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Echocardiography

Contractile Reserve Assessed Using Dobutamine Echocardiography Predicts Left Ventricular Reverse Remodeling after Cardiac Resynchronization Therapy: Prospective Validation in Patients with Left Ventricular Dyssynchrony

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Background: The presence of viable myocardium may predict response to cardiac resynchronization therapy (CRT). The aim of this study is to evaluate in patients with left ventricular (LV) dyssynchrony whether response to CRT is related to myocardial viability in the region of the pacing lead. Methods: Forty-nine consecutive patients with advanced heart failure, LV ejection fraction $< 35\%$, QRS duration > 120 ms and intraventricular asynchronism ≥ 50 ms were included. Dobutamine stress echocardiography was performed within the week before CRT implantation. Resting echocardiography was performed 6 months after CRT implantation. Viability in the region of LV pacing lead was defined as the presence of viability in two contiguous segments. Response to CRT was defined by evidence of reverse LV remodeling ($\geq$15% reduction in LV end-systolic volume). Results: Thirty-one patients (63%) were identified as responders at follow-up. The average of viable segments was 5.9 ± 2 in responders and 3.2 ± 3 in nonresponders ($P = 0.0003$). Viability in the region of the pacing lead had a sensitivity of 94%, a specificity of 67%, a positive predictive value of 83%, and a negative predictive value of 86% for the prediction of response to CRT. Conclusions: In patients with LV dyssynchrony, reverse remodeling after CRT requires viability in the region of the pacing lead. This simple method using echocardiography dobutamine for the evaluation of local viability (i.e., viability in two contiguous segments) may be useful to the clinician in choosing the best LV lead positioning. (Echocardiography 2010;27:668-676)

Key words: contractile reserve, dobutamine echocardiography, LV reverse remodeling, cardiac resynchronization therapy, heart failure

Intraventricular conduction delay is frequent in patients with dilated cardiomyopathy and can result in inefficient contraction and reduced ventricular performance. Cardiac resynchronization therapy (CRT) is a valuable therapeutic option for such patients and has been shown to improve heart failure symptoms, mitral regurgitation (MR), and to reduce hospitalization and mortality in well-selected patients.[1–7] Between 30% and 40% of patients with congestive heart failure and QRS duration > 120 ms, however, do not clinically improve after CRT.[6,8] Factors that influence whether patients will respond to a therapy are not completely understood. To date, the main approach identifying CRT candidates has been QRS prolongation and mechanical dyssynchrony.[9] Contractile reserve may represent a key element in the resynchronization process. Because electrical conduction and regional wall thickening are influenced by the extent of myocardial fibrosis, it has been hypothesized that long-term response to CRT could correlate with myocardial viability in patients with left ventricular (LV) dysfunction. Using nuclear myocardial perfusion imaging (2C1Ti),[10,11] magnetic resonance imaging (MRI)[12–14] or dobutamine stress echocardiography (DSE),[15–19] studies have demonstrated the importance of LV

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viability in predicting response to CRT. Furthermore, scar tissue in the LV pacing lead region may prohibit response to CRT.[20] This study sought to prospectively validate the potential impact of myocardial reserve (i.e., global and in the LV pacing lead) as assessed during DSE on LV reverse remodeling after CRT in patients with echocardiographic evidence of LV dyssynchrony at baseline.

Materials and Methods:

From May 2005 to March 2008, 50 patients (mean age 66 $\pm$ 12 years, 34 (69%) male) were prospectively enrolled. The inclusion criteria were as follow: (1) New York Heart Association (NYHA) functional class III and IV heart failure, (2) QRS duration $\geq$ 120 ms, (3) chronic LV systolic dysfunction (LV ejection fraction $\leq$ 35%), (4) basal LV dyssynchrony $\geq$ 50 ms, (5) optimal medical treatment for heart failure including angiotensin-converting enzyme inhibitors or AT1 receptor antagonists diuretics, beta-receptor blockers, and spironolactone when tolerated, and (6) sinus rhythm. Patients with recent myocardial infarction, coronary revascularization ($<$6 months), and presenting standard contraindications to DSE were excluded. One patient was subsequently excluded for the failure of CRT implantation. All patients underwent coronary angiograms before implantation to exclude treatable ischemic heart disease. Etiology was considered ischemic in the presence of significant coronary artery disease ($\geq$50% stenosis in one or more of the major epicardial coronary arteries) and/or a history of myocardial infarction or prior revascularization. All patients provided informed consent. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by local ethics committee.

