A Randomized Study of Cardiac Resynchronization Therapy Defibrillator Versus Dual-Chamber Implantable Cardioverter-Defibrillator in Ischemic Cardiomyopathy With Narrow QRS

The NARROW-CRT Study

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Background—Current recommendations require a QRS duration of ≥120 ms as a condition for prescribing cardiac resynchronization therapy (CRT). This study was designed to test the hypothesis that patients with heart failure (HF) of ischemic origin, current indications for defibrillator implantation, and QRS <120 ms may benefit from CRT in the presence of marked mechanical dyssynchrony.

Methods and Results—Patients with intraventricular dyssynchrony on echocardiography were randomly assigned to CRT or dual-chamber defibrillator implantation (CRT defibrillator and dual-chamber implantable cardioverter-defibrillator arm, respectively). The primary end point was the HF clinical composite response, which scores patients as improved, unchanged, or worsened. The secondary end point was the cumulative survival from HF hospitalization and HF death. An additional secondary end point was the composite of HF hospitalization, HF death, and spontaneous ventricular fibrillation. Twenty-three of 56 patients with CRT defibrillator showed an improvement in their clinical composite response at 1 year, compared with 9 of 55 patients with dual-chamber implantable cardioverter-defibrillator (41% versus 16%; P=0.004). After a median follow-up of 16 months, the CRT defibrillator arm showed a nonsignificant higher survival from HF hospitalization and HF death (P=0.077), and a significantly higher survival from the combined end point of HF hospitalization, HF death, and spontaneous ventricular fibrillation (P=0.028).

Conclusions—In this comparison of CRT defibrillator and dual-chamber implantable cardioverter-defibrillator, CRT improved clinical status in some patients with ischemic cardiomyopathy, mild-to-moderate symptoms, narrow QRS duration, and mechanical dyssynchrony on echocardiography.

Clinical Trial Registration—URL: http://clinicaltrials.gov. Unique identifier: NCT01577446.

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Key Words: CRT ● dyssynchrony ● heart failure ● narrow QRS
CRT in the presence of marked intraventricular mechanical dyssynchrony, regardless of narrow QRS duration.

Methods

Patients

The NARROW-CRT study was a prospective, randomized, single-blind, multicenter evaluation of CRT in patients who were candidates for cardioverter–defibrillator implantation, with New York Heart Association (NYHA) class II and III HF, ischemic cardiomyopathy, an ejection fraction of \( \leq 35\% \), a QRS interval of \( \leq 120 \) ms, and evidence of mechanical dyssynchrony as measured on echocardiography. Patients were excluded from the study if they had a conventional indication for cardiac pacing, persistent atrial fibrillation, or a life expectancy \(<1\) year.

Study Design

Patients meeting eligibility requirements underwent baseline evaluation, which included demographics and medical history, clinical examination, 12-lead ECG, estimation of NYHA functional class, and echocardiographic evaluation.

In the presence of intraventricular mechanical dyssynchrony on echocardiography, as defined below, patients were randomly assigned to CRT defibrillator (CRT-D) or dual-chamber implantable cardioverter-defibrillator (D-ICD) groups in a 1:1 ratio according to center, by sealed-envelope technique. Block randomization was by a computer-generated random number list prepared by an investigator with no clinical involvement in the trial.

In the absence of mechanical dyssynchrony, patients were included in a prospective registry and received a single- or dual-chamber defibrillator at the discretion of the implanting physician.

The CRT-D group underwent implantation of a CRT defibrillator with a standard right atrial, right ventricular defibrillator, and LV leads. The target location for the LV lead tip was the lateral or posterolateral segment. The D-ICD group received a dual-chamber defibrillator with a right atrial and right ventricular lead, by means of standard techniques.

In the D-ICD group, the defibrillator was programmed to minimize right ventricular pacing. In both groups, the ventricular fibrillation detection cutoff rate was required to be 200 beats/min.

