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Clinical Application of Echocardiographic Findings

Cardiac Resynchronization Therapy Tailored by Echocardiographic Evaluation of Ventricular Asynchrony

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OBJECTIVES The value of interventricular and intraventricular echocardiographic asynchrony parameters in predicting reverse remodeling after cardiac resynchronization therapy (CRT) was investigated.

BACKGROUND Cardiac resynchronization therapy has been suggested as a promising strategy in patients with severe heart failure and left bundle branch block (LBBB), but the entity of benefit is variable and no criteria are yet available to predict which patients will gain.

METHODS Interventricular and intraventricular mechanical asynchrony was evaluated in 20 patients (8 men and 12 women, 63 ± 10 years) with advanced heart failure caused by ischemic (n = 4) or nonischemic dilated cardiomyopathy (n = 16) and LBBB (QRS duration of at least 140 ms) using echocardiographic Doppler measurements. Left ventricular end-diastolic volume index (LVEDVI) and left ventricular end-systolic volume index (LVESVI) were calculated before and one month after CRT. Patients with a LVESVI reduction of at least 15% were considered as responders.

RESULTS Cardiac resynchronization therapy significantly improved ventricular volumes (LVEDVI from 150 ± 53 ml/m^2 to 119 ± 37 ml/m^2, $p < 0.001$; LVESVI from 116 ± 43 ml/m^2 to 85 ± 29 ml/m^2, $p < 0.0001$). At baseline, the responders had a significantly longer septal-to-posterior wall motion delay (SPWMD), a left intraventricular asynchrony parameter; only QRS duration and SPWMD significantly correlated with a reduction in LVESVI ($r = -0.54$, $p < 0.05$ and $r = -0.70$, $p < 0.001$, respectively), but the accuracy of SPWMD in predicting reverse remodeling was greater than that of the QRS duration (85% vs. 65%).

CONCLUSIONS In patients with advanced heart failure and LBBB, baseline SPWMD is a strong predictor of the occurrence of reverse remodeling after CRT, thus suggesting its usefulness in identifying patients likely to benefit from biventricular pacing. (J Am Coll Cardiol 2002;40:1615–22) © 2002 by the American College of Cardiology Foundation

Chamber enlargement in patients with chronic heart failure is often associated with asynchrony between right and left ventricular contractions and within the left ventricle. Late contraction of the left free wall gives rise to a further worsening of hemodynamic function (1,2), which contributes to the development of ventricular remodeling (3). It has been suggested that cardiac resynchronization therapy (CRT), which involves the simultaneous stimulation of the right ventricle and left free wall, reduces left ventricular volumes and increases the ejection fraction (4–7). However, the response in terms of reverse remodeling (7) and clinical benefit (6–9) is heterogeneous and difficult to predict (7,10–12).

Given the mechanisms by which resynchronization therapy works, it can be speculated that the greater the asynchrony, the greater the benefit. In clinical practice, a prolonged QRS duration and, in particular, complete left bundle branch block (LBBB) are regarded as the index of ventricular asynchrony, guiding patient selection for CRT (13). However, LBBB may not be precise enough to reflect interventricular or intraventricular mechanical asynchrony accurately and, if this is the case, the use of imaging techniques to visualize ventricular asynchrony may do better in identifying patients who will show reverse remodeling.

The aim of this prospective study was to evaluate whether interventricular or intraventricular asynchrony parameters identify patients with stable severe heart failure and LBBB who are most likely to benefit from CRT in terms of reverse remodeling.

METHODS

Study population. We studied patients with New York Heart Association (NYHA) functional class III, chronic heart failure of any origin who had been taking optimal drug therapy for at least three months; all of them were in sinus rhythm and had LBBB with a QRS duration ≥140 ms and a left ventricular ejection fraction (LVEF) ≤35%. Their condition had to be stable, without any spontaneous or provoked angina, or the need for revascularization procedures. The other exclusion criteria were acute heart failure,

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Abbreviations and Acronyms

AUC	= areas under the curve
CI	= confidence interval
CRT	= cardiac resynchronization therapy
ECG	= electrocardiogram/electrocardiographic/ electrocardiography
EIVD	= electrographic interventricular delay
ICC	= intraclass correlation coefficient
IVD	= interventricular delay
LBBB	= left bundle branch block
LVEDVI	= left ventricular end-diastolic volume index
LVEF	= left ventricular ejection fraction
LVEMD	= left ventricular electromechanical delay
LVESVI	= left ventricular end-systolic volume index
MR	= mitral regurgitation
MR_a	= mitral regurgitation area
MR_d	= mitral regurgitation duration
NYHA	= New York Heart Association
ROC	= receiver operating characteristic
SPWMD	= septal-to-posterior wall motion delay

coronary artery bypass graft surgery or myocardial infarction within the previous three months, valvular stenosis, previous valve replacement or reconstruction, the presence of a pacemaker or any indication for one, or a history of chronic atrial fibrillation.