Study Design:

Patients underwent clinical examination, 12-lead electrocardiography (EKG), resting echocardiography, and DSE, within the week before biventricular pacing implantation. Follow-up clinical and echocardiographic examinations were obtained at 6 months. Responders were defined by $\geq$ 15% decrease in LV end-systolic volume.

Echocardiographic Assessment:

Echocardiographic measurements were performed by two observers blinded to patient's status using Philips Sonos 5500 or 7500 instrument with a 2.5-MHz transducer (Philips Medical Systems, Amsterdam, The Netherlands). LV volumes and ejection fraction were measured using the modified biplane Simpson's rule. LV stroke volume was calculated by multiplying the LV outflow tract area by the LV outflow tract velocity–time integral measured by pulsed wave Doppler. The proximal isovelocity surface area (PISA) was used to assess MR severity and to measure effective regurgitant orifice (ERO) area and regurgitant volume.[21] Aortic and pulmonary Doppler flows were recorded in the pulsed mode from the apical four-chamber view and parasternal short-axis view, respectively. Aortic and pulmonary ejection delays were defined as the delay between the onset of the QRS complex on the surface EKG and the onset of the aortic and pulmonary waves. The interventricular delay was defined as the time difference between the aortic and pulmonary electromechanical delay.[22]

Intraventricular Asynchronism Measurement:

Tissue Doppler imaging (TDI) was performed in the pulsed-wave Doppler mode from apical views to assess longitudinal myocardial regional function, analyzing the septal, inferior, lateral, anterior, and posterior walls.[22] Velocity profiles were recorded with a sample volume placed in the middle of the basal segment of each wall. Gain and filters were adjusted as needed to eliminate background noise and to allow for a clear tissue signal. TDI signals were recorded at a sweep of 100 mm/s. The electromechanical delay defined as the delay between the onset of the QRS complex on the surface EKG and the onset of the systolic TDI wave were measured by an independent observer (MS or PG). Intraventricular asynchronism was defined as the time difference between the shortest and longest electromechanical delay among the five LV walls.[22]

Assessment of Contractile Reserve:

All patients underwent DSE according to a low-dose infusion protocol. Patients received 5, 10, 15, and 20 μg/kg per minute of dobutamine in 3-minute stage, with echocardiographic images recorded at each stage.[23,24] Heart rate and blood pressure were monitored during each stage. Criteria for stopping the dobutamine infusion included (1) hypotension (systolic blood pressure $<$ 90 mmHg), (2) angina, (3) significant arrhythmias (atrial fibrillation, bigeminy, ventricular tachycardia), (4) attainment of 85% maximal predicted heart rate. The regional wall motion was assessed by the 16-segment model recommended by the American Society of Echocardiography.[25] Thus, a normal or hyperkinetic segment was graded as 1, hypokinetic as 2, akinetic as 3, dyskinetic as 4. The stress images at the dobutamine dose showing the maximum augmentation of wall motion were compared with baseline images. A segment was considered to have contractile reserve if after dobutamine the wall motion improved by one grade. Viability in the region of the LV pacing lead was defined as the presence of viability in two contiguous segments.

CRT Implantation and LV Lead Position:
A coronary sinus venogram was obtained using balloon catheter, followed by the insertion of the LV pacing lead (Guidant Corporation, St Paul, MN, USA or Medtronic Inc, Minneapolis, MN, USA) in the coronary sinus. The preferred position was a lateral or posterolateral vein. The right atrial and ventricular leads were positioned conventionally. All leads were connected to a dual-chamber biventricular pacing (Guidant Corporation, or Medtronic Inc). One day after implantation, the LV lead position was assessed from a chest x-ray, using frontal and lateral views (scored anterior, lateral, or posterior).[26]

Statistical Analysis:
Results are expressed as mean $\pm$ SD. Inter- and intraobserver variability for measurement of the asynchrony as for quantification of wall motion score index (WMSI) was determined from the analysis of Doppler echocardiographic images of 15 randomly selected patients by two independent observers (MS and PG). Results were compared with a one-way analysis of variance, Pearson correlation coefficient, and Bland-Altman method. Baseline data of responders versus nonresponders group were compared for statistical significance using *t*-test or chi-square test, as appropriate. Baseline and post-CRT MR severity were compared within groups using paired *t*-test or chi-square test, as appropriate. Linear regression analyses were used to evaluate the relationship between CRT response, assessed as the percentage of change in LV volume, and the percentage of change in echocardiographic data.

