flush (Table 2).

The LV-dP/dt_{max} was calculated electronically from every heartbeat for a period of at least 10 s to ensure steady-state conditions. The results were averaged for the complete measurement period. A waiting period of at least 20 s was respected after any change in pacing settings or lead position to achieve hemodynamic stabilization (23). This method has previously been shown to reliably measure LV-dP/dt_{max} (12).

Hemodynamic measurement protocol and data analysis. An occlusive venogram was performed, and either Quickflex LV leads or Quartet Model 1458Q (programmed bipolar D1-M2) (St. Jude Medical, Sylmar, California) were placed in branches of the coronary sinus that were considered as potential targets to allow multiple measurements of dP/dt_{max}. In these sites LV-dP/dt_{max} was measured during intrinsic rhythm and atrial pacing (atrial antibradycardia pacing [AAI] 5 to 10 beats above intrinsic atrial rate to ensure consistent capture) and with LV coronary sinus pacing (dual-chamber [DDD]-LV [fixed atrioventricular delay 100 ms] or single-chamber ventricular pacing [patients in atrial fibrillation], 5 to 10 beats above intrinsic). In patients with atrial fibrillation, baseline was considered as RV pacing 5 to 10 beats above intrinsic ventricular rate (24).

Results at each pacing site were expressed as a percentage change from baseline. The baseline was reassessed before every new LV lead position, and the optimal LV lead

Abbreviations and Acronyms

AAI = atrial antibradycardia pacing
AHR = acute hemodynamic response
BIV = biventricular
CRT = cardiac resynchronization therapy
DCM = dilated cardiomyopathy
DDD = dual-chamber (pacing)
ESV = end-systolic volume
ICM = ischemic cardiomyopathy
IVMD = interventricular mechanical delay
LV = left ventricle/ventricular
LV-dP/dt_{max} = maximum rate of left ventricular pressure
LVEF = left ventricular ejection fraction
NYHA = New York Heart Association
ROC = receiver-operator characteristic
RR = reverse remodeling
RV = right ventricle/ventricular
SDI = systolic dyssynchrony index
TDI = tissue Doppler imaging

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Table 1 Patient Characteristics

	All Patients (n = 33)	DCM (n = 21)	ICM (n = 12)	p Value DCM vs. ICM
Age (yrs)	63.6 ± 12.1	62.3 ± 12.7	65.9 ± 10.9	NS
Male/female	29/4	18/3	11/1	NS
NYHA functional class III	30	20	10	NS
QOL score pre-CRT	52 ± 22	50 ± 23	53 ± 21	NS
QRS duration (ms)	160 ± 23	162 ± 28	156 ± 13	NS
Rhythm	27 SR	16 SR	11 SR	NS
	6 AF	5 AF	1 AF	
Ejection fraction (%)	25 ± 8	24.4 ± 9.4	25.6 ± 4.9	NS
End-diastolic volume (ml)	239 ± 69	250 ± 83	229 ± 56	NS
ESV (ml)	185 ± 67	193 ± 77	170 ± 43	NS
Beta-blockers (%)	86	88	75	
ACE/ARB (%)	100	100	100	
Diuretics (%)	64	78	45	
Aldosterone antagonists (%)	39	41	36	

ACE = angiotensin-converting enzyme; AF = atrial fibrillation; ARB = angiotensin receptor blocker; CRT = cardiac resynchronization therapy; DCM = dilated cardiomyopathy; ESV = end-systolic volume; ICM = ischemic cardiomyopathy; NYHA = New York Heart Association; QOL = quality of life questionnaire; SR = sinus rhythm.

position was arbitrarily defined as the location with the largest percentage rise in LV-dP/dt$_{max}$ from baseline. The number of measurements varied, depending on the number of target branches. To determine baseline drift in dP/dt$_{max}$, the SD in the baseline was calculated for each patient over the course of the implant and then the mean SD for all the procedures. At the end of the procedure, pressure wire-guided atrioventricular and interventricular optimization was performed.

