JACC: CARDIOVASCULAR IMAGING VOL. 4, NO. 4, 2011

ISSN 1936-878X/$36.00

PUBLISHED BY ELSEVIER INC.

DOI:10.1016/j.jcmg.2011.01.010

Dependency of Cardiac Resynchronization Therapy on Myocardial Viability at the LV Lead Position

Michael Becker, MD,* Christian Zwicker, MD,* Markus Kaminski, MD,* Andreas Napp, MD,* Ertunc Altiok, MD,* Christina Ocklenburg, MSc,† Zvi Friedman, PhD,‡ Dan Adam, PhD,‡ Patrick Schauerte, MD,* Nikolaus Marx, MD,* Rainer Hoffmann, MD*

Aachen, Germany; and Haifa, Israel

OBJECTIVES This study sought to analyze the effectiveness of cardiac resynchronization therapy (CRT) related to the viability in the segment of left ventricular (LV) lead position defined by myocardial deformation imaging.

BACKGROUND Echocardiographic myocardial deformation analysis allows determination of LV lead position as well as extent of myocardial viability.

METHODS Myocardial deformation imaging based on tracking of acoustic markers within 2-dimensional echo images (GE Ultrasound, GE Healthcare, Horton, Norway) was performed in 65 heart failure patients (54 ± 6 years of age, 41 men) before and 12 months after CRT implantation. In a 16-segment model, the LV lead position was defined based on the segmental strain curve with earliest peak strain, whereas the CRT system was programmed to pure LV pacing. Nonviability of a segment (transmural scar formation) was assumed if the peak systolic circumferential strain was >−11.1%.

RESULTS In 47 patients, the LV lead was placed in a viable segment, and in 18 patients, it was placed in a nonviable segment. At 12-month follow-up there was greater decrease of LV end-diastolic volumes (58 ± 13 ml vs. 44 ± 12 ml, $p = 0.0388$) and greater increase of LV ejection fraction (11 ± 4% vs. 5 ± 4%, $p = 0.0343$) and peak oxygen consumption (2.5 ± 0.9 ml/kg/min vs. 1.7 ± 1.1 ml/kg/min, $p = 0.0465$) in the viable compared with the nonviable group. The change in LV ejection fraction and the reduction in LV end-diastolic volumes at follow-up correlated to an increasing peak systolic circumferential strain in the segment of the LV pacing lead ($r = 0.61$, $p = 0.0274$ and $r = 0.64$, $p = 0.0412$, respectively). Considering only patients with ischemic heart disease, differences between viable and nonviable LV lead position group were even greater.

CONCLUSIONS Preserved viability in the segment of the CRT LV lead position results in greater LV reverse remodeling and functional benefit at 12-month follow-up. Deformation imaging allows analysis of viability in the LV lead segment. (J Am Coll Cardiol Img 2011;4:366–74) © 2011 by the American College of Cardiology Foundation

From the *Department of Cardiology, RWTH Aachen University, Aachen, Germany; †Department of Medical Statistics, RWTH Aachen University, Aachen, Germany; and the ‡Department of Biomedical Engineering, Technion, Haifa, Israel. This study was supported by a research grant from the German-Israeli Foundation for Scientific Research and Development (GIF, I-873-77.10/2005). The authors have reported that they have no other relationships to disclose.

Manuscript received October 11, 2010; revised manuscript received January 3, 2011, accepted January 7, 2011.

Cardiac resynchronization therapy (CRT) is used for the treatment of advanced drug-refractory heart failure of ischemic and nonischemic origin (1–5). However, up to one-third of patients do not respond to CRT using standard clinical selection criteria (5,6). Factors influencing the patient's response to CRT are not completely understood. Echocardiographic parameters suggested to evaluate mechanical dyssynchrony and predict CRT success have not been confirmed in a large multicenter study (7–9). Technical and procedural factors such as optimal left ventricular (LV) lead placement seem to have an important impact. Butter et al. (10) demonstrated in an experimental analysis that the LV lead should be placed in the area of greatest delay in mechanical contraction and electrical activation to achieve the optimal resynchronization effect. Clinical studies confirmed that concurrence of the LV lead position and the LV segment with latest contraction before CRT results in significantly better effectiveness of CRT on LV function and clinical outcome (11,12). Ischemic etiology of heart failure has been identified as a predictor of impaired responsiveness (13). The extent of scar tissue has been shown to define the response to CRT (14–17). The response to CRT may thus be directly related to the extent of myocardial viability in the area of the LV lead and nonresponse in ischemic heart failure may be the consequence of the LV lead being positioned in a scarred segment without functional capacity.

See page 375

Myocardial deformation imaging can be used to define CRT LV lead position and determine myocardial viability. Temporal analysis of segmental myocardial deformation curves has been shown to allow definition of LV lead position (11,18). The magnitude of peak segmental myocardial strain closely relates to segmental viability (19,20).