Results:

Patients:
Table I summarizes baseline characteristics of the population before CRT. Device implantation was successful in all patients and one patient developed pneumothorax after CRT implantation. LV pacing threshold were not different between responders and nonresponders (1.18 ± 0.70 vs. 1.75 ± 0.5, $P = 0.17$). In the subgroup of patients with CAD, no patients experience angina, electric, or regional wall motion modification at peak stress (20 μg/kg per minute) suggestive of ischemia.

Reproducibility of Asynchronism and WMSI:
There were excellent correlations ($r \geq 0.96$) between intra- and interobserver analysis of viability in the region of the pacing lead and for WMSI. Intra- and interobserver relative differences were $< 3\%$ for all parameters. The Bland-Altman method showed an excellent agreement between inter- and intraobserver measurement in both low and high values of asynchronism or WMSI.

TABLE I

Demographic and Clinical Data

Variables	All Patients (n = 49)	Responders (n = 31, 63%)	Nonresponders (n = 18, 37%)	P-Value
Demographic data				
Age (years)	66 ± 12	67 ± 10	65 ± 14	0.55
Male, n (%)	34 (69)	21 (68)	16 (72)	0.74
CAD, n (%)	34 (69)	20 (65)	14 (78)	0.32
Clinical data				
QRS duration (ms)	164 ± 30	166 ± 31	153 ± 26	0.14
LBBB, n (%)	30 (61)	20 (65)	10 (56)	0.53
RBBB, n (5)	3 (6)	2 (6)	1 (6)	0.90
IVCD, n (%)	8 (16)	3 (10)	5 (28)	0.10
PR, ms	185 ± 42	175 ± 32	202 ± 51	0.05
Pre-CRT pacing, n (%)	8 (16)	6 (19)	2 (11)	0.45
NYHA III/IV, n (%)	33 (67)/16 (33)	23 (74)/8 (26)	10 (56)/8 (44)	0.18
Medication				
Diuretic, n (%)	49 (94)	29 (94)	17 (94)	0.90
Beta-blockers, n (%)	46 (94)	28 (90)	18 (100)	0.09
ACEi, n (%)	34 (69)	21 (68)	13 (72)	0.74
AR Blockers, n (%)	14 (29)	10 (33)	4 (22)	0.41
Digoxin, n (%)	14 (29)	5 (16)	9 (50)	0.01
Spironolactone, n (%)	31 (63)	17 (55)	14 (78)	0.10

CAD = coronary arteries disease; LBBB = left bundle branch block; RBBB = right bundle branch block; IVCD = intraventricular conduction defect; ACEi = angiotensin converting enzyme inhibitors; and AR = angiotensin receptors.

TABLE II

Echocardiographic Data

Variables	All Patients (n = 49)	Responders (n = 31, 63%)	Nonresponders (n = 18, 37%)	P-Value
LV geometry and function				
LV End-Diastolic Volume (ml)				
Pre-CRT	216 ± 65	207 ± 65	231 ± 65	0.22
Late post-CRT	205 ± 74	180 ± 64*	248 ± 73*	0.0013
LV End-Systolic Volume (ml)				
Pre-CRT	180 ± 62	173 ± 63	191 ± 60	0.32
Late post-CRT	158 ± 68	131 ± 56*	203 ± 65*	0.0002
LV Stroke Volume (ml)				
Pre-CRT	43 ± 12	39.5 ± 11	48 ± 14	0.02
Late post-CRT	50 ± 12	52 ± 9*	48 ± 15	0.31
LV Ejection Fraction (%)				
Pre-CRT	19 ± 7	18.5 ± 7	20 ± 7	0.59
Late post-CRT	24 ± 9	27.5 ± 9*	19 ± 6	0.0009
Mitral regurgitation				
ERO (mm^2)				
Pre-CRT	18 ± 13	18 ± 12	20 ± 15	0.67
Late post-CRT	11 ± 12	6 ± 6*	21 ± 14	<0.0001
Regurgitant Volume (ml)				
Pre-CRT	30 ± 26	30 ± 28	29.5 ± 22	0.9
Late post-CRT	20 ± 19	12 ± 13*	33 ± 22	<0.0001
Severe MR, n (%)				
Pre-CRT	23 (47)	14 (45)	9 (50)	0.74
Late post-CRT	12 (24.5)	2 (6.5)*	10 (55.5)	<0.0001

LV = left ventricular; CRT = cardiac resynchronization therapy; ERO = effective regurgitant orifice area; and MR = mitral regurgitation; severe MR: ≥ 20 mm^2, *Significant difference (P < 0.05) between pre-CRT and late post-CRT data.

