Reduced Ventricular Volumes and Improved Systolic Function With Cardiac Resynchronization Therapy

A Randomized Trial Comparing Simultaneous Biventricular Pacing, Sequential Biventricular Pacing, and Left Ventricular Pacing

Rajni K. Rao, MD; Uday N. Kumar, MD; Jill Schafer, MS; Esperanza Viloria, RN, MS; David De Lurgio, MD; Elyse Foster, MD

Background—Cardiac resynchronization therapy has emerged as an important therapy for advanced systolic heart failure. Among available cardiac resynchronization therapy pacing modes that restore ventricular synchrony, it is uncertain whether simultaneous biventricular (BiV), sequential BiV, or left ventricular (LV) pacing is superior. The Device Evaluation of CONTAK RENEWAL 2 and EASYTRAK 2: Assessment of Safety and Effectiveness in Heart Failure (DECREASE-HF) trial is the first randomized trial comparing these 3 cardiac resynchronization therapy modalities.

Methods and Results—The DECREASE-HF Trial is a multicenter trial in which 306 patients with New York Heart Association class III or IV heart failure, an LV ejection fraction ≤35%, and a QRS duration ≥150 ms were randomized to simultaneous BiV, sequential BiV, or LV pacing. LV volumes and systolic and diastolic function were assessed with echocardiography at baseline, 3 months, and 6 months. All groups had a significant reduction in LV end-systolic and end-diastolic dimensions (P<0.001). The simultaneous BiV pacing group had the greatest reduction in LV end-systolic dimension (P=0.007). Stroke volume (P<0.001) and LV ejection fraction (P<0.001) improved in all groups with no difference across groups.

Conclusions—Compared with LV pacing, simultaneous BiV pacing was associated with a trend toward greater improvement in LV size. There is little difference between simultaneous BiV pacing and sequential BiV pacing as programmed in this trial. (Circulation. 2007;115:2136-2144.)

Key Words: echocardiography • heart failure • pacing • remodeling

Cardiac resynchronization therapy (CRT), in which both the right ventricle (RV) and left ventricle (LV) are paced to synchronize ventricular contraction, may improve mechanical synchrony and ventricular performance in patients with systolic heart failure (HF). Recent trials have shown a significant mortality benefit with CRT with simultaneous left and right biventricular (BiV) pacing.1–3 The mortality benefit was accompanied by an improvement in LV function, New York Heart Association class, 6-minute walk distance, and peak oxygen consumption (V̇O₂) with exercise.1,2,4,5 CRT also has been shown to result in significant reductions in ventricular size.6–12

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Three major CRT modalities have emerged: simultaneous BiV pacing, sequential BiV pacing, and LV pacing. It has been hypothesized that LV pacing may be preferable to the other 2 CRT pacing modes in patients with left bundle-branch block because the LV lateral wall is the region in which electric conduction and mechanical contraction are the most delayed.1,2,4–6,8,13 Smaller studies of LV pacing have shown comparable, and sometimes superior, hemodynamic and functional benefits for simultaneous BiV pacing.14–19

In sequential BiV pacing, the timing of RV and LV stimulation (VV timing) can be programmed to allow 1 ventricle to be activated before the other. Several studies have shown superiority of optimized sequential BiV pacing over simultaneous BiV pacing in short-term outcomes such as hemodynamics, contractility (dP/dt), and tissue Doppler changes.20–22 However, a recent randomized trial did not prove superiority of sequential over simultaneous BiV pacing.23 These mixed results may be explained by the varied parameters used to optimize VV timing, which have included blood pressure, dP/dt, stroke volume, tissue Doppler synchrony, and various other echocardiographic parameters. No large studies have shown the superiority of 1 method of VV
optimization over another. A study is underway that will evaluate which echocardiographic measures best predict CRT response and may shed further light on this issue.\textsuperscript{24}