This study sought to determine CRT effectiveness related to the viability of the segment with the LV lead position as well as the area surrounding the LV lead segment. Viability was defined by analysis of myocardial deformation.

METHODS

Patients. We included in this study 65 consecutive patients (mean age 55 ± 4 years, 39 men) with end-stage heart failure severe LV systolic dysfunction (ejection fraction [EF] <35%), scheduled for new implantation of a biventricular pacemaker. Patients had to be in New York Heart Association functional class III (n = 48) or IV (n = 17) despite optimal pharmacologic therapy and show sinus rhythm with a QRS interval duration >120 ms. Etiology of heart failure was ischemic in 46 patients and nonischemic in 19 patients based on coronary angiography. No studies to assess myocardial viability were performed before CRT implantation. This study was approved by the local ethical committee and all subjects gave written informed consent.

Biventricular device implantation. The LV pacing lead was inserted by a transvenous approach through the coronary sinus into a cardiac vein of the free wall. An average of 2.1 veins were tried intraoperatively to achieve an optimal LV lead position. Optimal LV lead position was considered to be when the width of the QRS complex was minimized and the arterial systolic pressure increased. No information about presence of myocardial viability or area of latest activation was provided intraoperatively. The right atrial and ventricular leads were positioned conventionally. All patients received a biventricular cardioverter-defibrillator (Attain-System with InSync Marquis, Medtronic, Minneapolis, Minnesota [n = 40] or Aesula-System with Epic HF V-339, St. Jude Medical, St. Paul, Minnesota [n = 25]).

Post-operatively the optimal atrioventricular time was determined by Doppler echocardiography and set between 100 and 150 ms (mean time 122 ± 10 ms) in 61 patients and between 70 and 85 ms (mean time 75 ± 8 ms) in 4 patients. The ventriculo-ventricular time was set to 0 in all patients. Thresholds for sensing and pacing of the LV lead at the final position were documented.

To exclude LV lead dislocation and change of AV time, the device was controlled at 6- and 12-month follow-up. Seven days after implantation of the CRT system, transient programming of the device to pure LV pacing was performed during an echocardiographic examination to determine the LV lead position.

Echocardiography. All studies were performed before CRT, one day after implantation, and at 12 (± 3)-month follow-up using a Vivid Seven digital ultrasound scanner (General Electric, Horton, Norway). Using apical 4- and 2-chamber views, LVEF and left ventricular end-diastolic volume (LVEDV) were determined employing biplane Simpson method. The physician performing the echocardio-

ABBREVIATIONS AND ACRONYMS

CRT = cardiac resynchronization therapy

EF = ejection fraction

LV = left ventricle/ventricular

LVEDV = LV end-diastolic volume

ROC = receiver-operator characteristic

VO_2max = peak oxygen consumption

graphic analyses was blinded to the physician performing the LV lead placement.

Analysis of myocardial deformation. For analysis of LV myocardial deformation, the 16-segment model was applied on 3 parasternal short-axis views: 6 segments each on the basal and on the papillary muscle levels and 4 segments on the apical level. The frame rate was between 56 and 92 frames/s, the focus was adjusted to the center of the LV cavity for optimized characterization of myocardial tissue. Using 2 consecutive cardiac cycles, myocardial deformation analysis was performed offline with the aid of a customized software package (EchoPAC BT 05.2, General Electric). This software follows acoustic markers within the myocardium during several consecutive frames (21) and calculates mean strain values for whole pre-defined LV segments (22). It is assumed that these natural acoustic markers change their position from frame to frame in accordance with the surrounding tissue motion. Visual control of width between endocardial and pericardial trace as well as tracking quality was performed to ensure accurate analysis. End-systole was determined in the apical long-axis view as aortic valve closure. The time difference from the QRS complex was transferred to the other views. The focus was adjusted to the center of the LV cavity to optimize myocardial speckle characteristics of all segments.

Circumferential strain relates to circumferential deformation along the LV curvature. It is calculated as mean over the whole segment. Myocardial deformation analysis was used to define the LV lead position. The LV lead position was defined as the segment with the earliest peak on the segmental strain curve analysis, whereas the CRT system was programmed to pure LV pacing (18).

Viability of LV segments was determined based on the segmental peak systolic circumferential strain before CRT implantation. This information was not provided to the physician performing the implantation procedure. A peak systolic circumferential strain ≤−11.1% was considered to indicate myocardial viability (no scar or nontransmural scar), whereas a peak systolic circumferential strain >−11.1% was considered to indicate nonviability (transmural scar formation) as shown before (19) (Fig. 1). In addition, viability of the adjacent segments of the LV lead position segment was evaluated. This assessment was based on application of a 16-segment LV model. There were 4 adjacent segments in case of midventricular LV lead position and 3 adjacent segments in case of basal or apical LV lead position. Viability of the surrounding area of the LV lead segment was defined as viability in at least 3 adjacent segments in case of midventricular LV lead position, and as viability in at least 2 adjacent segments in case of basal or apical LV lead position.