CRT Response and Echocardiographic Parameters:

Thirty-one patients (63%) were classified as responders to CRT, according to the predefined criterion of reduction in LV end-systolic volume. The response rate of patients with ischemic and nonischemic cardiomyopathy was not statistically significant (59% vs. 73%, P = 0.52). Before CRT, LV stroke volume was significantly higher in nonresponders (Table II) and there was no other significant difference between the two groups with regard to baseline echocardiographic data. In responders, LV ejection fraction improved significantly from 19 ± 7% to 28 ± 9% (P < 0.05), and a significant reduction in LV end-diastolic (207 ± 65 ml to 180 ± 64 ml) and LV end-systolic volume (173 ± 63 ml to 131 ± 56 ml) was observed (Table II). Prevalence of MR between responders and nonresponders was not statistically different before CRT (89% vs. 87%, P = 0.85). Moreover, there was no significant difference between groups regarding the prevalence of severe MR (ERO ≥ 20 mm^2) and MR severity. In responders, ERO and regurgitant volume were significantly reduced following CRT (66 ± 25%, from 18 ± 12 mm^2 to 6 ± 6 mm^2, P < 0.001; 62 ± 29%, from 30 ± 28 ml to 12 ± 13 ml, P < 0.0001).

Contractile Reserve and LV Remodeling:

All patients completed DSE protocol without complications. During low-dose dobutamine infusion, responders had less akinetic segments (8 ± 3 vs. 10 ± 3, P = 0.02) and significantly higher number of viable segments (5.9 ± 2 vs. 3.2 ± 3, P = 0.0003) than nonresponders (Table III). Reduction in LV end-systolic volume after CRT was mainly related to the improvement in WMSI during dobutamine infusion (r = 0.49, P = 0.0003) (Fig. 1).

Viability in the Region of the Pacing Lead and Response to CRT:

The presence of viability in the region of the pacing lead was more frequent in responders than in nonresponders (94% vs. 33%, P < 0.0001). In nonresponders, 12 patients had LV lead placed in myocardial region without viability. In contrast, LV lead positioned in a region with viability was observed in 29 of the 31 responders (Fig. 2) and was associated with greater end-systolic volume reduction (8.6 ± 3.0 vs. 21 ± 3, P < 0.0001) (Fig. 3). Viability in the region of the pacing lead had a sensitivity of 94%, a specificity of 67%, a positive predictive value of 83% and a negative predictive value of 86% for the prediction of response to CRT.

TABLE III

Baseline LV Asynchronism, Function, and Viability Data

Variables	All Patients (n = 49)	Responders (n = 31, 63%)	Nonresponders (n = 18, 37%)	P-Value
Asynchronism				
Interventricular (ms)	45 ± 28	45 ± 30	46 ± 24	0.92
Intraventricular (ms)	82 ± 25	84 ± 25	82.5 ± 26	0.87
No. of akinetic segments				
Rest	10 ± 3	9 ± 3.5	10.5 ± 3	0.16
Stress	8.5 ± 3	8 ± 3*	10 ± 3*	0.02
Wall motion score index				
Rest	3.5 ± 0.4	3.5 ± 0.4	3.6 ± 0.2	0.16
Stress	3.1 ± 0.5	3 ± 0.4*	3.3 ± 0.4*	0.0069
Viability				
No. of viable segments	4.9 ± 2.7	5.9 ± 2	3.2 ± 3	0.0003
≥ 4 viable segments, n (%)	31 (75)	30 (97)	7 (39)	<0.0001
Viability in the region of the lead, n (%)	35 (71)	29 (94)	6 (33)	<0.0001
Lead placement				
Posterior, n (%)	32 (65)	21 (68)	11 (61)	0.87
Lateral, n (%)	15 (31)	10 (32)	5 (28)	0.33
Anterior, n (%)	2 (4)	0 (0)	2 (11)	. . .

*Significant difference ($P < 0.05$) between pre-CRT and late post-CRT data.

Viability in the region of the pacing lead was a better predictor of response in the group of patients with nonischemic cardiomyopathy versus patients with ischemic cardiomyopathy (sensibility 100% vs. 90%, specificity 75% vs. 64%, positive predictive value 100% vs. 78%, and negative predictive value 100% vs. 82%).