Remodeling and responders. Patients were deemed to have RR if there was a ≥15% reduction in LV end-systolic volume (ESV) (20,25). Symptomatic response was evaluated by NYHA functional class and quality-of-life questionnaire repeated at 6 months (26). Acute response was defined as a ≥10% rise in dP/dt$_{max}$ from baseline to assess sensitivity and specificity for dP/dt$_{max}$ to predict RR. This cutoff value has been used in previous studies (11,27). Patients were labeled clinical responders if the NYHA functional class fell by ≥1 or if there was a ≥10% reduction in quality-of-life questionnaire score.

Table 2 Implant Details

	Implant
Device	8 St. Jude Promote Q CD3221
	16 St. Jude Promote RF 3213-36
	5 St. Jude Pacesetter Atlas II HF v-367
	4 St. Jude Frontier II 5596
LV lead position	2 posterior vein
	19 posterolateral vein
	11 lateral vein
	1 middle cardiac vein
	1 anterolateral vein
Types of LV lead	27 Quickflex (St. Jude Medical)
	6 Quartet Model 1458Q (St. Jude Medical)
LV lead threshold	1.4 ± 0.7
RV lead threshold	0.7 ± 0.3

LV = left ventricular; RV = right ventricular.

Statistical analysis. Statistical analysis was performed on JMP (version 8.0.2, Marlow, Buckinghamshire, United Kingdom). A Shapiro-Wilk test was used to ensure variables were normally distributed. Continuous variables were expressed as mean ± SD and compared with parametric (1-way analysis of variance) and nonparametric (Wilcoxon rank sum) tests. Changes in variables were compared with paired *t* tests. Nominal variables are expressed as absolute count and percentages and compared with a Fisher exact test. Outcomes were assessed with logistic regression to create receiver-operator characteristic (ROC) curves. Optimal cutoffs were selected as the level with the highest (sensitivity − [1 − specificity]). Values of $p < 0.05$ were considered statistically significant.

Results

Patients. Thirty-three patients were studied (29 men, age 63.6 ± 12.1 years), with a mean ejection fraction of 25 ± 8%. All patients had left bundle branch block (QRS duration 160 ± 23 ms). Twelve had ischemic cardiomyopathy (ICM), and 21 had dilated cardiomyopathy (DCM) (Table 1). The LV-dP/dt$_{max}$ was successfully measured in all patients (Table 2). Average procedure time was 138 ± 38 min and fluoroscopy time 20.7 ± 7.4 min. One groin hematoma and one wound hematoma occurred, neither requiring intervention. One RV lead displacement occurred requiring repositioning the following day. One patient had a coronary sinus dissection; however, an LV lead was successfully implanted. One patient with ICM had excessive diaphragmatic pacing, which led to the LV lead being turned off, and was excluded from follow-up.

Mean intrinsic LV-dP/dt$_{max}$ was 722 ± 148 mm Hg/s, increasing to 801 ± 194 mm Hg/s ($p < 0.001$) with AAI/RV pacing (baseline). Average number of baseline readings was 5.8 ± 1.3. Baseline drift in LV-dP/dt$_{max}$ over the course of the

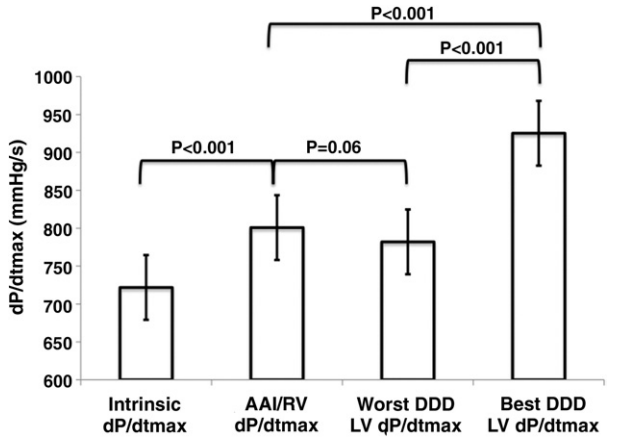

Figure 1 **Change in LV-dP/dt$_{max}$ for Various Pacing Modes and Difference Between Best and Worst LV-dP/dt$_{max}$ for DDD-LV Pacing**