The study was approved by the local ethics committee, and all of the patients gave written, informed consent.

Protocol. Between 10 and 5 days before implantation, all of the patients underwent a clinical examination, 12-lead electrocardiography (ECG), and mono-dimensional and two-dimensional echocardiographic and Doppler evaluations. The same evaluations were repeated one month after implantation (during which time care was taken to keep the drug treatment unchanged), when the patients were paced using the optimal mode and settings. The QRS duration was measured as the maximum of leads II, V_1, and V_6; the PQ interval duration was calculated as the longest interval found on the 12-lead ECG.

ECHOCARDIOGRAPHIC EXAMINATION. Mono-dimensional and two-dimensional echocardiography recordings were made using a phased-array echocardiographic Doppler system (Sonos 5500, Hewlett-Packard [Agilent], Andover, Massachusetts) equipped with a 3-MHz transducer. Briefly, after resting for 10 min, the patients were examined in the left lateral recumbent position using standard parasternal short- and long-axis and apical views. Left ventricular end-diastolic and end-systolic volumes were calculated using Simpson's rule (14) and indexed for body surface area. Reverse remodeling was assessed on the basis of the reduction in the left ventricular end-systolic volume index (LVESVI). The patients were considered as responders if LVESVI decreased by 15%, and as nonresponders in all other cases (7,15). Left ventricular systolic function was evaluated using LVEF (14). Mitral regurgitation (MR) was quantified by calculating the area (MR_a) and duration (MR_d) of the regurgitation (16).

Intraventricular asynchrony was evaluated on the basis of the left ventricular electromechanical delay (LVEMD) (i.e., the time [ms] from QRS onset to aortic flow onset) (6) and the delay between the motion of the septum and left posterior wall (septal-to-posterior wall motion delay [SPWMD]; ms), calculated as the shortest interval between the maximal posterior displacement of the septum and the maximal displacement of the left posterior wall using a mono-dimensional short-axis view at the papillary muscle level (Fig. 1). Interventricular asynchrony (interventricular delay [IVD]; ms) was evaluated on the basis of the delay in LVEMD in comparison with the right electromechanical delay (measured as the time between the simultaneously recorded onset of the QRS interval and pulmonary flow) (6).

The intraobserver and interobserver reproducibilities of all of the aforementioned echocardiographic measures of asynchrony were calculated.

The data obtained before implantation were compared with those found during follow-up by two skilled and independent operators (R. R. and B. R.), who were unaware of the baseline interventricular and intraventricular conduction delays.

PACEMAKER IMPLANTATION. Twenty-one consecutive patients were implanted with a biventricular pacemaker (Guidant Contak TR CHFD, Guidant Inc., St. Paul, Minnesota or Medtronic InSync III 8040, Medtronic Inc., Minneapolis, Minnesota), and four received a biventricular cardioverter-defibrillator (Guidant Contak CD CHFD or Contak Renewal, Guidant Inc.; or Medtronic InSync ICD 7272, Medtronic Inc.). Left ventricular pacing was obtained transvenously in all cases. After coronary sinus angiography, a unipolar lead with an over-the-wire system (Easytrak, Guidant Inc. or Medtronic 4193-78, Medtronic Inc.) was advanced into the lateral or posterolateral cardiac vein. The final position was chosen on the basis of visual inspection by using the right and left anterior oblique views; the most lateral region was reached (15 through the lateral and 10 through the posterolateral vein), and the final position was validated on the basis of both the best left ventricular stimulation threshold (1.48 ± 0.81 V/0.5 ms; minimum 0.3 V; maximum 3.0 V) and the best left ventricular amplitude signal. The right atrium and ventricle were then stimulated by positioning standard bipolar catheters in the right atrial appendage and right ventricular apex, respectively. During cardioverter-defibrillator implantation, a dual-coil catheter for right ventricular pacing, sensing, and cardioversion/ defibrillation was inserted in the right ventricle. The biventricular pacing mode was programmed in DDD, and the lower rate was set at 40 beats/min. The atrioventricular interval was optimized for maximal diastolic filling by Doppler echocardiography (17). In the control group, the pacing mode was programmed in DDD, with a lower rate of 40 beats/min and an atrioventricular delay of 300 ms. If these settings resulted in ventricular pacing, the device was programmed in VVI, with lower rate at 40 beats/min.