Discussion:

The main finding of the present study showed that for long-term response in ischemic and nonischemic cardiomyopathy, CRT requires the presence of myocardial viability. A direct relation between improvement in WMSI, assessed using low-dose dobutamine infusion, and the

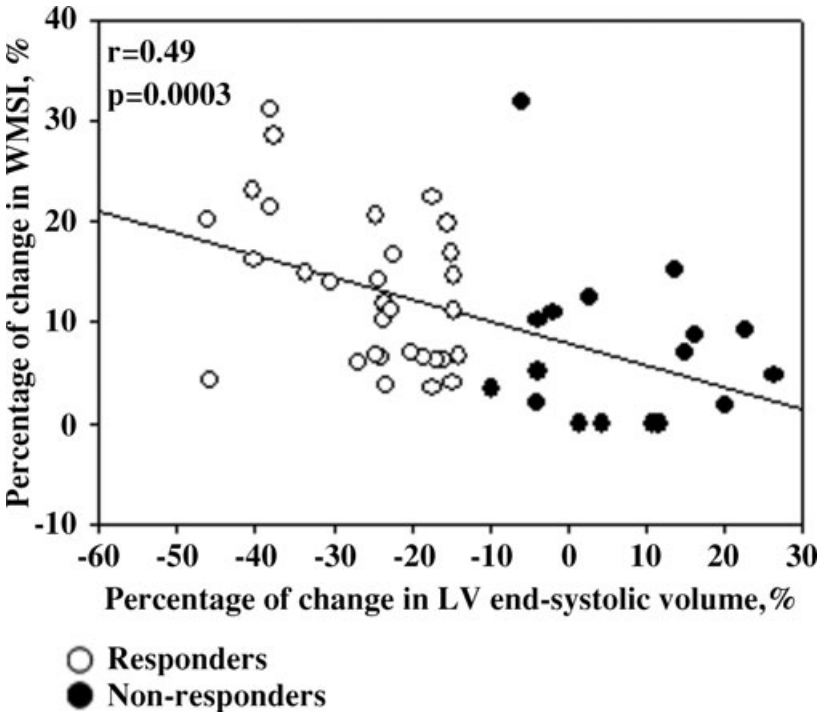

Figure 1. Correlation between changes in WMSI (rest/dobutamine) and changes in LV end systolic volume after CRT.

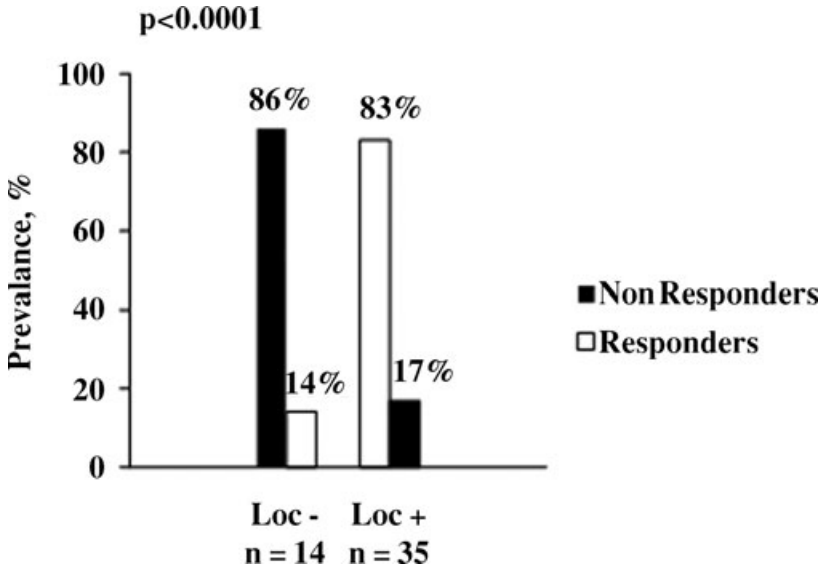

Figure 2. Percentage of responders to CRT based on the presence or absence of viability in the region of the pacing lead (local+/local −).

improvement in LV volume after CRT was observed. More importantly, our results suggest that for LV remodeling in patients with significant LV dyssynchrony, CRT requires the presence of myocardial viability in the LV lead target site. This underlines the importance of assessing viability before device implantation in order to guide LV lead positioning to ensure a pacing benefit.

Comparisons with Previous Studies:
Various studies have demonstrated that patients with QRS duration $\geq$ 120 ms and extensive baseline LV dyssynchrony have a high likelihood of response to CRT, whereas patients without baseline LV dyssynchrony do not respond to CRT. More recently, studies have evaluated the relation between myocardial viability and CRT. However, the results are scarce and patients included in those studies did not necessarily have significant intraventricular asynchronism. Using contrast-enhanced MRI, Bleeker et al.[20] demonstrated in 40 patients with ischemic cardiomyopathy that CRT did not reduce LV dyssynchrony when transmural scar tissue in the posterolateral LV segments is present. Only 14% of patients with posterolateral scar showed response to CRT. Even in the subset of patients with intra-ventricular asynchrony and posterolateral scar, the response rate was low (n = 2, 18%). Ypenburg et al. recently observed in 31 CRT patients that responders showed an increase in strain in the region of the pacing lead during low-dose dobutamine infusion while nonresponders had no contractile reserve.[17] Furthermore, Lim et al.,[16] demonstrated