Enrolled patients returned for regular clinic visits at 6 and 12 months, and every 6 months thereafter until the last patient reached the 1-year evaluation. In addition to clinical evaluation, device-recorded arrhythmic episodes were retrieved from the defibrillator memory at each follow-up visit. In addition, echocardiography was performed at the 1-year follow-up visit in patients with CRT-D. The Institutional Review Boards approved the study, and all patients gave written informed consent.

End Points

The primary end point of the study was the HF clinical composite score.\cite{14} In detail, at the 12-month follow-up evaluation, patients were classified according to a score, which assigns subjects to 1 of 3 response groups—improved, worsened, or unchanged. Patients were judged to have worsened if they died or were hospitalized because of worsening HF (at any time during the 12 months), or displayed worsening in NYHA functional class or patient global assessment at their 12-month visit. Patients were judged to have improved if they had not worsened, and had displayed improvement in NYHA functional class and patient global assessment at 12 months. Patients who had neither worsened nor improved were classified as unchanged. Only hospitalizations requiring \( \geq 1 \) overnight stay, and which were adjudicated by a blinded End Point Advisory Committee, contributed to the end point.

Implanting physicians and study site personnel involved in device management were unblinded to randomization assignment. Conversely, patients, treating physicians, and site personnel taking the functional measurements of NYHA classification did not know to which arm the subject had been randomized.

The secondary end point was the cumulative survival from HF hospitalization and HF death. An additional secondary end point was the composite of HF hospitalization, HF death, and spontaneous ventricular fibrillation.\cite{15} Spontaneous sustained arrhythmic episodes detected by the device were validated by 2 blinded electrophysiologists. If a consensus could not be reached, a third electrophysiologist was called on to adjudicate. A sustained arrhythmia was defined a priori as one treated by the device. All device-detected arrhythmias correctly classified as ventricular fibrillations and appropriately terminated by shock therapy were counted as end points.

The effects of CRT on echocardiographic parameters were evaluated by comparing the baseline values with those recorded at the 12-month follow-up examination of surviving patients. Moreover, the cumulative survival from death or HF hospitalization and from the combined end point of HF death or hospitalization, and shock-terminated spontaneous ventricular fibrillation in the study arms were also compared with those of the parallel group with no baseline mechanical dyssynchrony.

Echocardiographic Analysis

Echocardiographic analysis was performed at the baseline evaluation in all screened patients and at follow-up visits in patients with CRT-D. The level of intraventricular mechanical dyssynchrony was determined by means of tissue Doppler imaging.

As previously described,\cite{4} color Doppler imaging was performed by first acquiring standard apical views of 2 chambers, 3 chambers, and 4 chambers at high frame rates. The sample volume was placed offline in the basal portions of the septal and lateral walls, and velocity curves were generated. Peak systolic velocities and time-to-peak systolic velocities were recorded. A difference between the septal and lateral delays of 260 ms was defined as a significant intraventricular mechanical delay.\cite{5} Echocardiographic recordings were reviewed in a core laboratory to confirm eligibility of enrolled patients. If the presence of intraventricular mechanical dyssynchrony was not confirmed by the operator, a second sonographer at the core laboratory was called on to adjudicate. If the absence of dyssynchrony criteria was verified, the patient exited the study.

The following parameters were also recorded: LV end-diastolic and end-systolic volumes and diameters, and ejection fraction assessed by means of Simpson equation.

Statistical Analysis

All end points were analyzed according to the intention-to-treat principle, and analyses were stratified by center. For the prespecified analysis of the primary end point, the percentage of patients in the 2 study groups who had improved was compared by means of the Mantel–Haenszel \( \chi^2 \) test to assess the efficacy of CRT.

The sample size (60 patients per treatment group) was estimated on the basis of the assumption that the study would have 80% power to detect a difference of 25% in improved HF clinical composite responses, as reported in previous CRT trials.\cite{16,17} The proportion of patients in the CRT-D group who would improve was assumed to be 38%,\cite{18} with an attrition rate of 10% from randomization to the end of study.

Kaplan–Meier analysis was used to analyze cumulative survival from HF hospitalization and HF death and cumulative survival from the combined end point of HF hospitalization, HF death, and spontaneous ventricular fibrillation. The log-rank test was used to assess significance. Additionally, Cox model with robust standard errors was used to analyze end points to account for intrasite correlation.