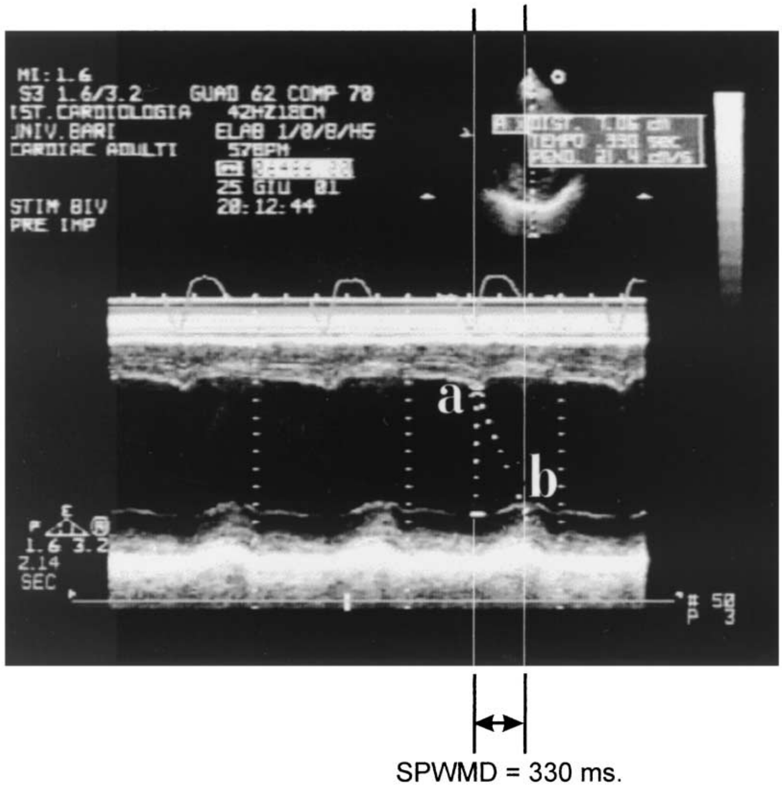

Figure 1. Mono-dimensional short-axis view of the echocardiographic image taken at the level of the papillary muscles. Calculation of septal-to-posterior wall motion delay (SPWMD) obtained by measuring the shortest interval between the maximal posterior displacement of the septum **(a)** and the posterior wall **(b)**.

At the site of the best left ventricular pacing, the local left electrogram was recorded and the conduction time between the right and left electrograms was calculated as a measure of IVD (electrographic interventricular delay [EIVD]; ms).

CONTROL GROUP. Interventricular and intraventricular asynchrony measures were analyzed in five patients with chronic heart failure who, in accordance with another study protocol, underwent device implantation followed by a six-month period during which it was kept inactive. These control subjects were used to evaluate whether the interventricular and intraventricular asynchrony measures had any post-implantation spontaneous modification not related to CRT. Once again, the measurements at one month after implantation were taken by operators who had no knowledge of the baseline values.

Statistical analysis. The data are shown as the mean value ± SD. Continuous variables were compared using the *t* test, and frequencies using the Fisher exact test. The percent variations were compared using the Mann-Whitney *U* test. Correlations between variables were assessed using Pearson's linear correlation. Interobserver and intraobserver reproducibilities were evaluated by means of the intraclass correlation coefficient (ICC) (18), with reproducibility being considered almost perfect if the ICC was between 0.81 and 1.0. The receiver operating characteristics (ROC) curves for sensitivity and specificity were constructed to evaluate the predictive values of the studied variables, and the areas under the curve (AUC) were statistically compared to estimate the accuracy of the variables. The tests were considered statistically significant at $p < 0.05$.

RESULTS

We enrolled 25 patients: 5 with ischemic and 20 with nonischemic heart disease (by World Health Organization criteria) (19). The demographic, clinical, and therapeutic characteristics of the patient population are shown in Table 1.