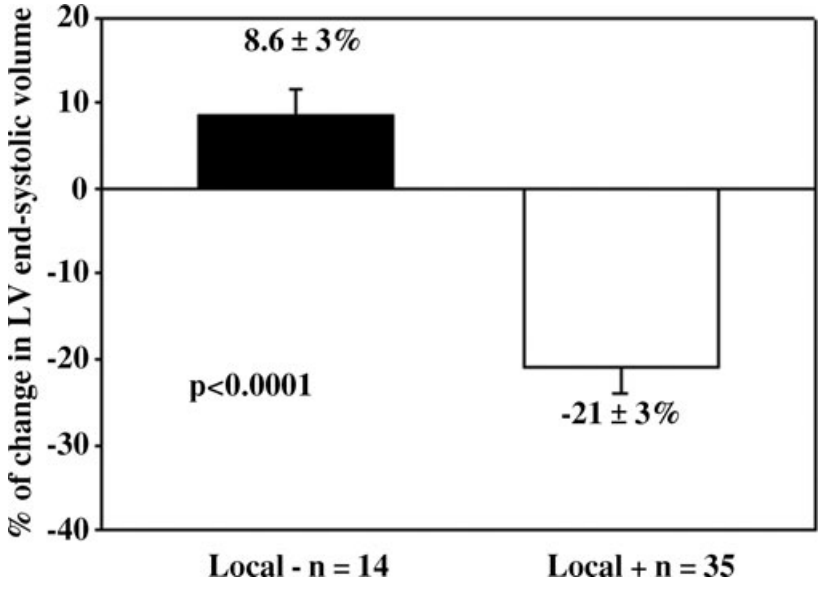

Figure 3. Changes in LV end systolic volume after CRT based on the presence of viability in the region of the pacing lead (local+/local −).

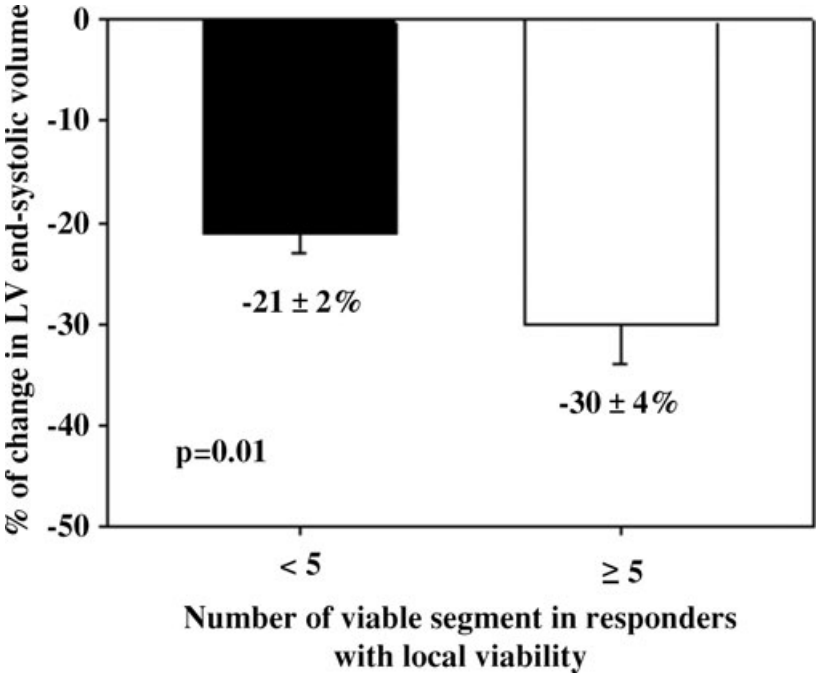

Figure 4. Changes in LV end systolic volume after CRT based on the number of viable segments (<5 vs. ≥5) in responders with viability on the region of the pacing lead.