Descriptive statistics are reported as means\(\pm SD\) for normally distributed continuous variables or medians with 25th to 75th percentiles in the case of skewed distribution. Differences between mean data were compared by means of a \( t \) test for gaussian variables. The Mann–Whitney test and the Wilcoxon nonparametric test were used to compare nongaussian variables for independent and paired samples, respectively. Differences in proportions were compared by applying \( \chi^2 \) analysis or Fisher exact test, as appropriate.
A *P* value <0.05 was considered significant for all tests. All statistical analyses were performed by using STATISTICA software, version 7.1 (StatSoft, Inc., Tulsa, OK).

Results

Study Timelines and Population

From January 2008 through May 2010, a total of 1290 patients referred to the 6 centers for cardioverter–defibrillator implantation for primary prevention of sudden cardiac death were initially screened. Of these, 233 patients met eligibility requirements and underwent the baseline evaluation. On echocardiographic analysis, mechanical dyssynchrony was detected in 120 patients, who were randomly assigned to the CRT-D or D-ICD arms. In 3 additional patients, mechanical dyssynchrony was diagnosed at the local site but not confirmed after core laboratory review. Thus, these patients exited the study before randomization.

Demographic data, clinical parameters, and pharmacological treatment were similar between the study arms at the time of enrollment (Table 1). The majority of LV leads (42 out of 60; 70%) were deployed in a lateral or posterolateral cardiac vein. Two patients in the CRT-D arm did not undergo successful implantation of the LV lead; these received a dual-chamber defibrillator, but remained in the CRT-D arm in accordance with the intention-to-treat design of the analysis. During the course of the study, 9 patients were lost to follow-up or exited the study (4 in the CRT-D arm and 5 in the D-ICD arm), while there were no crossovers (Figure 1). The median length of follow-up was comparable between groups: 16 months (12–24) versus 15 months (9–24; *P*=0.325).

The median percentage of biventricular pacing in the CRT-D arm was 97% (93–100) at 6 months and 99% (96–100) at 1 year. In the D-ICD arm, the median percentage of right ventricular pacing was 1% (0–8) at 6 months and 1% (0–7) at 1 year.

Effects on Primary and Secondary End Points

Of the 56 patients assigned to CRT-D, 23 (41%) patients displayed an improvement in their HF clinical composite response at 1 year compared with 9 (16%) of the 55 patients randomized to D-ICD (*P*=0.004; Figure 2). Details of the components considered in the calculation of the end points are listed in Table 2.

By the end of the study, 4 patients in the CRT-D arm had died (2 of pump failure and 2 of noncardiac causes) and 5 D-ICD patients had died of pump failure. One patient in the CRT-D arm and 1 patient in the D-ICD arm died of pump failure during the first 12 months. All the remaining patients completed their 12-month follow-up visit.