Reproducibility of echocardiographic asynchrony parameters. The intraobserver reproducibility of SPWMD, LVEMD, and IVD (ICC: 0.96, 0.96, and 0.95, respectively), as well as the interobserver reproducibility (ICC: 0.91, 0.92, and 0.83, respectively), was very high. The values of these parameters before and one month after implantation were similar to those of the control group, thus again showing a very high degree of reproducibility (ICC: 0.97, 0.94, and 0.92, respectively).

Correlations between asynchrony parameters before implantation. The baseline QRS duration significantly correlated only with SPWMD ($r = 0.62$, $p < 0.01$); LVEMD and IVD did not correlate with the QRS interval, SPWMD, or EIVD. Baseline EIVD significantly and positively correlated with LVEMD ($r = 0.50$, $p < 0.05$), but not with the QRS duration, SPWMD, or IVD.

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Table 1. Baseline Clinical Characteristics of All Patients, Responders, Nonresponders, and Controls

	All Patients (n = 25)	Responders (n = 12)	Nonresponders (n = 8)	Controls (n = 5)
Age (yrs)	62 ± 11	65 ± 10	61 ± 11	60 ± 12
Male/female (n)	11/14	4/8	4/4	3/2
NYHA functional class	III	III	III	III
Underlying cardiomyopathy (%)				
Ischemic	20	0	50	20
Nonischemic	80	100	50	80
Concomitant therapy (%)				
ACE inhibitors	80	75	75	100
AT_1 receptor antagonists	20	25	13	0
Beta-blockers	76	67	88	80
Digitalis	72	83	50	80
Diuretics	100	100	100	100
Aldosterone antagonists	72	75	63	80

Data are presented as the mean value ± SD, number, or percentage of patients.
ACE = angiotensin-converting enzyme; AT_1 = angiotensin type 1; NYHA = New York Heart Association.

ECG and asynchrony parameters changes after CRT. Changes in the electrocardiographically and echocardiographically studied variables after one month of CRT are shown in Table 2. As expected, there was a significant reduction in the PQ interval and QRS duration, but no significant change in the heart rate. There was a significant reduction in all of the parameters reflecting intraventricular and interventricular asynchrony, and left ventricular volumes, ejection fractions, and MR significantly improved.

Correlations between baseline asynchrony parameters and reverse remodeling. The SPWMD and QRS duration measures before implantation significantly correlated with the reductions in both left ventricular end-diastolic volume index (LVEDVI) ($r = -0.73$, $p < 0.001$ and $r = -0.55$, $p < 0.05$, respectively) and LVESVI (Figs. 2 and 3) (i.e., the longer the baseline SPWMD and QRS duration, the greater the reverse remodeling). In contrast, LVEMD, IVD, and EIVD did not significantly correlate with the changes in left ventricular volumes.

Table 2. Differences in Electrocardiographic and Echocardiographic Parameters Before and After One Month of Cardiac Resynchronisation Therapy

	Before CRT (n = 20)	One Month After CRT (n = 20)	p Value
Heart rate (beats/min)	71 ± 14	68 ± 11	NS
PQ interval (ms)	203 ± 28	125 ± 19	< 0.0001
QRS duration (ms)	169 ± 16	132 ± 12	< 0.0001
SPWMD (ms)	192 ± 92	14 ± 67	< 0.0001
LVEMD (ms)	167 ± 35	141 ± 27	< 0.05
IVD (ms)	59 ± 29	39 ± 21	< 0.05
LVEDVI (ml/m^2)	150 ± 53	119 ± 37	< 0.001
LVESVI (ml/m^2)	116 ± 43	85 ± 29	< 0.0001
LVEF (%)	24 ± 5	29 ± 6	< 0.001
MR_d (ms)	560 ± 59	470 ± 59	< 0.0001
MR_a (mm^2)	10.4 ± 3.7	6.6 ± 3.4	< 0.01

Data are presented as the mean value ± SD.
CRT = cardiac resynchronization therapy; IVD = difference between LVEMD and right ventricular electromechanical delay (interval between onset of QRS and onset of pulmonary flow); LVEDVI = left ventricular end-diastolic volume indexed for body surface area; LVEF = left ventricular ejection fraction; LVEMD = left ventricular electromechanical delay (interval between onset of QRS and onset of aortic flow); LVESVI = left ventricular end-systolic volume indexed for body surface area; MR_a = mitral regurgitation area; MR_d = mitral regurgitation duration; SPWMD = septal-to-posterior wall motion delay.