The p values are derived from paired *t* tests and reflect the change in maximum rate of left ventricular pressure (LV-dP/dt$_{max}$) between pacing positions and baseline dP/dt$_{max}$. AAI = atrial antibradycardia pacing; DDD = dual-chamber (pacing); LV = left ventricular; RV = right ventricular.

implants was 68 ± 17 mm Hg/s. Average number of coronary sinus LV sites tested was 3.3 ± 1.2. There was a highly significant increase in LV-dP/dt$_{max}$ from baseline to DDD-LV pacing in the optimal (best AHR) position (801 ± 194 mm Hg/s to 924 ± 203 mm Hg/s, $p < 0.001$, 18 ± 18% rise) (Fig. 1, Table 3). In 30 of the patients at least 2 separate branches of the coronary sinus were paced. There was a highly significant difference between best and worst LV pacing site (924 ± 203 mm Hg/s best site vs. 782 ± 160 mm Hg/s worst site, $p < 0.001$) (Figs. 1 and 2). With a 10% cutoff to define acute response, 23 (70%) of patients acutely responded to DDD-LV pacing.

Response and remodeling. Pre-implant LVESV and LVEF were 185 ± 67 ml and 24.8 ± 8.0%, respectively. These improved at follow-up to 157 ± 69 ml and 32.8 ± 9.7%, representing a 15% relative reduction in LVESV and a 41% relative improvement in LVEF (both $p < 0.001$). Eighteen (56%) patients remodeled with a significant relationship for percentage rise in dP/dt$_{max}$ and RR for DDD-LV pacing ($p < 0.001$) (Fig. 3A). There was a good relationship between QRS duration and RR ($p < 0.001$). Echocardiographic measures of dyssynchrony, left ventricular pre-ejection time, IVMD, and SDI measured with 3-dimensional echocardiography were found to have a significant relationship for RR ($p = 0.01$, $p < 0.001$, and $p = 0.01$, respectively). Septal-lateral delay with TDI showed no relationship for RR ($p = 0.8$) (Fig. 4).

A >10% improvement in LV-dP/dt$_{max}$ from baseline with DDD-LV pacing was more sensitive at predicting remodeling than echocardiographic parameters (Table 4). Seventeen (94%) of 18 patients that remodeled had a ≥10% rise in LV-dP/dt$_{max}$, with only 1 patient that had a 10% rise in LV-dP/dt$_{max}$ not RR (sensitivity 0.94, $p < 0.001$, compared with best echo parameter left ventricular pre-ejection time sensitivity 0.82, $p = 0.06$). ROC (Table 5) showed an 11.1% rise in LV-dP/dt$_{max}$ from baseline had a sensitivity of 0.94 and specificity of 0.86 ($p = 0.009$) to predict RR, supporting the use of a 10% cutoff value to distinguish between responders and nonresponders. A QRS duration cutoff of 146 ms was found to be a good predictor of RR. With ROC analysis, the only echocardiographic parameter of dyssynchrony that had comparable sensitivity and specificity was IVMD with a cutoff of 29 ms (sensitivity 0.94, specificity 0.79, $p = 0.003$).

Etiology and remodeling. Thirteen (61%) patients with DCM exhibited RR, compared with 5 (45%) with ICM. (Table 6). There was a nonsignificant trend toward patients with DCM having a greater percentage reduction in ESV (19 ± 21% vs. 8 ± 28%). There was a strong relationship for AHR and RR for both DCM and ICM patients ($p = 0.01$ and $p = 0.006$, respectively) (Figs. 3B and 3C). A similar relationship was found with QRS duration and RR for both DCM and ICM patients ($p = 0.01$ and $p = 0.04$, respectively). For patients with DCM, there was a statistically significant relationship between SDI and RR ($p = 0.004$) and also between IVMD and RR ($p = 0.006$). For patients with ICM, the only echocardiographic parameter with statistically significant relationships was IVMD and RR ($p = 0.006$).