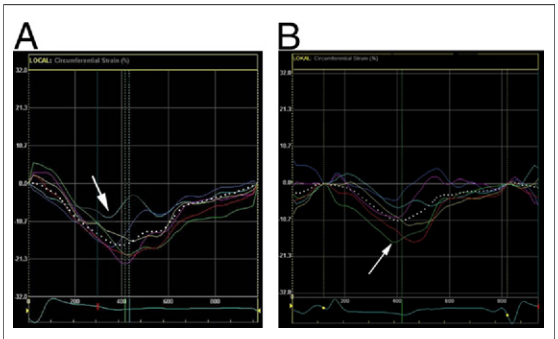

Figure 1. CS Tracings Related to CRT Response

(A) Circumferential strain (CS) tracings during left ventricular (LV) pacing. The anterior segment at the mid-ventricular level showed earliest peak strain among all 16 segments and was defined as LV lead position. The segment was defined as nonviable, as the peak CS was –9.8% and, therefore, less than the viability cutoff value of >−11.1%. This patient was a nonresponder to cardiac resynchronization therapy (CRT) (increase of left ventricular ejection fraction [LVEF] 2% and reduction of left ventricular end-diastolic volume [LVEDV] 18 ml). **(B)** The lateral segment at the mid-ventricular level was defined as LV lead position and as viable (peak CS = –17.2%). This patient was a responder to CRT (increase of LVEF 8% and reduction of LVEDV 44 ml).

Peak oxygen consumption. Patients underwent bicycle cardiopulmonary exercise testing (10 W per min increments) at baseline and after 12 (±3) months of CRT. The peak oxygen consumption (VO_2max) at peak exercise was defined as the highest oxygen consumption measured during the symptom-limited exercise test and expressed as ml/kg/min.

Statistics. Continuous data are expressed as mean ± SD and have been compared using Student *t* test or analysis of variance as appropriate. Pearson correlation coefficient was determined and linear regression analysis was performed to define the relationship between parameters with continuous data. Categorical data are presented as frequencies and were compared with Pearson chi-square test. The receiver-operator characteristics (ROC) curve for peak circumferential systolic strain in the segment of the LV pacing lead was examined to define the optimal cutoff for prediction of CRT response. The area under ROC curve was calculated. A p value of <0.05 was considered statistically significant.

RESULTS

Baseline characteristics. Clinical baseline characteristics of all patients related to viability in the segment of the LV pacing lead are given in Table 1. There were no significant differences in patient characteristics as well as medication. Myocardial deformation analysis could be performed in 946 of 1,040 segments. Based on analysis of segmental peak circumferential strain, 683 segments were found to be viable and 263 segments were found to be nonviable.

LV lead position. The LV lead position was defined considering the segment with earliest peak strain during pure LV pacing as follows: 18 anterior (10 basal, 8 medial), 29 lateral (17 basal, 9 medial, 3 apical), 12 posterior (5 basal, 7 medial), and 6 inferior (4 basal, 2 apical).

Impact of myocardial viability at LV lead position. Forty-seven patients were found to have preserved viability at the LV pacing lead segment and 18 patients had not. Within these segments, mean peak systolic circumferential strain was −14.8 ± 2.9% and −8.3 ± 2.6%, respectively. Sensing thresholds were 19 ± 6 mV and 13 ± 4 mV for LV leads positioned in viable and nonviable segments, respectively ($p = 0.042$). Pacing thresholds were 1.6 ± 0.4 V and 2.4 ± 0.5 V for LV leads positioned in viable and nonviable segments, respectively ($p = 0.059$). Comparison of baseline results and results obtained at 12 months after CRT implantation demonstrated a greater increase in LVEF (ΔLVEF 11 ± 4% vs. 5 ± 4%, $p = 0.0343$), reverse remodeling (ΔLVEDV 58 ± 13 ml vs. 44 ± 12 ml, $p = 0.0388$), and peak oxygen consumption (ΔVO_2max 2.5 ± 0.9 ml/kg/min vs. 1.7 ± 1.1 ml/kg/min, $p = 0.0465$) for patients with the LV pacing lead placed in a viable segment compared with the nonviable group (Table 2).