### Table 1. Demographics, Baseline Clinical Parameters, and Pharmacological Treatment of the Study Population

<table>
<thead>
<tr>
<th>Parameters</th>
<th>CRT-D Arm (n=60)</th>
<th>D-ICD Arm (n=60)</th>
<th>No-Dysynchrony Group (n=113)</th>
<th><em>P</em> Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>53 (88)</td>
<td>50 (83)</td>
<td>99 (88)</td>
<td>0.646</td>
</tr>
<tr>
<td>Age, y</td>
<td>65±9</td>
<td>68±9</td>
<td>64±9</td>
<td>0.219</td>
</tr>
<tr>
<td>QRS duration, ms</td>
<td>107±14</td>
<td>104±14</td>
<td>99±15</td>
<td>0.003</td>
</tr>
<tr>
<td>NYHA class</td>
<td></td>
<td></td>
<td></td>
<td>0.003</td>
</tr>
<tr>
<td>Class II, n (%)</td>
<td>23 (38)</td>
<td>25 (42)</td>
<td>67 (59)</td>
<td></td>
</tr>
<tr>
<td>Class III, n (%)</td>
<td>37 (62)</td>
<td>35 (58)</td>
<td>46 (41)</td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction, n (%)</td>
<td>54 (90)</td>
<td>52 (87)</td>
<td>96 (85)</td>
<td>0.065</td>
</tr>
<tr>
<td>Previous CABG, n (%)</td>
<td>19 (32)</td>
<td>16 (27)</td>
<td>28 (25)</td>
<td>0.451</td>
</tr>
<tr>
<td>Previous angioplasty, n (%)</td>
<td>32 (53)</td>
<td>33 (55)</td>
<td>53 (47)</td>
<td>0.268</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>30 (50)</td>
<td>35 (58)</td>
<td>48 (43)</td>
<td>0.074</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>24 (40)</td>
<td>19 (33)</td>
<td>33 (29)</td>
<td>0.281</td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>28±5</td>
<td>29±5</td>
<td>28±5</td>
<td>0.884</td>
</tr>
<tr>
<td>LVEDV, mL</td>
<td>201±69</td>
<td>194±63</td>
<td>176±46</td>
<td>0.226</td>
</tr>
<tr>
<td>LVESV, mL</td>
<td>148±54</td>
<td>136±52</td>
<td>113±41</td>
<td>0.065</td>
</tr>
<tr>
<td>LVEDD, mm</td>
<td>66±9</td>
<td>66±10</td>
<td>61±7</td>
<td>0.047</td>
</tr>
<tr>
<td>LVESD, mm</td>
<td>53±10</td>
<td>56±9</td>
<td>50±8</td>
<td>0.117</td>
</tr>
<tr>
<td>Intraventricular mechanical delay, ms</td>
<td>79±19</td>
<td>81±21</td>
<td>30±18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ß-Blocker use, n (%)</td>
<td>52 (87)</td>
<td>55 (92)</td>
<td>95 (84)</td>
<td>0.253</td>
</tr>
<tr>
<td>ACE-inhibitor use, n (%)</td>
<td>48 (80)</td>
<td>46 (77)</td>
<td>84 (74)</td>
<td>0.472</td>
</tr>
<tr>
<td>Diuretic use, n (%)</td>
<td>51 (85)</td>
<td>52 (87)</td>
<td>89 (79)</td>
<td>0.157</td>
</tr>
<tr>
<td>Class III antiarrhythmic use, n (%)</td>
<td>20 (33)</td>
<td>22 (37)</td>
<td>32 (28)</td>
<td>0.274</td>
</tr>
</tbody>
</table>

ACE indicates angiotensin-converting-enzyme; CABG, coronary artery bypass grafting; CRT-D, cardiac resynchronization therapy defibrillator; D-ICD, dual-chamber implantable cardioverter-defibrillator; LV, left ventricular; LVEDD, LV end-diastolic diameter; LVEDV, LV end-diastolic volume; LVESD, LV end-systolic diameter; LVESV, LV end-systolic volume; and NYHA, New York Heart Association.

*No-Dysynchrony vs randomized patients (CRT-D + D-ICD).
The Kaplan–Meier analysis showed a nonsignificant higher survival from HF hospitalization and HF death ($P=0.077$), and a significantly higher survival from the combined end point of HF hospitalization, HF death, and spontaneous ventricular fibrillation ($P=0.028$) in the CRT-D arm (Figure 3).

During follow-up, incisional infections at the pocket site were reported in 2 patients in the CRT-D arm and in 1 patient in the D-ICD arm; phrenic-nerve stimulation was reported in 3 CRT-D patients, and was corrected by means of device reprogramming. Moreover, 1 CRT-D patient and 1 D-ICD patient had pocket hematoma.

A significant increase in LV ejection fraction was observed in the CRT-D arm after 12 months (Table 3), together with a reduction in systolic dimensions (LV end-systolic volume and LV end-systolic diameter), whereas diastolic dimensions (LV end-diastolic volume and LV end-diastolic diameter) did not show significant changes. CRT significantly reduced the intraventricular mechanical delay, and 21% of patients with CRT-D presented at the 1-year visit with a mechanical delay of ≤60 ms.