Comparison between responders and nonresponders. Twelve patients were responders (reduction in LVESVI ≥15%). At baseline, there were no differences between the responders and nonresponders in terms of the heart rate, QRS duration, ventricular volumes, and MR, but the responders had a longer PQ interval and a longer SPWMD (Table 3).

In Table 4, the percent variations of the studied parameters in responders and nonresponders are shown. The reductions in LVEDVI, LVESVI, and MR_a were significantly greater in responders than in nonresponders. No differences between the two groups were found when ECG parameters, asynchrony measures, LVEF, and MR_d variations were taken into account. Seventeen patients improved in their NYHA functional class, from III to II. The responders were more likely to improve their NYHA functional class, as compared with nonresponders (100% vs. 63%; $p < 0.05$).

Predictive value of asynchrony parameters. The ROC curves for post-CRT reverse remodeling showed that the AUC for SPWMD (0.95; confidence interval [CI] 0.76 to 0.99) was significantly greater than those for the QRS duration (0.59; CI 0.35 to 0.80) (Fig. 4), LVEMD (0.60; CI 0.34 to 0.83), IVD (0.68; CI 0.38 to 0.89), or EIVD (0.54; CI 0.30 to 0.76), but not statistically different from that of the PQ interval (0.78; CI 0.54 to 0.93). All of the responders had a baseline SPWMD ≥130 ms, a QRS duration ≥150 ms, and a PQ interval ≥180 ms. Using these cut-off values, the specificity of SPWMD was 63%, with a positive predictive value of 80% and an accuracy of 85%, whereas the specificity of both the QRS duration and PQ interval was 13%, with a positive predictive value of 63% and an accuracy of 65%.