The change in LVEF and the reduction in LVEDV at 12-month follow-up correlated to an increasing peak systolic circumferential strain in the segment of the LV pacing lead ($r = 0.61$, $p = 0.0274$ and $r = 0.64$, $p = 0.0412$, respectively) (Fig. 2). Patients with an improvement in LVEF of ≥5% were classified as responders. Referring to this definition, 5 (of 47) patients in the viable and 15 (of 18) patients in the nonviable LV pacing lead region were nonresponders to CRT.

The ROC analysis for prediction of CRT response considering the peak systolic circumferential strain in the segment of the LV pacing lead demonstrated a cutoff value of −11.9%. The area under the curve was 0.757 (95% confidence interval: 0.693 to 0.818). Considering this cutoff value for peak systolic circumferential strain, sensitivity and specificity to predict CRT response were 73% and 77%, respectively.

There was an incremental increase in EF as well as decrease in LVEDV dependent on viability of the LV lead segments as well as viability of the surrounding area. Whereas changes in EF and LVEDV were lowest if the LV lead segment as well as the surrounding area were nonviable, changes in EF and LVEDV were greatest if the LV lead segment as well as the surrounding area were viable (Fig. 3). Considering viability of the total LV, there was a correlation between amount of total LV viability and change in EF as well as LVEDV at follow-up. The greater the amount of viability of the LV was, the greater was found to be the increase in EF as well as the decrease in LVEDV (Fig. 4).

Impact of viability in patients with ischemic cardiomyopathy. Considering only the 46 patients with ischemic cardiomyopathy, there were 32 patients with the LV lead being placed in a viable segment and 14 patients with the LV lead being placed in a nonviable segment. The difference between patients with the LV lead being placed in a viable or a nonviable segment was more pronounced than when considering all patients (Table 3). Considering the 46 patients with ischemic car-

Table 1. Patient Characteristics at Baseline Before CRT Related to Viability in the LV Lead Segment

	LV Lead Segment		
	Viable (n = 47)	Nonviable (n = 18)	p Value
Age, yrs	54 ± 5	53 ± 7	0.642
Men	28 (59%)	11 (61%)	0.478
Ischemic cardiomyopathy	33 (71%)	13 (74%)	0.297
QRS duration, ms	160 ± 9	159 ± 10	0.329
NYHA functional classification	3.2 ± 0.5	3.2 ± 0.7	0.451
LVEDV, ml	311 ± 81	306 ± 86	0.352
VO_2max, ml/kg/min	13.7 ± 1.5	13.5 ± 1.6	0.628
LVEF, %	31 ± 4	30 ± 6	0.337
Concomitant therapy			
ACE inhibitors	37 (78%)	13 (74%)	0.427
ARBs	9 (19%)	3 (16%)	0.683
Beta-blockers	42 (90%)	16 (88%)	0.559
Digitalis	15 (31%)	6 (34%)	0.673
Diuretics	21 (45%)	8 (46%)	0.548
Aldosterone antagonists	30 (64%)	11 (61%)	0.281

The LV lead position was defined with myocardial deformation imaging during pure LV pacing.
ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blockers; LVEDV= left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; VO_2max = peak oxygen consumption.

Table 2. LVEF, LVEDV, and VO_2max Before CRT and at 12-Month Follow-Up for Patients With Viable or Nonviable LV Lead Segment

	LV Lead Position Determined During Pure LV Pacing
LVEF, %	
Viable segment of LV lead position	
Baseline LVEF	31 ± 5
Follow-up LVEF	42 ± 6
ΔLVEF	11 ± 4
Nonviable segment of LV lead position	
Baseline LVEF	30 ± 7
Follow-up LVEF	35 ± 6
ΔLVEF	5 ± 4
Difference in ΔLVEF	
(viable – nonviable group)	6.0
(95% CI)	(2.5–7.9)
p value for ΔLVEF (viable vs. nonviable group)	0.0343
LVEDV, ml	
Viable segment of LV lead position	
Baseline LVEDV	321 ± 54
Follow-up LVEDV	263 ± 62
ΔLVEDV	58 ± 13
Nonviable segment of LV lead position	
Baseline LVEDV	316 ± 59
Follow-up LVEDV	272 ± 60
ΔLVEDV	44 ± 12
Difference in ΔLVEDV	
(viable – nonviable group)	14.0
(95% CI)	(8.6–16.3)
p value for ΔLVEDV (viable vs. nonviable group)	0.0388
VO_2max, ml/kg/min	
Viable segment of LV lead position	
Baseline VO_2max	13.4 ± 1.3
Follow-up VO_2max	15.9 ± 1.6
Δ VO_2max	2.5 ± 0.8
Nonviable segment of LV lead position	
Baseline VO_2max	13.4 ± 1.3
Follow-up VO_2max	15.1 ± 1.5
Δ VO_2max	1.7 ± 1.1
Difference in Δ VO_2max, ml/kg/min	
(viable – nonviable group)	1.0
(95% CI)	(0.4–1.8)
p value for ΔVO_2max (viable vs. nonviable group)	0.0465