The baseline characteristics of the patients included in the registry of subjects with no mechanical dyssynchrony on baseline evaluation and treated with non-CRT devices (Table 1) were comparable with those of the patients in analysis who underwent randomization, except for slightly shorter QRS duration, smaller LVEDD, a significantly higher proportion of patients in NYHA class II. Obviously, also the mean intraventricular mechanical delay was markedly shorter. During the course of the study, 15 patients in the registry were lost to follow-up, 7 patients died (6 of pump failure and 1 of non-cardiac causes), and 11 patients were hospitalized because of worsening HF. Moreover, 7 patients had a shock-terminated spontaneous ventricular fibrillation.

Kaplan–Meier estimates of survival from HF hospitalization and death and from the combined end point of HF hospitalization, HF death, and spontaneous ventricular fibrillation were made for patients with no baseline mechanical dyssynchrony; these were then compared with the estimates made in the CRT-D and D-ICD study arms (Figure 4). The CRT-D group displayed an event rate comparable with that of the group with no evidence of mechanical dyssynchrony, whereas the D-ICD group presented a significantly worse outcome.

**Discussion**

**Primary End Point Analysis**

In the NARROW-CRT trial, CRT improved clinical status, as measured by the clinical composite score, in patients with HF with ischemic cardiomyopathy and marked intraventricular mechanical dyssynchrony, regardless of narrow QRS duration. Among patients with current indications, that is, QRS ≥120 ms, those with significant QRS prolongation seem to derive
the most benefit from CRT and to have a better prognosis, according to the post hoc analyses of large CRT trials. Moreover, left bundle-branch block QRS morphology was found to be a predictor of functional status improvement, and reduction in HF progression and in the risk of ventricular tachyarrhythmias. This seems to contradict the well-known association between prolonged QRS duration and poor prognosis. The lesser efficacy of CRT in patients with HF with normal QRS duration may reflect the lower prevalence of mechanical dysynchrony in such patients. Indeed, although some studies on the effect of CRT in patients with narrow QRS have enrolled unselected patients, the majority have adopted additional selection methods to detect amenable mechanical dysynchrony and to identify potential candidates for CRT.

Although the majority of single-center experiences have shown a positive response to CRT in patients with narrow QRS, a randomized study that enrolled patients with QRS duration of <130 ms (the RethinQ [Resynchronization Therapy in Normal QRS] trial) did not show any improvement in peak oxygen consumption on CRT. Peak oxygen consumption, however, is poorly associated with symptoms and, thus, is not an adequate surrogate measure of symptomatic benefit in patients with HF. Indeed, in the Multicenter InSync ICD Randomized Clinical Evaluation II (MIRACLE ICD II) trial, CRT failed to improve peak oxygen uptake, despite a significant improvement in NYHA class. Moreover, the RethinQ trial did demonstrate both an improvement in NYHA class and fewer HF events in the CRT group.

As the primary end point of our study, we adopted the clinical composite score, because this combines the occurrence of major events, such as HF hospitalization and mortality, with NYHA functional class. This score has proved to be sensitive in detecting the presence or absence of a true CRT effect in both moderate and mild HF and, thus, in the stages of disease considered in the present study. Unlike the RethinQ trial, we also enrolled patients in NYHA class II, in line with current CRT recommendations. However, although CRT indication was extended to mildly symptomatic patients in the recent update of the European guidelines, the QRS width cutoff was increased from 120 to 150 ms in these patients, because randomized trials had seemed to demonstrate that the favorable effect of CRT was limited to patients with longer QRS duration.

### Secondary End Point Analysis

Our trial showed that CRT could improve survival from clinical events, such as death or hospitalization for worsening of HF, with NYHA functional class. This score has proved to be sensitive in detecting the presence or absence of a true CRT effect in both moderate and mild HF and, thus, in the stages of disease considered in the present study. Unlike the RethinQ trial, we also enrolled patients in NYHA class II, in line with current CRT recommendations. However, although CRT indication was extended to mildly symptomatic patients in the recent update of the European guidelines, the QRS width cutoff was increased from 120 to 150 ms in these patients, because randomized trials had seemed to demonstrate that the favorable effect of CRT was limited to patients with longer QRS duration.