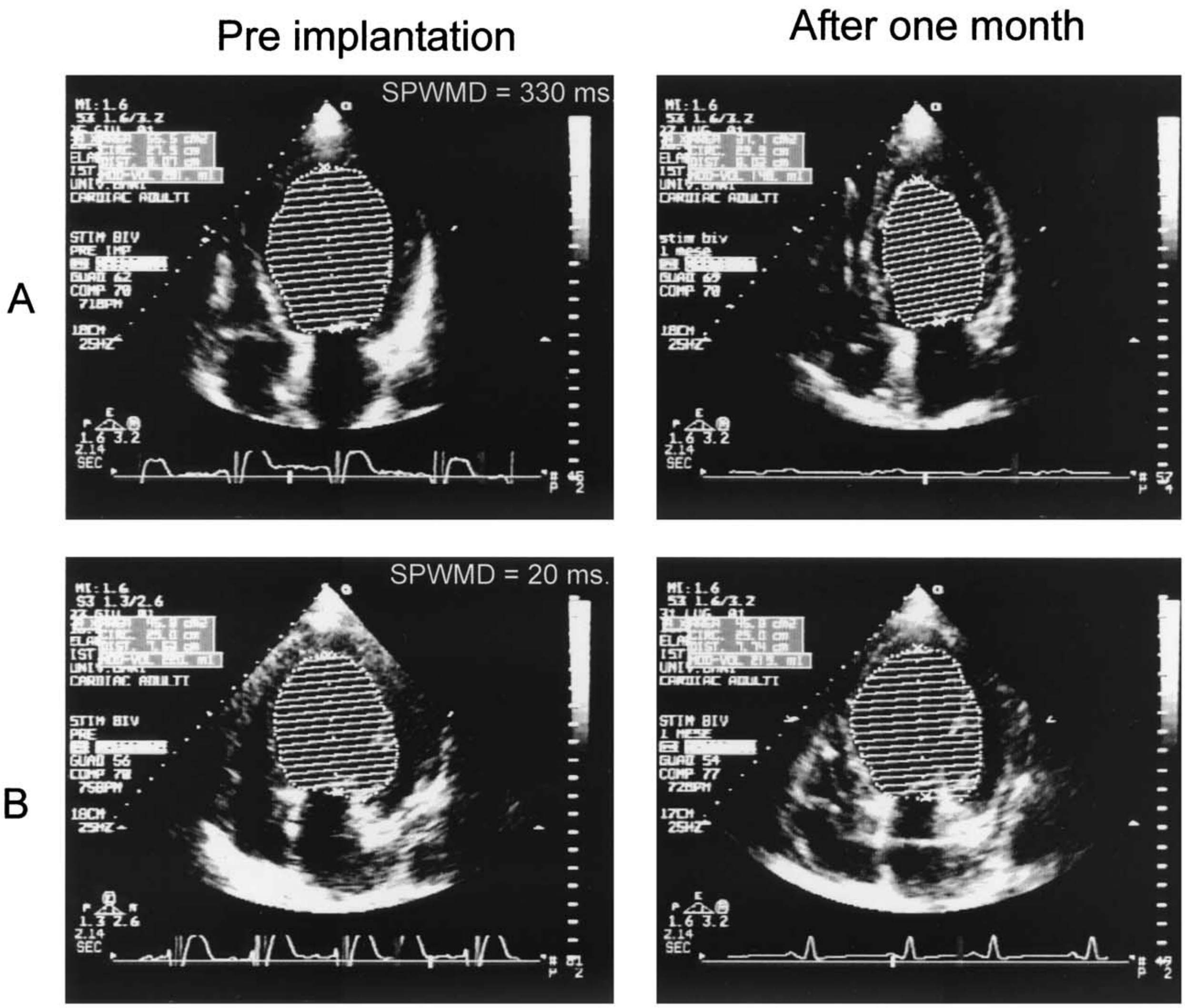

Figure 2. Two-dimensional apical four-chamber view of echocardiographic images. Left ventricular end-systolic volumes before (pre) device implantation **(left images)** and one month after cardiac resynchronization therapy **(right images)** in two different patients. **(A)** This patient had a prolonged pre-implantation septal-to-posterior wall motion delay (SPWMD) and a marked left ventricular end-systolic volume reduction after one month. **(B)** This patient had a short pre-implantation SPWMD and no reverse remodeling.

DISCUSSION

Cardiac resynchronization has recently been proposed as a long-term treatment for patients with severe heart failure despite optimal medical therapy. This electrical strategy is currently offered to patients with complete LBBB in the belief that this ECG parameter reflects mechanical asynchrony (1,2), but a benefit in terms of improved symptoms and ventricular reverse remodeling is evident in only some patients (6–8).

The main result of the present study is that an echocardiographically derived measure of intraventricular mechanical asynchrony identifies patients with severe heart failure who are likely to show reverse remodeling more accurately than LBBB alone. The relevance of our findings comes from the fact that they are the result of pathophysiologic speculation (1–3,20), and this sheds new light on the possibility of changing the selection criteria used to identify heart failure patients suitable for CRT.

Left ventricular remodeling is the result of the complex interaction between structural and functional abnormalities favoring the progressive dilation of the left ventricle (21), which takes on a spherical shape that is unfavorable from an energetic point of view and becomes dyssynergic (i.e., the posterolateral wall contracts later than does the septum). These abnormalities are responsible for MR and further hemodynamic deterioration (22) and are worsened by the appearance of LBBB (2). It is believed that stimulation of the left posterolateral wall in order to synchronize this area with the septum blunts these alterations and gives rise to so-called "reverse remodeling."

However, the possibility of achieving this favorable result depends on a number of factors, such as the presence of a left ventricular area with delayed contraction, the possibility

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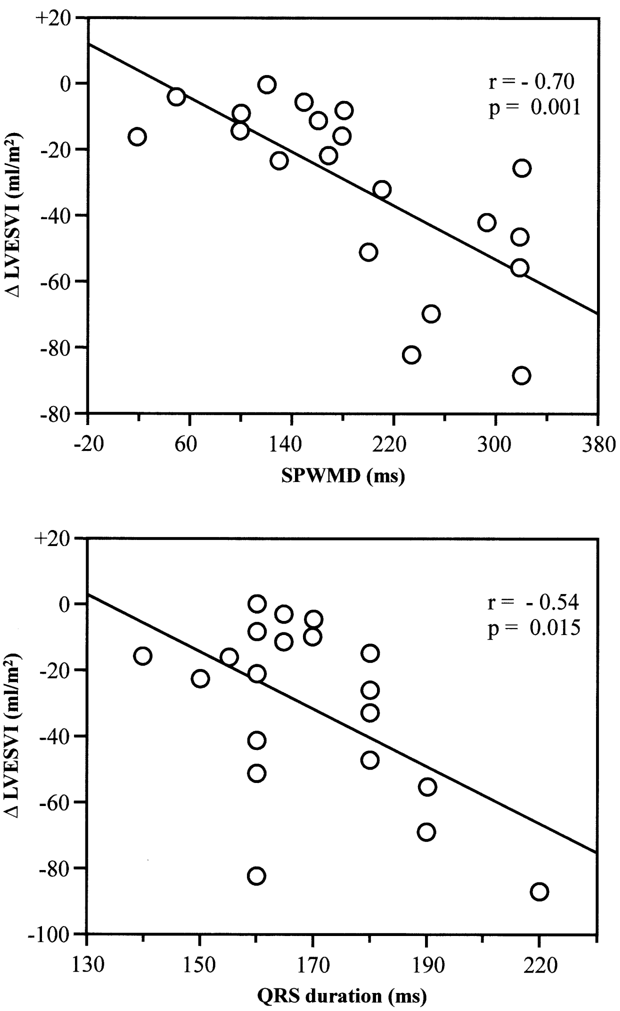