The Device Evaluation of CONTAK RENEWAL 2 and EASYTRAK 2: Assessment of Safety and Effectiveness in Heart Failure (DECREASE-HF) trial is a randomized, double-blind, 3-arm study designed to show treatment equivalence of sequential BiV and LV pacing to simultaneous BiV pacing in patients with advanced systolic HF, an LV ejection fraction (LVEF) ≤35\%, and a wide QRS (≥150 ms). This is the first randomized study comparing these 3 CRT modalities. The DECREASE-HF trial has shown equivalence of simultaneous and sequential CRT on a composite primary endpoint of peak VO\(_2\) and LV end-systolic dimension and showed a weaker improvement with LV pacing alone (D. De Lurgio et al, manuscript submitted for publication, 2007). In this article, we report the secondary echocardiographic end points of the DECREASE-HF trial. Echocardiographic data, including measurements of ventricular dimensions, systolic and diastolic function, and dyssynchrony, were obtained at baseline, 3 months, and 6 months and were compared among the 3 pacing groups.

**Methods**

The study rationale and design have been described elsewhere.\textsuperscript{25} Briefly, patients were included if they were ≥18 years of age and had New York Heart Association class III or IV HF, an LVEF ≤35\%, and a life expectancy >6 months. A QRS duration of ≥150 ms was required for inclusion because these patients have been shown to derive more benefit from LV pacing than those with a QRS duration of 120 to 150 ms.\textsuperscript{26} All patients were treated with optimal pharmacological therapy, and enrollment required at least 30 days of angiotensin-converting enzyme inhibitor and β-blocker therapy at stable doses. Patients were excluded if they had prior CRT, had a bradycardia indication for pacing, or were excluded if they had prior CRT, had a bradycardia indication for pacing, or were continued to receive CRT. Echocardiographic measurements and analysis were performed at a core laboratory by a single experienced observer blinded to the pacing mode and were reviewed by the laboratory director (E.F.). LV internal dimensions were measured with the leading-edge technique directly from the 2-dimensional parasternal long-axis view or from M-mode recordings. LV volumes and LVEF were calculated with Simpson’s rule (biplane method of disks at end diastole and end systole in the orthogonal apical 2- and 4-chamber views). Doppler measurements of systolic function included LV stroke volume (LV outflow tract velocity-time integral multiplied by the LV outflow tract area), cardiac output (product of stroke volume and heart rate), and mitral regurgitation (MR) dP/dt\(_{\text{max}}\) (derived by dividing 32 mm Hg by the time for the velocity rise from 1 to 3 m/s). Diastolic function was measured by transmitral Doppler flow. Tissue Doppler data for analysis of diastolic function was not assessed. The myocardial performance index, which is a combined index of systolic and diastolic function, was calculated by dividing the sum of isovolumic contraction and relaxation times by the LV ejection time. MR severity was graded on a scale of 0 to 3 of increasing severity using a combination of color and continuous Doppler flow and jet characteristics.

The present study was powered for analysis of the primary composite end point (peak VO\(_2\) and LV end-systolic dimension). Demographic data are presented as mean ± SD or frequencies. A value of \(P<0.05\) was considered statistically significant. Unless otherwise noted, all continuous variables were analyzed with ANOVA to examine the difference in the sample means (SAS/STAT version 9.1, SAS Institute, Inc, Cary, NC).

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

**Results**

Between March 2003 and April 2004, 360 patients were enrolled in the DECREASE-HF study; 2 patients withdrew from the study before undergoing the implant procedure. The investigational system was successfully implanted in 342 patients. Three of these patients died, 1 withdrew before randomization, and 32 patients were assigned to the safety arm because of an inability to complete baseline testing (n=13) or because of a simultaneous BiV pacing recommendation by Expert Ease (n=19). The remaining 306 patients were randomized to 1 of the 3 arms; 272 (89\%) had paired echocardiographic data at 6 months. Of the remaining 34 patients (11\%), 1 patient’s baseline echocardiogram was not located, 11 patients died within 6 months of study entry (2 in the simultaneous BiV group, 4 in the sequential BiV group, and 5 in the LV group), 9 patients withdrew from the study, 7 patients missed the 6-month echocardiography visit, 1 patient had an uninterpretable echocardiogram, and 5 patients had no 6-month echocardiogram for other reasons. There was no statistically significant difference in the dropout rate between the various pacing groups for any of the above reasons \((P=0.56\) to 1.00). The mean VO\(_2\) offset in the sequential BiV group was 48±14 ms (median, 50 ms; range, 0 to 80 ms). One patient randomized to the sequential BiV group was programmed by his or her physician to a VO\(_2\) offset of 0 ms; another patient was programmed to a VO\(_2\) offset of 10

lay) – 20 ms. All patients in these studies had LV stimulation before RV stimulation.