Lead position. In 18 (54%) patients, the largest rise in LV-dP/dt$_{max}$ was in a posterolateral vein (1 patient had the LV lead turned off, due to phrenic nerve stimulation). Of these, 11 (64%) remodeled. In 11 (33%) patients, the largest rise in

Table 3 **Responders and Hemodynamic Response Depending on LV Lead Position**

				DDD-LV Pacing	
	≥15% Reduction in ESV	Intrinsic Mean dP/dt$_{max}$	AAI Pacing Mean dP/dt$_{max}$	Mean dP/dt$_{max}$	% Change
All patients*, n = 33	18 (56%)	722 ± 148†	801 ± 194	924 ± 203†	18 ± 18
LV lead posterolateral vein*, n = 18	11 (64%)	730 ± 123†	828 ± 174	978 ± 222†	19 ± 16
LV lead lateral vein, n = 11	5 (45%)	725 ± 164	795 ± 255	894 ± 178†	18 ± 23
LV lead posterior vein, n = 2	1 (50%)	745	831	978	18
LV lead middle cardiac vein, n = 1	1 (100%)	519	516	599	15
LV lead anterolateral vein, n = 1	0 (0%)	780	948	982	4

Values are n (%), mean ± SD, or n. *One patient excluded from long-term follow-up. †Significant difference from atrial antibradycardia pacing (AAI) ($p < 0.05$).
DDD = dual-chamber (pacing); ESV = end-systolic volume; LV = left ventricular; RV = right ventricular.

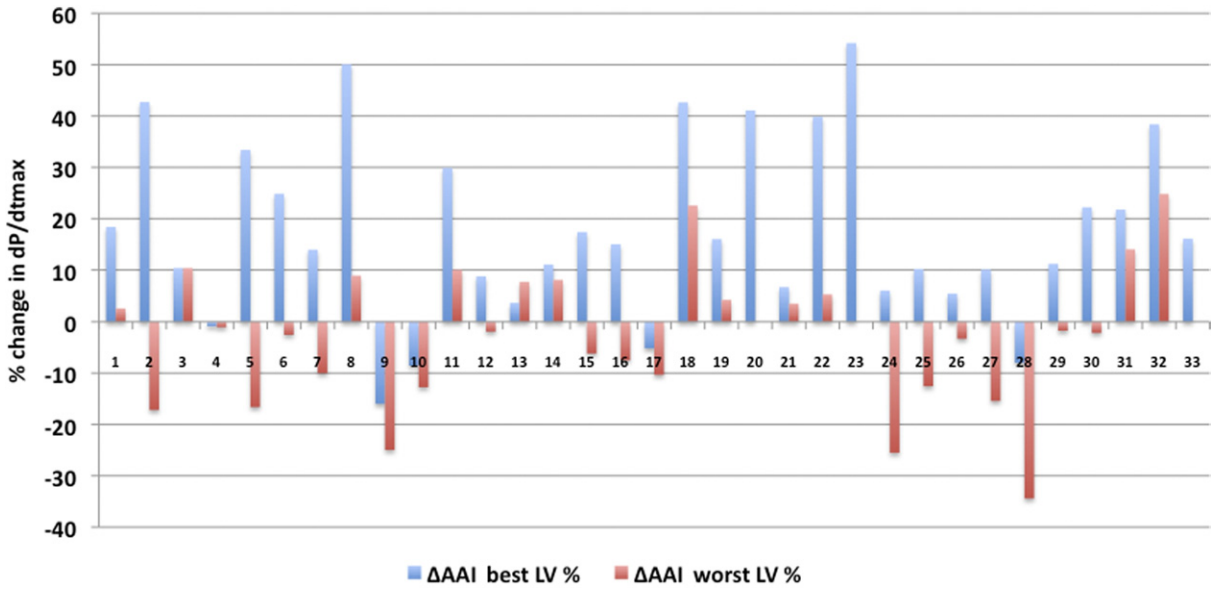

Figure 2 Best and Worst Sites for Each Individual Pacing Position

Percentage of change in LV-dP/dt_{max} from AAI or RV baseline LV-dP/dt_{max} for each individual patient at best **(blue bars)** and worst **(red bars)** LV lead position. Abbreviations as in Figure 1.