Figure 3. **(Top)** The correlation between the baseline values of septal-to-posterior wall motion delay (SPWMD) and ΔLVESVI. **(Bottom)** Correlation between baseline QRS duration and ΔLVESVI. ΔLVESVI = difference between post- and pre-implantation left ventricular end-systolic volumes indexed for body surface area.

of identifying it, and, finally, the ability to reach and stimulate this area by using a catheter positioned through the coronary sinus. The first two factors are particularly relevant for guiding patient selection. On the basis of these considerations and our results, it is possible to hypothesize that nonresponders are the consequence of inadequate patient selection, which is currently based on the presence of LBBB (13). This ECG abnormality should be considered as only a generic marker of conduction disturbance, because the fact that left intraventricular asynchrony is often associated with LBBB is not sufficient to presume that the latter is a specific marker of any degree of mechanical asynchrony. Also, LBBB may be the result of abnormalities that do not necessarily cause late contraction of the left free wall (e.g., peripheral conduction defect or global left ventricular dysfunction).

Seen in this light, the weak correlation between QRS duration and echocardiographically visualized mechanical asynchrony is not surprising. Furthermore, our hypothesis

Table 3. Comparison of Baseline Characteristics of Responders and Nonresponders

	Responders (n = 12)	Nonresponders (n = 8)	p Value
ECG parameters			
Heart rate (beats/min)	68 ± 15	76 ± 12	NS
PQ interval (ms)	213 ± 27	186 ± 23	< 0.05
QRS duration (ms)	173 ± 18	164 ± 12	NS
Echocardiographic parameters			
SPWMD (ms)	246 ± 68	110 ± 55	< 0.001
LVEMD (ms)	176 ± 40	163 ± 55	NS
IVD (ms)	59 ± 19	73 ± 21	NS
LVEDVI (ml/m^2)	162 ± 65	132 ± 23	NS
LVESVI (ml/m^2)	125 ± 52	103 ± 19	NS
LVEF (%)	24 ± 4	23 ± 5	NS
MR_d (ms)	559 ± 63	561 ± 58	NS
MR_a (mm^2)	9.8 ± 1.8	10.2 ± 5.5	NS

Data are presented as the mean value ± SD.
ECG = electrocardiographic; other abbreviations as in Table 2.

explains the low specificity of even a very wide QRS interval (as in the case of our patient population) in predicting the occurrence of reverse remodeling. In contrast, by providing information on the delayed mechanical asynchrony between the left free wall and septum, the echocardiographic parameter is highly specific and has a positive predictive value: the longer the delay, the greater the reduction in ventricular volumes.

The parameter analyzing IVD by taking into account the onset of the QRS interval and aortic flow does not provide the same information as that of SPWMD. It is possible that this measure is not sufficiently precise to identify the presence of delayed left free wall contraction and, in particular, its asynchrony with the septum. This echocardiographic Doppler parameter correlates well with the electrical delay recorded between the right and left catheter during implantation. In addition, EIVD is not useful in predicting reverse remodeling. The electrogram recorded at

Table 4. Comparison of One-Month Percent Variations Occurring in the Studied Parameters Between Responders and Nonresponders

	Responders (n = 12)	Nonresponders (n = 8)	p Value
ECG parameter changes (%)			
Heart rate	1 ± 19	−7 ± 10	NS
PQ interval	−39 ± 11	−36 ± 8	NS
QRS duration	−21 ± 9	−22 ± 10	NS
Echocardiographic parameter changes (%)			
SPWMD	−97 ± 37	−85 ± 56	NS
LVEMD	−4 ± 13	−21 ± 32	NS
IVD	−16 ± 32	−42 ± 32	NS
LVEDVI	−29 ± 12	−2 ± 4	< 0.05
LVESVI	−36 ± 12	−8 ± 5	< 0.05
LVEF	27 ± 18	18 ± 32	NS
MR_d	−44 ± 12	−21 ± 28	NS
MR_a	−19 ± 10	−11 ± 7	< 0.05

Data are presented as the mean value ± SD.
ECG = electrocardiographic; other abbreviations as in Table 2.