that only patients (n = 19) with contractile reserve in the LV target site for pacing (lateral, posterolateral) presented a decrease in LV dyssynchrony with CRT. The authors also showed that the mean increase of LV stroke volume was greater in patients with contractile reserve (22% vs. 0%). In line with these results, the present study demonstrated that responders to CRT showed viability in the region of the pacing lead significantly more often than nonresponders. Of interest, 29 of 31 responders (94%) had viability in the region of the pacing lead. In the nonresponders group, 7 patients (39%) had $\geq$ 5 total viable segments (6.1 $\pm$ 1.5) in the absence of viability in the region of the pacing lead. Moreover, in the responders group, 16 patients (58%) had $\leq$ 5 total viable segments (4.3 $\pm$ 0.8) in the presence of viability in the region of the pacing lead. Therefore, it appears likely that viability of the paced segments is the crucial factor mediating the influence of viability (local viability vs. global) on response to CRT. However, in accordance with other studies concerning the relation between the burden of global viability and LV remodeling after CRT, responders with viability in the region of the pacing lead and with $\geq$ 5 total viable segments demonstrated a more important LV end-systolic reduction after CRT (30 $\pm$ 4% vs. 21 $\pm$ 2%, P = 0.01) than those with < 5 total viable segments (Fig. 4). In line with our results, Ypenburg et al.[15] evaluated and demonstrated that beside the presence of LV dyssynchrony, myocardial contractile reserve (resulting in $\geq$ 7.5% increase in LV ejection fraction during dobutamine infusion) predicts LV reverse remodeling and improvement in LV function, 6 months after CRT implantation. Another study[19] with 67 patients including 34% ischemic cardiomyopathy revealed that the presence of contractile myocardial reserve was an independent predictor of event-free survival after CRT. Using a cutoff value of 25% increase in dobutamine LV ejection fraction exhibits a sensitivity of 70% and a specificity of 62% for predicting major cardiac events. Hummel et al.,[18] in 21 CRT patients (100% ischemic), evaluated myocardial viability by myocardial contrast echocardiography. The LV systolic performance was assessed by echocardiography on the day after implantation. In that study, acute improvement in LV stroke volume was significantly correlated with the degree of viability as determined by the perfusion score index.

Mechanisms of LV Remodeling Following CRT: There are several potential mechanisms by which myocardial viability may influence LV remodeling following CRT. An intuitive explanation is that resynchronization reverses wasted work toward cardiac output only in viable segments where some potential for wall thickening exists. Akinetic regions that are largely nonviable contribute little to systolic performance, whether or not their relatively passive motion dyssynchronized. Also, slower conduction velocities through fibrotic region could preclude electrical resynchronization. In agreement with this hypothesis, in the study by Bleeker et al.,[20] patients with posterolateral scar did not show improvement on echocardiographic

parameters and LV dyssynchrony remained unchanged after CRT implantation. Our present results confirm earlier suggestions that the absence of viability in the region of the pacing lead may prohibit response to CRT; also the positive predictive value of echocardiographic response is high in presence of viability in the region of the pacing lead; moreover, in those patients, the magnitude of LV remodeling is clearly influenced by the burden of global viability. Of interest, in our study, the criterion used to define the presence of "significant" viability in the region of the LV pacing lead (presence of viability in 2 contiguous segments) is simple, rapid, and easily applicable in the context of clinical evaluation before CRT. This underlines the importance of assessing local viability in order to guide LV positioning. Region of myocardium without viability should be avoided as a final resting place for LV lead placement to maximize the possibility of therapeutic benefit.

Study Limitations:

Some limitations should be acknowledged. Our study contains only patients with current criteria for CRT implantation and significant LV dyssynchrony. The population studied was not completely homogenous since it was composed of patients with myocardial dysfunction of ischaemic and nonischemic origin. However, this represents our daily patients referred for CRT. Moreover, biventricular pacing is still a challenging therapy in both settings. Although, the accuracy of x-ray for assessing the lead position is imperfect, there was a good correlation between viability in the region of the pacing lead and response to CRT.

Conclusion:

In patients with heart failure and LV dyssynchrony, reverse remodeling after CRT requires viability in the region of the pacing lead. Identification of myocardial viability should therefore be routinely performed before CRT to guide LV pacing lead implantation and improve patient's prognosis.