### Table 2. Clinical Events and Clinical Composite Score Details in the CRT-D and D-ICD Groups

<table>
<thead>
<tr>
<th>Patients With Clinical Events</th>
<th>CRT-D Arm (n=56)</th>
<th>D-ICD Arm (n=55)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause death, n (%)</td>
<td>4 (7)</td>
<td>5 (9)</td>
<td>0.707</td>
</tr>
<tr>
<td>Death attributable to worsening HF, n (%)</td>
<td>2 (4)</td>
<td>5 (9)</td>
<td>0.232</td>
</tr>
<tr>
<td>From baseline to 12-mo visit,* n (%)</td>
<td>1 (2)</td>
<td>1 (2)</td>
<td>1.000</td>
</tr>
<tr>
<td>Hospitalization attributable to worsening HF, n (%)</td>
<td>5 (9)</td>
<td>11 (20)</td>
<td>0.097</td>
</tr>
<tr>
<td>From baseline to 12-mo visit,* n (%)</td>
<td>3 (5)</td>
<td>8 (14)</td>
<td>0.105</td>
</tr>
<tr>
<td>Improved NYHA class at 12-mo visit,* n (%)</td>
<td>25 (45)</td>
<td>13 (24)</td>
<td>0.020</td>
</tr>
<tr>
<td>Improved global assessment at 12-mo visit,* n (%)</td>
<td>30 (54)</td>
<td>18 (33)</td>
<td>0.027</td>
</tr>
<tr>
<td>Shock-terminated spontaneous ventricular fibrillation, n (%)</td>
<td>2 (4)</td>
<td>7 (13)</td>
<td>0.077</td>
</tr>
</tbody>
</table>

Subjects may be included in >1 event category. CRT-D indicates cardiac resynchronization therapy defibrillator; D-ICD, dual-chamber implantable cardioverter-defibrillator; HF, heart failure; and NYHA, New York Heart Association.

*Components of the primary end point.
of HF hospitalization, HF death, and spontaneous ventricular fibrillation, adopted as end points in previous large CRT trials,\textsuperscript{16,18} was significantly improved.

It had previously been shown that CRT could reduce sudden death,\textsuperscript{25} but this ability was seen to be delayed and seemed to depend on improvements in cardiac function. Indeed, CRT is associated with a reversal of structural remodeling and has been shown to lessen the risk of malignant arrhythmia.\textsuperscript{24}

Identification of Mechanical Dyssynchrony and Patient Selection

The method that we selected to identify mechanical dyssynchrony is one of the most frequently adopted in the literature\textsuperscript{6} and is the same as was used in the RethinQ trial. In the PROSPECT (Predictors of Response to Cardiac Re-Synchronization Therapy) trial,\textsuperscript{25} the time difference between lateral and septal peak systolic wall velocities was the only tissue Doppler imaging–based test, which demonstrated a significantly higher level of CRT response among patients meeting the cutoff criterion.

In our series, we only included patients with HF of ischemic origin. Among patients with narrow QRS, conduction delays and consequent inhomogeneities in ventricular activation are more frequently caused by ischemic endocardial damage rather than by discrete bundle–branch disease. This was apparent both in the post hoc MADIT-CRT analysis, in which the group with narrow QRS was mainly composed of ischemic patients,\textsuperscript{18} and in the recent study by Foley et al,\textsuperscript{26} who tested the efficacy of CRT in patients with normal QRS complex (<120 ms) who were not selected on the basis of mechanical dyssynchrony. In line with our findings, these authors were able to demonstrate an improvement in symptoms, exercise capacity, and quality of life on CRT. In their randomized study, they used late gadolinium–enhancement cardiovascular magnetic resonance scans to deploy the LV lead over nonscarred myocardium. However, although the avoidance of pacing myocardial scars could have produced a more favorable response to CRT, no other studies have used such a technique, and further studies are needed to confirm this hypothesis.