The LV lead position was defined with myocardial deformation imaging during pure LV pacing.
CI = confidence interval; other abbreviations as in Table 1.

diomyopathy, the distribution was as follows: 33 patients were classified as responder (3 of 14 patients in the nonviable group and 30 of 32 patients in the viable group), and 13 patients were classified as nonresponders. In nonischemic cardiomyopathy, the difference in ΔLVEF and ΔLVEDV at follow-up between patients with the LV lead being placed in a segment with circumferential strain >−11.1% or ≤−11.1% tended to be less (ΔLVEF = 5.0% and ΔLVEDV = 11.4%).

DISCUSSION

The major findings of this study are the following: 1) preserved viability in the segment of the LV lead position results in greater LV reverse remodeling and functional benefit at 12-month follow-up; 2) there is incremental CRT effectiveness with preserved viability of the LV pacing lead segment as well as the surround segments; and 3) considering only patients with ischemic cardiomyopathy, the influence of viability of the LV lead segment is pronounced.

Optimal LV lead position in CRT. Several studies have demonstrated that a significant rate of patients do not respond positively to CRT using standard selection criteria (1–3). Technical factors such as an optimal LV pacing site have been identified as important parameters to determine the success of

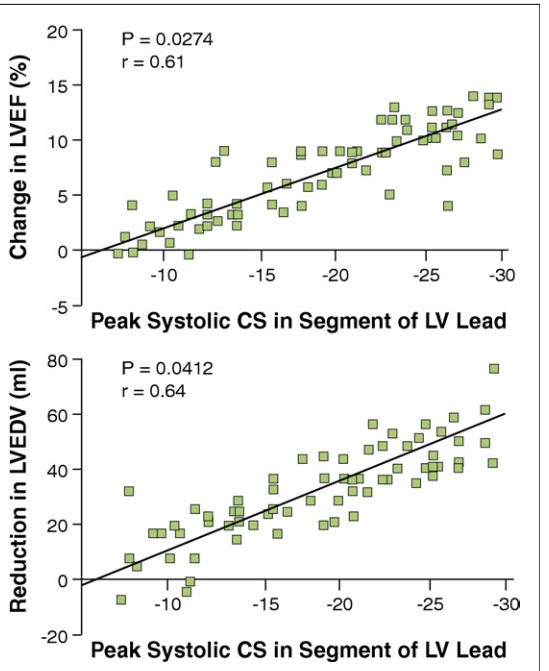

Figure 2. Change in LV Function Related to CS at Baseline

(A) Increase in LVEF from baseline to 12-month follow-up related to peak systolic CS in the segment of the LV pacing lead. The LV lead segment was defined as the segment with earliest peak systolic CS during pure LV pacing. **(B)** Reduction in LVEDV from baseline to 12-month follow-up related to peak systolic CS in the segment of the LV pacing lead. Abbreviations as in Figure 1.

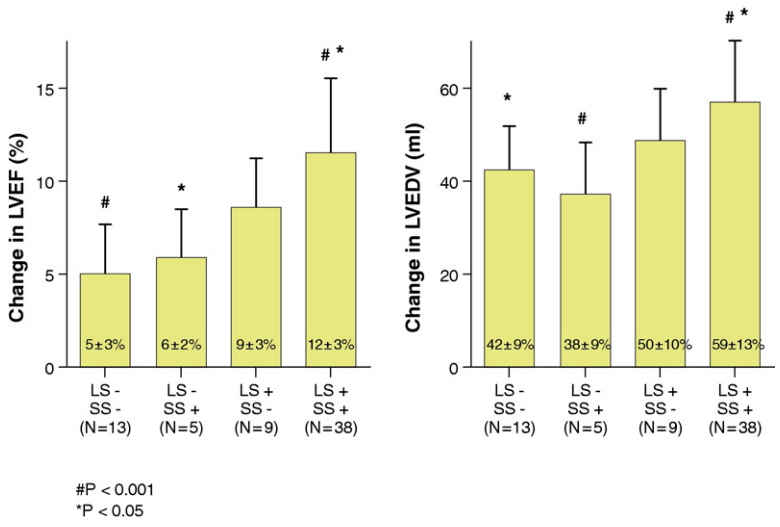

Figure 3. Change in LV Function and Volumes Related to Viability

Increase in LVEF and reduction in LVEDV related to viability (+: viability,−: no viability) of LV segment with assumed LV lead position (LS) and viability of surrounding segments (SS). #p < 0.001; *p < 0.05. Abbreviations as in Figure 1.