LV-dP/dt_{max} was in a lateral vein, and 5 (45%) remodeled. In 2 patients, the largest rise in LV-dP/dt_{max} was in a posterior vein, with 1 patient remodeling. In 1 patient, optimal LV-dP/dt_{max} was in the middle cardiac vein, and the patient remodeled. In 1 patient, the best position was the anterolateral vein, but the subject did not remodel (Table 3).

Clinical response. Twenty-nine (91%) patients improved by at least 1 NYHA functional class, and 30 (94%) patients had a ≥10% reduction in quality-of-life score. There was a statistically significant relationship between percentage rise in LV-dP/dt_{max} and improvement in NYHA functional class and 10% reduction in quality-of-life score ($p = 0.02$ for both). No relationship between QRS duration or echocardiographic measures of dyssynchrony and measures of clinical improvement were found.

Discussion

With invasive acute hemodynamic measurements at the time of CRT implant we have shown: 1) there is a strong relationship between the magnitude of rise in LV-dP/dt_{max} from baseline for DDD-LV pacing and RR; 2) a ≥10% increase in LV-dP/dt_{max} with DDD-LV pacing is a highly sensitive and specific predictor of remodeling, which was underpinned by the ROC giving a cutoff of 11.1%; 3) percentage rise in LV-dP/dt_{max} for LV pacing is better at

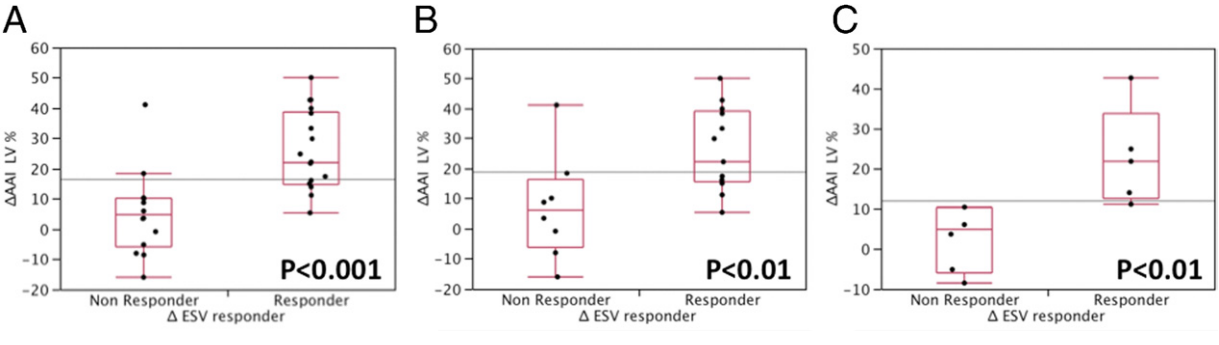

Figure 3 Percentage Change in LV-dP/dt_{max} From Baseline for DDD-LV Pacing Plotted Against the Presence or Absence of LV RR

(A) All patients; **(B)** patients with dilated cardiomyopathy; and **(C)** patients with ischemic cardiomyopathy. ESV = end-systolic volume; RR = reverse remodeling; other abbreviations as in Figure 1.