About half of our patients with a QRS interval of ≤120 ms presented evidence of mechanical dyssynchrony on baseline echocardiography. This finding closely matches that reported by Foley et al,\textsuperscript{26} despite the different technique adopted for intraventricular dyssynchrony assessment. Confirming their results, in the CRT-D group, we observed a significant reduction in the septal-to-lateral wall motion delay, which in 21% of patients turned out to have normalized during follow-up. Moreover, the rate of clinical events in the CRT-D group was

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Baseline</th>
<th>12 mo</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV ejection fraction, %</td>
<td>27±5</td>
<td>12 (10 to 13)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEDV, mL</td>
<td>194±52</td>
<td>−18 (−47 to 6)</td>
<td>0.070</td>
</tr>
<tr>
<td>LVESV, mL</td>
<td>143±40</td>
<td>−30 (−48 to −11)</td>
<td>0.003</td>
</tr>
<tr>
<td>LVEDD, mm</td>
<td>64±8</td>
<td>−3 (−5 to 0)</td>
<td>0.060</td>
</tr>
<tr>
<td>LVESD, mm</td>
<td>51±9</td>
<td>−5 (−7 to −2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intraventricular mechanical delay, ms</td>
<td>85±28</td>
<td>−36 (−44 to −27)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Twelve-month follow-up data are mean differences (95% confidence interval). CRT-D indicates cardiac resynchronization therapy defibrillator; LV, left ventricular; LVEDD, LV end-diastolic diameter; LVEDV, LV end-diastolic volume; LVESD, LV end-systolic diameter; and LVESV, LV end-systolic volume.
The use of CRT-D devices in the control arm, with inhibited our primary end point was relatively subjective, and some bias functional status were blinded to randomization assignment, Moreover, although patients and the physicians measuring not powered to detect differences in its secondary end points. The sample size was small and, although the statistical power was sufficient to address the primary end point, the study was Limitations

The sample size was small and, although the statistical power was sufficient to address the primary end point, the study was not powered to detect differences in its secondary end points. Moreover, although patients and the physicians measuring functional status were blinded to randomization assignment, our primary end point was relatively subjective, and some bias could have entered into the decision to hospitalize the patient. The use of CRT-D devices in the control arm, with inhibited ventricular pacing, would have improved the study blinding, but increased procedural and long-term risks.

Measuring additional outcome variables (eg, quality of life, 6-minute walking distance, peak oxygen consumption) would have enhanced the validity of the present findings. Furthermore, the lack of follow-up echocardiographic data in the D-ICD arm did not permit us to exclude the occurrence of similar changes among patients with dual-chamber defibrillators.

Conclusions

On the basis of the results of the NARROW-CRT study, which compared CRT defibrillators with dual-chamber defibrillators, it can be hypothesized that CRT improves clinical status in some patients with mild-to-moderate HF of ischemic origin and mechanical dyssynchrony, regardless of narrow QRS duration. However, pending the final results of the ongoing EchoCRT (Echocardiography Guided Cardiac Resynchronization Therapy) trial, this hypothesis remains to be verified.

Appendix

Echocardiographic core laboratory investigators: Raffaele Iengo and Michelangelo Canciello (Ospedale S. Maria di Loreto Mare, Napoli).

Enrolling centers contributed as follows: Ospedale S. Maria di Loreto Mare, Napoli (36 patients); Casa di cura “Montevergine” Mercogliano (27 patients); CdC Villa dei Fiori, Acerra (23 patients); CdC Villa Bianca, Bari (18 patients); CdC Villa Verde Taranto (11 patients); and Ospedale Buon Consiglio Fatebenefratelli, Napoli (5 patients).

Disclosures

The NARROW-CRT trial was an independent study. The Advisory Committee designed the trial. Boston Scientific provided technical support and supervised the implementation of the study, but had no access to the database and did not participate in the analysis of the results or the writing of the article. A Boston Scientific representative (Carmine Ciardiello) commented on the article before its submission. The other authors report no conflict.

References


A Randomized Study of Cardiac Resynchronization Therapy Defibrillator Versus Dual-Chamber Implantable Cardioverter-Defibrillator in Ischemic Cardiomyopathy With Narrow QRS: The NARROW-CRT Study

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