CRT. Experimental data suggested placing the LV lead in the area of the latest contraction before CRT (10). Clinical studies confirmed the importance of optimal LV lead placement site, demonstrating improved exercise tolerance, greater improvement in LV function, and better outcome for patients with concordance of LV lead position to site of latest contraction before CRT (11,12). Different imaging techniques have been used to define the LV lead site. Fluoroscopy has been used in a large study demonstrating differences in patient outcome depending on the LV lead site defined by fluoroscopy (12). However, because of the limited fluoroscopic views applied in clinical studies, the segmental definition of the lead position is con-

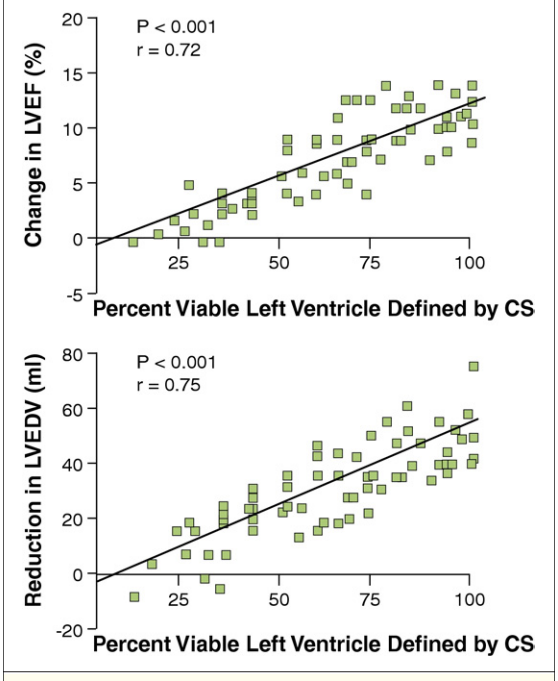

Figure 4. LV Viability and Follow-Up Change in LV Function and Volumes

Correlation between percentage of viable segments determined by myocardial deformation analysis (peak systolic circumferential strain ≤–11.1%) and effectiveness of CRT defined as increase in LVEF **(A)** and reduction in LVEDV **(B)**. Abbreviations as in Figure 1.

Table 3. Comparison of Baseline to 12-Month Follow-Up Results (LVEF, LVEDV, and VO_2max) Considering Only Patients With Ischemic Cardiomyopathy (n = 46)

	LV Lead Position Determined During Pure LV Pacing
Difference in ΔLVEF, %	
(viable – nonviable group)	7.0
(95% CI)	(3.7–9.8)
p value for ΔLVEF (viable vs. nonviable)	<0.001
Difference in ΔLVEDV, ml	
(viable – nonviable group)	16.0
(95% CI)	(11.3–19.7)
p value for ΔLVEDV (viable vs. nonviable)	<0.001
Difference in ΔVO_2max, ml/kg/min	
(viable – nonviable group)	1.4
(95% CI)	(0.6–2.6)
p value for ΔVO_2max (viable vs. nonviable)	<0.001

Abbreviations as in Tables 1 and 2.

fined. Techniques based on myocardial deformation imaging have been shown to allow improved definition of LV lead position (11,18). In this study, we used a technique that defines the LV lead position as the segment with earliest mechanical activity during pure LV pacing. It has been demonstrated to provide facilitated access to the LV pacing site (18).

Impact of viability on response to CRT. It has also been suggested that the extent of scar tissue as well as the extent of viable myocardium are important factors defining the response to CRT (14–17). Bleeker et al. (23) suggested that pacing the LV in nonviable or scared myocardium results in a less optimal response to CRT. Some studies have found global extent of LV scar to be important (15,16), whereas other studies found the size of septal or lateral scar significant (17). A study by Ypenburg et al. (17) demonstrated a direct association between viability determined by gated single-photon emission computed tomography and response to CRT. The increase in LV function and the decrease of LV end-systolic and end-diastolic volumes at 6-month follow-up were linearly related to the extent of viability. Additionally, the extent of scar tissue was also important for the response to CRT as reflected by an inverse relation between the scar tissue and the change in LV function and LV volumes.

In an echocardiographic study, transmural scar was diagnosed based on measurement of an end-diastolic wall thickness ≤0.5 cm associated with increased tissue acoustic reflectance (24). The echocardiographic extent of scar tissue was significantly associated with LV reverse remodeling. The greater the pre-implant myocardial scar tissue, the lower the reverse remodeling effect of CRT. This is in line with results by Mangiavacchi et al. (25), who reported that the number of scar segments evaluated by echocardiography was less in CRT responders than in nonresponders. However, these studies did not specifically focus on myocardial viability of the LV pacing segment.