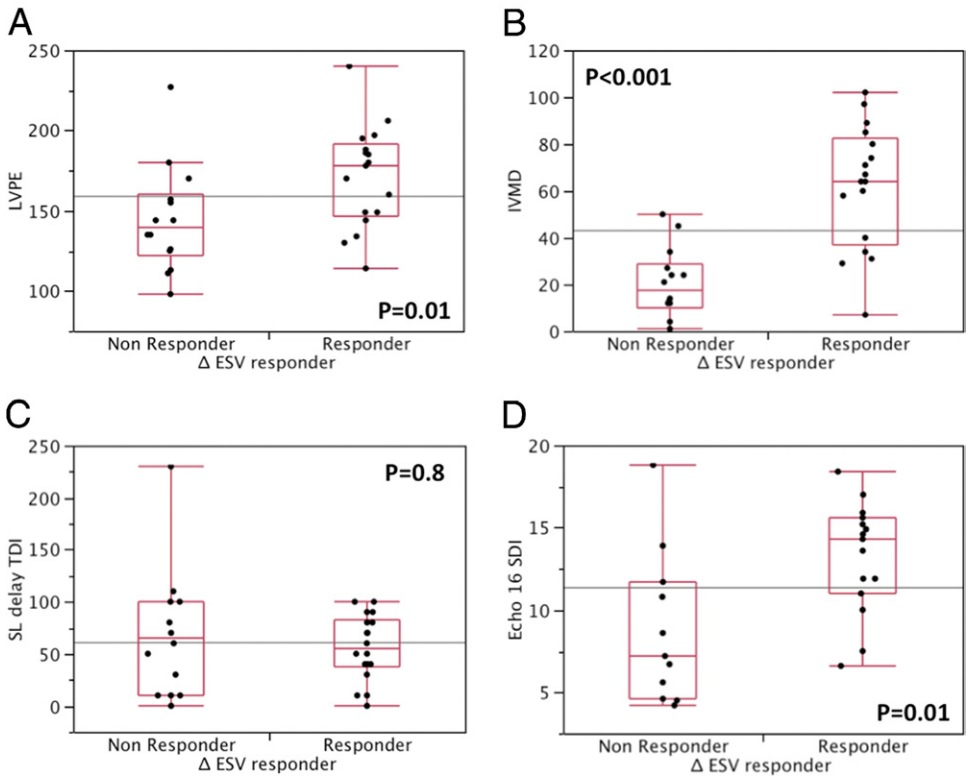

Figure 4 Relationship for Echocardiographic Parameters Presence or Absence of Left Ventricular Reverse Remodeling

(A) The left ventricular pre-ejection (LVPE) period; **(B)** interventricular mechanical delay (IVMD); **(C)** septal lateral (SL) delay measured with tissue Doppler imaging (TDI); and **(D)** systolic dyssynchrony index (SDI) measured with 3-dimensional echocardiography (Echo). ESV = end-systolic volume.

predicting remodeling than QRS duration ≥120 ms and at least as good as the best echocardiographic parameters of dyssynchrony (IVMD); and 4) LV-dP/dt_{max} varies significantly, depending on site of LV lead positioning, and might be useful for guidance.

Remodeling and etiology. There was a nonsignificant trend toward increased remodeling in DCM versus ICM patients (61% vs. 45%). Acute response seemed similarly predictive of remodeling in both groups. Fewer ICM patients remodeling might be explained by the presence of myocardial scar, producing a more varied response to CRT. Nevertheless, the rise in LV-dP/dt_{max} might reflect contractile reserve and therefore provides an indicator of how likely a patient is to respond (28), independent of etiology. There was a good relationship between QRS duration and remodeling in both DCM and ICM. For echocardiographic parameters of dyssynchrony only IVMD delay was predictive of response in ICM patients, suggesting that LV-dP/dt_{max}

Table 4 Sensitivity and Specificity for 10% Rise in LV-dP/dt_{max} for LV Pacing and Standard Echocardiographic Measures of Dyssynchrony Predicting 15% Reduction in ESV

Assessment Method	Cutoff Met?	Total	n	%	Sensitivity	Specificity	p Value
% rise LV-dP/dt_{max} ≥10%, n = 322	Yes	22	17	77	0.94	0.64	<0.001
	No	10	1	10			
LVPE ≥140 ms, n = 31	Yes	21	14	67	0.82	0.5	0.06
	No	10	3	30			
IVMD ≥40 ms, n = 31	Yes	15	13	86	0.76	0.86	<0.001
	No	16	4	25			
TDI septal lateral ≥80 ms, n = 32	Yes	8	4	50	0.22	0.71	0.7
	No	24	14	56			
SDI ≥10.3%, n = 26	Yes	16	12	75	0.8	0.64	0.02
	No	10	3	30			

ESV = end-systolic volume; IVMD = interventricular mechanical delay; LV-dP/dt_{max} = maximum rate of left ventricular pressure; LVPE = left ventricular pre-ejection time; SDI = systolic dyssynchrony index; TDI = tissue Doppler imaging.