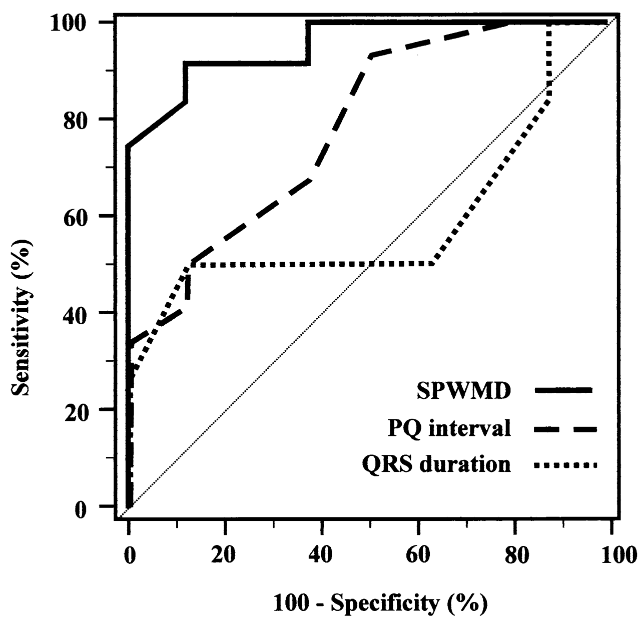

Figure 4. The receiver operating characteristic curves for septal-to-posterior wall motion delay (SPWMD), PQ interval, and QRS duration to predict reverse remodeling. The areas underlying SPWMD and QRS duration are statistically different.

the level of the lateral free wall is greatly influenced by the position of the catheter in the coronary sinus tree and, therefore, by its anatomy. Furthermore, in patients with a previous myocardial infarction, the presence of slowed conduction in the peri-infarcted myocardium may give rise to a locally prolonged delay that does not reflect real intraventricular asynchrony.

Another interesting finding is the very high predictive value of the baseline PQ interval: the longer the interval, the greater the improvement. It has been previously suggested that prolonged atrioventricular conduction has pathophysiologic significance (23–25) and may lead to worsening hemodynamic function that is independent of intraventricular asynchrony (26). Although the number of patients enrolled in this study did not allow us to perform multivariate analysis, analysis of the independent and incremental value of these parameters would be of interest in defining patient selection criteria.

To the best of our knowledge, this is the first study that has prospectively demonstrated the value of electrocardiographically and echocardiographically derived Doppler measures in predicting reverse remodeling in patients receiving CRT. However, it must to be acknowledged that Stellbrink et al. (7) have recently suggested that patients with very large left ventricular volumes at baseline are unlikely to benefit from CRT. This hypothesis was not confirmed in our patient population, because a long SPWMD retained its ability to predict improvement, even in the presence of a very dilated heart. This difference may be due to the fact that Stellbrink et al. (7) analyzed ventricular volumes without considering the degree of left lateral wall motion delay. Therefore, it is possible that their patients with very dilated ventricles had global hypokinesia with little intraventricular asynchrony (a phenomenon that is not unusual in markedly remodeled hearts).

The intraventricular asynchrony parameter we suggest combines the advantages of the echocardiographic technique with a high level of accuracy in identifying responders. It is therefore a very promising measure in the clinical setting. The use of mono-dimensional echocardiography to evaluate all patients with severe heart failure, LBBB, and a wide QRS interval would make it possible to avoid implanting the device in those whose cardiac function is unlikely to improve.

Conclusions. This study suggests that patients with stable and severe heart failure (while receiving optimal therapy) and LBBB need to be further evaluated echocardiographically to identify the possible presence of a long SPWMD, which would allow the selection of patients most likely to achieve reverse remodeling after CRT. However, LBBB alone (even if the QRS duration is very prolonged) cannot be considered an adequate marker of intraventricular asynchrony and, therefore, cannot be used as the only parameter guiding the decision to implant a biventricular device.

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