In the present study, a peak systolic circumferential strain of ≤−11.1% was used to define segmental myocardial viability. This value was determined in a recent study and had a sensitivity of 70% and a specificity of 71% to detect transmural myocardial infarction defined by magnetic resonance imaging (19). In this study, we evaluated LV volumes and functional capacity at baseline and at 12 months after CRT implantation related to viability of the LV lead segment. A greater increase in LVEF, reverse remodeling, and peak oxygen consumption could be demonstrated for patients with viability at the LV pacing lead position versus patients in the nonviable group. Furthermore, the improvement in LVEF and the reduction in LVEDV correlated to an increasing peak systolic circumferential strain in the region of LV pacing lead as a marker of increasing viability. The similarity of the cutoff value found in the ROC analysis on peak systolic circumferential strain in the segment with the LV pacing lead for prediction of CRT response to a previously reported cutoff value for circumferential strain to predict myocardial viability (19) stresses the importance of myocardial viability at the LV lead position for CRT effectiveness.

The results on importance of myocardial viability for CRT effectiveness are consistent to results by Mangiavacchi et al. (25) as well as Chalil et al. (26), who reported an association between increasing extent and transmurality of scar and poor response to CRT. Patients with scar transmurality of ≥52% showed only one-half symptomatic responder rate (improvement was New York Heart Association functional class ≥1 or 6-min walking distance ≥25%) observed in patients with a scar transmurality of ≤51%. Considering the results of these studies, there may be a limit of scar size beyond which resynchronization becomes ineffective. Several factors might contribute to this finding: 1) a substantial amount of viable myocardium is needed for improvement in systolic LV function after CRT, whereas scar tissue does not contract; 2) pacing of scar tissue is likely to result in suboptimal resynchronization of the neighboring myocardium as electrical conduction is delayed. Evaluation of the extent and location of scar tissue should be considered in the selection process for CRT to avoid nonresponse, especially for the area of latest contraction as optimal segment for the LV lead placement.

Study limitations. Because there was an insufficient number of echocardiographic images, myocardial deformation parameters for analysis of myocardial viability and optimal location for LV lead could not be determined in 9% of segments. Thus, the segment with assumed LV lead position may have been missed in some patients. However, this should not have affected the principle findings of this study.

The location of the LV lead was determined based on the assumption that the electric current of the LV lead will affect the nearest segment strongest and first. This assumption was affirmed before

by a high match in the LV lead position determined by fluoroscopy (11).

There are potential difficulties of speckle tracking imaging. Circumferential strain values may be impaired owing to very tight coronary stenosis (>90%) inducing acute myocardial ischemia (27). This study focused on analysis of circumferential strain. This focus considered former analysis demonstrating superiority of circumferential strain to longitudinal motion analysis in terms of adequate demonstration of CRT benefit (28).

The analysis approach used in this study may simplify the complexity of many factors having an impact on CRT effectiveness. This relates in particular to technical and procedural factors that are not all considered. However, myocardial viability, optimal location of LV lead position, and actual LV lead position are 3 important factors that influence CRT effectiveness, and the applied analysis gives access to all 3 parameters using 1 modality. The study was not intended to analyze differences between ischemic and nonischemic cardiomyopathies. This study found a more pronounced impact of viability in patients with ischemic heart disease but further studies should address this issue within proportionate subgroups. The viability cutoff value defined for ischemic cardiomyopathy was applied also to patients with nonischemic cardiomyopathy. However, as the definition of viability based on deformation analysis relates to functional capacity, application of the same cutoff value for nonischemic cardiomyopathy to predict functional response to CRT should be a valid approach.

CONCLUSIONS

Myocardial deformation imaging provides information on LV lead position and myocardial viability. Preserved viability in the segment of the LV lead results in greater LV reverse remodeling and functional benefit at 12-month follow-up. The impact of viability in the LV lead position is particularly pronounced in patients with ischemic heart disease.

Reprint requests and correspondence: Dr. Rainer Hoffmann, Medical Clinic I, RWTH Aachen University, Pauwelsstrasse 30, 52057 Aachen, Germany. *E-mail: rhoffmann@UKAACHEN.de.*