Table 5 Sensitivity, Specificity, and AUC for 15% Reduction in ESV

Assessment Method	AUC	Cutoff	Sensitivity	Specificity
QRSD (ms), n = 32	0.84	146.0	1.00	0.64
% rise LV dP/dt$_{max}$, n = 32	0.89	11.1	0.94	0.86
LVPE (ms), n = 31	0.75	160.0	0.65	0.79
IVMD (ms), n = 31	0.91	29.0	0.94	0.79
TDI septal lateral (ms), n = 32	0.5	90.0	0.88	0.29
SDI (%), n = 26	0.8	11.9	0.73	0.82

Table uses receiver-operator characteristic curve analysis to investigate whether changing the cutoff values used in Table 4 could give a better prediction of improvement in ESV.

AUC = area under the receiver-operator characteristic curve; QRSD = QRS duration; other abbreviations as in Table 4.

might be particularly useful in determining which ICM patients are likely to respond when conventional methods are less helpful.

LV pacing site. In most patients the greatest percentage rise in LV-dP/dt$_{max}$ was in the posterolateral or lateral vein (88%). In 4 patients (12%), although the LV-dP/dt$_{max}$ was assessed in the posterolateral and lateral vein, the optimum position based on LV-dP/dt$_{max}$ was a posterior, middle, or anterolateral vein. Of these 4 patients, 50% remodeled. One of these 4 had ICM with extensive transmural inferior lateral scar, and the lead was placed in the anterolateral vein. They had a <10% increase in LV-dP/dt$_{max}$ and did not remodel. It is unlikely this patient would have remodeled, due to position and extent of scar. Recent published data have demonstrated that pacing the site of latest mechanical activation produces a better long-term prognosis and remodeling at 6 months (29). A further study (8) using an individually based approach showed marked individual variation between patients and LV-dP/dt$_{max}$ at different LV pacing sites and concluded that an individually based approach might be superior to empirical lead placement in a posterolateral or lateral vein. We used epicardial pacing via the coronary sinus, which limits the potential targets (3 patients had only 1 suitable vein). However, we found that, with a targeted approach with LV-dP/dt$_{max}$, empirical implantation of the LV lead in a posterolateral or lateral vein does not always produce the best AHR. Notably some LV lead positions were no better than AAI or RV pacing (Figs. 1 and 2), emphasizing the importance of optimizing LV lead placement.

Role of LV-dP/dt$_{max}$. Patients were recruited on the basis of QRS duration ≥120 ms. On this basis, only 18 (56%) patients remodeled. For LV-dP/dt$_{max}$, 17 (94%) of the 18 patients that remodeled had a ≥10% rise in LV-dP/dt$_{max}$ and only 1 patient with a ≥10% rise in LV-dP/dt$_{max}$ did not remodel. The ROC showed that a QRS cutoff of 146 ms was a far more sensitive predictor of RR than 120 ms. Of 10 patients with a QRS between 120 and 149 ms, only 1 remodeled; this patient did have a ≥10% rise in LV-dP/dt$_{max}$. Although the numbers are small, it is possible that LV-dP/dt$_{max}$ could be beneficial in determining responders in this group, because it would seem that if the QRS is <150 ms and there is a <10% rise in dP/dt$_{max}$ it is very unlikely remodeling will occur.

The IVMD was nearly equivalent in its predictive value for remodeling as dP/dt$_{max}$. When groups were separated into DCM and ICM only IVMD was found to be predictive of remodeling for both etiologies. We found no relationship for septal lateral delay and remodeling. Three-dimensional echo-derived SDI was predictive of RR overall and in DCM patients but did not give superior discrimination compared with QRS duration alone and was not helpful in ICM patients. Furthermore, 7 (22%) datasets were not analyzable, due to poor image quality.