References

1. Cazeau S, Leclercq C, Lavergne T, et al: Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. *N Engl J Med* 2001;344:873–880.
2. Auricchio A, Stellbrink C, Sack S, et al; Pacing Therapies I Congestive Heart Failure (PATH-CHF) Study Group: Long-term clinical effect of hemodynamically optimized cardiac resynchronization therapy in patients with heart failure and ventricular conduction delay. *J Am Coll Cardiol* 2002;39:2026–2033.
3. Higgins SL, Hummel JD, Niazi IK, et al: Cardiac resynchronization therapy for the treatment of heart failure in patients with intraventricular conduction delay and malignant ventricular arrhythmias. *J Am Coll Cardiol* 2003;42:1454–1459.
4. Abraham WT, Fisher WG, Smith AL, et al: MIRACLE Study Group. Multicenter insync randomized clinical evaluation. Cardiac resynchronization in chronic heart failure. *N Engl J Med* 2002;346:1845–1853.
5. Bristow MR, Saxon LA, Boehmer J, et al; Comparison of Medical Therapy, Pacing and Defibrillation in Heart Failure (COMPANION) Investigators: Cardiac resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. *N Engl J Med* 2004;350:2140–2150.
6. 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;352:1539–1549.
7. Tournoux FB, Alabiad C, Fan D, et al: Echocardiographic measure of acute haemodynamic response after cardiac resynchronization therapy predicts long term clinical outcome. *Eur Heart J* 2007;28:1143–1148.
8. Gorscan III J, Kanzaki H, Bazaz R, et al: Usefulness of echocardiographic tissue synchronization imaging to predict acute response to cardiac resynchronization therapy. *Am J Cardiol* 2004;93:1178–1181.
9. Bleeker GB, Mollema SA, Holman ER, et al: Left ventricular resynchronization is mandatory for response to cardiac resynchronization therapy: Analysis in patients with echocardiographic evidence of left ventricular dyssynchrony at baseline. *Circulation* 2007;116:1440–1448.
10. Ypenburg C, Schalij MJ, Bleeker GB, et al: Extent of viability to predict response to cardiac resynchronization therapy in ischemic heart failure patients. *J Nucl Med* 2006;47:1565–1570.
11. Henneman MM, Van Der Wall EE, Ypenburg C, et al: Nuclear imaging in cardiac resynchronization therapy. *J Nucl Med* 2007;48:2001–2010.
12. White JA, Yee R, Yuan X, et al: Delayed enhancement magnetic resonance imaging predicts response to cardiac resynchronization therapy in patients with intraventricular dyssynchrony. *J Am Coll Cardiol* 2006;48:1953–1960.
13. Bilchick RC, Dimaanov V, Wu KC, et al: Cardiac magnetic resonance assessment of dyssynchrony and myocardial scar predicts function class improvement following cardiac resynchronization therapy. *JACC Card Imaging* 2008;5:561–568.
14. Chalil S, Foley PWX, Muyhaldeen SA, et al: Late gadolinium enhancement-cardiovascular magnetic resonance as a predictor of response to cardiac resynchronization therapy in patients with ischaemic cardiomyopathy. *Europace* 2007;9:1031–1037.
15. 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;154:1160–1165.
16. Lim P, Bars C, Mitchell-Hegg L, et al: Importance of contractile reserve for CRT. *Europace* 2007;9:739–743.
17. Ypenburg C, Schalij MJ, Bleeker GB, et al: Impact of viability and scar tissue on response to cardiac resynchronization therapy in ischaemic heart failure patients. *Eur Heart J* 2007;28:33–41.
18. Hummel JP, Lindner JR, Belcik JT, et al: Extent of myocardial viability predicts response to biventricular pacing in ischemic cardiomyopathy. *Heart Rhythm* 2005;2:1211–1217.
19. Da Costa A, Thévenin J, Roche F, et al: Prospective validation of stress echocardiography as an identifier of cardiac resynchronization therapy responders. *Heart Rhythm* 2006;3:406–413.
20. Bleeker GB, Kaandorp TAM, Lamb JH, et al: Effect of posterolateral scar tissue on clinical and echocardiographic improvement after cardiac resynchronization therapy. *Circulation* 2006;113:969–976.
21. Zoghbi WA, Enriquez-Sarano M, Foster E, et al: Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler

echocardiography. *J Am Soc Echocardiogr* 2003;16:777–802.
22. 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;43:248–256.
23. deFilippi CR, Willett DL, Irani WN, et al: Comparison of myocardial contrast echocardiography and low-dose dobutamine stress echocardiography in predicting recovery of left ventricular function after coronary revascularization in chronic ischemic heart disease. *Circulation*. 1995;92:2863–2868.
24. Cigarroa CG, deFilippi CR, Brickner ME, et al: Dobutamine stress echocardiography identifies hibernating myocardium and predicts recovery of left ventricular function after coronary revascularization. *Circulation* 1993;88:430–436.
25. Schiller NB, Shah PM, Crawford M, et al: Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. *J Am Soc Echocardiogr*. 1989;2:358–367.
26. Butter C, Auricchio A, Stellbrink C, et al: Effect of resynchronization therapy stimulation site on the systolic function of heart failure patients. *Circulation* 2001;104:3026–3029.