REFERENCES

1. Cleland JG, Daubert JC, Erdmann E, et al., for CARE-HF Study Investigators. The effect of cardiac resynchronization on morbidity and mortality in heart failure. N Engl J Med 2005;352:1539–49.
2. Abraham WT, Fisher WG, Smith AL, et al, for MIRACLE Study Group. Multicenter InSync Randomized Clinical Evaluation. Cardiac resynchronization in chronic heart failure. N Engl J Med 2002;346:1845–53.
3. Linde C, Leclercq C, Rex S, et al. Long-term benefits of biventricular pacing in congestive heart failure: results from the multisite stimulation in cardiomyopathy (MUSTIC) study. J Am Coll Cardiol 2002;40:111–8.
4. Auricchio A, Stellbrink C, Sack S, et al., for 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;39:2026–33.
5. Bristow MR, Saxon LA, Boehmer J, et al., for COMPANION Investigators. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med 2004;350:2140–50.
6. Young JB, Abraham WT, Smith AL, et al., for MIRACLE ICD Trial Investigators. Combined cardiac resynchronization and implantable cardioversion defibrillation in advanced chronic heart failure: the MIRACLE ICD trial. JAMA 2003;289:2685–94.
7. Penicka M, Bartunek J, De Bruyne B, et al. Improvement of left ventricular function after cardiac resynchronization therapy is predicted by tissue Doppler imaging echocardiography. Circulation 2004;109:978–83.
8. 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.
9. Chung ES, Leon AR, Tavazzi L, et al. Results of the Predictors of Response to CRT (PROSPECT) trial. Circulation 2008;117:2608–16.
10. Butter C, Auricchio A, Stellbrink C, et al., for Pacing Therapy for Chronic Heart Failure II Study Group. Effect of resynchronization therapy stimulation site on the systolic function of heart failure patients. Circulation 2001;104:3026–9.
11. Becker M, Kramann R, Franke A, et al. Impact of left ventricular lead position in cardiac resychronization therapy on left ventricular remodeling. A circumferential strain analysis based on 2D echocardiography. Eur Heart J 2007;28:1211–20.
12. Ypenburg C, Van Bommel RJ, Delgado V, et al. Optimal left ventricular lead position predicts reverse remodeling and survival after cardiac resynchronization therapy. J Am Coll Cardiol 2008;52:1402–9.
13. Díaz-Infante E, Mont L, Leal J, et al., for SCARS Investigators. Predictors of lack of response to resynchronization therapy. Am J Cardiol 2005;95:1436–40.
14. Hummel JP, Lindner JR, Belcik JT, et al. Extent of myocardial viability predicts response to biventricular pacing in ischemic cardiomyopathy. Heart Rhythm 2005;2:1211–7.
15. 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.
16. Buch E, Lellouche N, De Diego C, et al. Left ventricular apical wall motion abnormality is associated with lack of response to cardiac resynchronization therapy in patients with ischemic cardiomyopathy. Heart Rhythm 2007;4:1300–5.

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. Becker M, Altiok E, Ocklenburg C, et al. Analysis of left ventricular lead position in cardiac resynchronization therapy using different imaging modalities. J Am Coll Cardiol Img 2010; 3:472–81.
19. Becker M, Hoffmann R, Kuehl H, et al. Analysis of myocardial deformation based on ultrasonic pixel tracking to determine transmurality in chronic myocardial infarction. Eur Heart J 2006;27:2560–6.
20. Hanekom L, Jenkins C, Jeffries L, et al. Incremental value of strain rate analysis as an adjunct to wall-motion scoring for assessment of myocardial viability by dobutamine echocardiography: a follow-up study after revascularization. Circulation 2005;112: 3892–3900.
21. Reisner S, Lysyansky P, Agmon Y, Mutlak D, Lessick J, Friedman Z. Global longitudinal strain: a novel index of left ventricular systolic function. J Am Soc Echocardiogr 2004;17: 630–3.
22. Leitman M, Lysyansky P, Sidenko S, et al. Two-dimensional strain-a novel software for real-time quantitative echocardiographic assessment of myocardial function. J Am Soc Echocardiogr 2004;17:1021–9.
23. Bleeker GB, Kaandrop TAM, Lamb HJ, et al. Effect of posterolateral scar tissue on clinical and echocardiographic improvement after cardiac resynchronization therapy. Circulation 2006;113:969–76.
24. Mele D, Agricola E, Galderisi M, et al. Echocardiographic myocardial scar burden predicts response to cardiac resynchronization therapy in ischemic heart failure. J Am Soc Echocardiogr 2009;22:702–8.
25. Mangiavacchi M, Gaspaarini M, Faletra F, Klersy C, Morenghi E, Galimberti P. Clinical predictors of marked improvement in left ventricular performance after cardiac resynchronization therapy in patients with chronic heart failure. Am Heart J 2006;151:477,e1–6.
26. Chalil S, Stegemann B, Muhyaldeen SA, et al. Effect of posterolateral left ventricular scar on mortality and morbidity following cardiac resynchronization therapy. Pacing Clin Electrophysiol 2007;30:1201–9.
27. Reant P, Labrousse L, Lafitte S, et al. Experimental validation of circumferential, longitudinal, and radial 2-dimensional strain during dobutamine stress echocardiography in ischemic conditions. J Am Coll Cardiol 2008;51:149–57.
28. 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.

Key Words: cardiac resynchronization therapy ■ echocardiography ■ heart failure ■ left ventricular function ■ myocardial deformation imaging.