Assessment of dP/dt$_{max}$ is highly invasive (requires arterial access), whereas conventional 2-dimensional echocardiographic assessment of dyssynchrony is not. However, dp/dt measurement is a more practical method to assess response during the procedure, whereas echocardiography would be more difficult. The real benefit of the 2 predictors is complementary. Echocardiography should be used to predict who would respond before procedure, whereas dp/dt should be used intra-procedure to identify best site for response.

Clinical implications. Symptomatically, 29 (91%) patients improved by at least 1 NYHA functional class, and 30 (94%) patients had a ≥10% reduction in quality of life questionnaire score. There was a statistically significant relationship between percentage rise in LV-dP/dt$_{max}$ and improvement in quality of life questionnaire and NYHA functional class. For QRS duration and echocardiographic parameters, no relationship was found. Up to 28% of patients experience clinical response without significant LV RR (30). It could be inferred that using LV-dP/dt$_{max}$ to guide LV lead placement produces higher clinical responder rates. However, there are few clinical nonresponders, and a larger study is required to understand the relationship between rise in LV-dP/dt$_{max}$ and clinical response.

Table 6 Differences in Hemodynamic and Chronic Response Between DCM and ICM

				DDD-LV Pacing	
	% Decrease in ESV	≥15% Decrease in ESV	AAI Pacing Mean dP/dt$_{max}$	Mean dP/dt$_{max}$	% Change
All, n = 32	16 ± 24	18 (56%)	798 ± 197	910 ± 188*	16 ± 17
DCM, n = 21	19 ± 21	13 (61%)	766 ± 205	887 ± 185*	19 ± 18
ICM, n = 11	8 ± 28	5 (45%)	857 ± 173	953 ± 193*	12 ± 14

Values are mean ± SD or n (%). *Significant difference between AAI pacing ($p < 0.05$).

DCM = dilated cardiomyopathy; ICM = ischemic cardiomyopathy; other abbreviations as in Table 3.

Study limitations. Due to the small number of ICM patients, it is difficult to fully understand the relationship between rise in LV-dP/dt_{max} and remodeling. We have been able to show that LV-dP/dt_{max} is helpful at predicting remodeling in all patients undergoing CRT, and although we have shown that rise in LV-dP/dt_{max} seems to be helpful in predicting response in DCM and ICM patients, greater numbers are required to fully understand this relationship. The high clinical responder rate means that this study is underpowered to determine whether LV-dP/dt_{max} can predict which patients are likely to improve symptomatically.

We used DDD-LV pacing to determine the LV lead position rather than biventricular (BIV) pacing. It could be argued that determining the LV lead position with DDD-BIV pacing would be superior and more comparable to a normal resynchronization pacing strategy, but using DDD-LV pacing was the only option to ensure steady rate for accurate hemodynamic measurements throughout the study. Also, previous studies have demonstrated the noninferiority of DDD-LV pacing compared with DDD-BIV pacing (9,11,31). Further studies are required with the LV lead position optimized with BIV pacing to see whether there are differences in final lead placement and whether this changes the long-term outcome, although a protocol optimizing every lead position with BIV pacing would run the risk of having unfeasible procedure times.

The absence of a control group is a major limitation; however, our results highlight the potential of LV-dP/dt_{max} to guide LV lead placement and improve response rates. This study emphasizes the need for a randomized control study of a guided versus conventional approach to CRT.

Conclusions

We have shown that a rise in LV-dP/dt_{max} from baseline to guide LV lead position is helpful in predicting which patients are likely to reverse remodel after CRT. Using a 10% rise in LV-dP/dt_{max} is superior to QRS duration and at least as good as the best echocardiographic parameters at selecting which patients are likely to remodel both for DCM and ICM patients. This work supports the use of LV-dP/dt_{max} to aid in lead placement, and this might improve the responder rates in CRT with respect to determining which patients will remodel.

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