Echocardiographic data were obtained according to a predefined protocol based on standards defined by the American Society of Echocardiography at baseline (2 weeks after device implantation but before initiation of CRT) and at 3 and 6 months while patients were continuing to receive CRT. Echocardiographic measurements and analysis were performed at a core laboratory by a single experienced observer blinded to the pacing mode and were reviewed by the laboratory director (E.F.). LV internal dimensions were measured with the leading-edge technique directly from the 2-dimensional parasternal long-axis view or from M-mode recordings. LV volumes and LVEF were calculated with Simpson’s rule (biplane method of disks at end diastole and end systole in the orthogonal apical 2- and 4-chamber views). Doppler measurements of systolic function included LV stroke volume (LV outflow tract velocity-time integral multiplied by the LV outflow tract area), cardiac output (product of stroke volume and heart rate), and mitral regurgitation (MR) dP/dt\(_{\text{max}}\) (derived by dividing 32 mm Hg by the time for the velocity rise from 1 to 3 m/s). Diastolic function was measured by transmitral Doppler flow. Tissue Doppler data for analysis of diastolic function was not assessed. The myocardial performance index, which is a combined index of systolic and diastolic function, was calculated by dividing the sum of isovolumic contraction and relaxation times by the LV ejection time. MR severity was graded on a scale of 0 to 3 of increasing severity using a combination of color and continuous Doppler flow and jet characteristics.

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These patients are included in the sequential BiV analysis (intention to treat). The mean programmed atrioventricular delay was 97±1006, 96±1008, and 97±27 ms in the simultaneous BiV, sequential BiV, and LV pacing groups, respectively. The baseline (pre-CRT) PR intervals are listed in Table 1.

There were no significant differences in baseline characteristics, including age, LVEF, QRS duration, HF origin, and background medication use among the groups (Table 1). Most patients were in New York Heart Association class III. The mean qualifying LVEF (which was obtained by echocardiography, multiple gated acquisition scan, or left ventriculography at the enrolling site within 14 days before enrollment) was 22.6±6.6% in the simultaneous BiV, sequential BiV, and LV pacing groups, respectively. The baseline LVEF as measured by the core laboratory at the time of randomization across all groups was 28.1±0.4%. Most patients had a left bundle-branch block or nonspecific intraventricular conduction delay, except for 1 patient in the LV pacing group who developed a new right bundle-branch block after device implantation but before CRT initiation. The baseline heart rate was similar among all groups. Most patients in all pacing groups had an LV lead placed in the midlateral wall, and overall there were no significant differences in lead placement location across pacing groups. The echocardiographic measurements at baseline, 3 months, and 6 months for the LV,
sequential BiV, and simultaneous BiV groups are reported in Tables 2 through 5.

**LV Size**

Changes in chamber dimensions are presented in Table 2. At baseline, patients had marked LV enlargement with a mean LV end-diastolic dimension of 66.9 ± 0.5 mm and a mean LV end-diastolic volume (LVEDV) of 229 ± 4 mL. All groups had a significant reduction in LV end-diastolic dimension, LV end-systolic dimension, and LV end-systolic volume (LVESV) at 6 months. There was a trend toward greater improvement in LV dimensions and volumes with simultaneous BiV pacing. Only sequential and simultaneous BiV pacing led to a significant reduction in LVEDV. When all groups were combined, 27% of patients had a marked (≥15%) reduction in LVEDV. The simultaneous BiV pacing group had more patients with a marked (≥15%) reduction in LVEDV (36%, 23%, and 22% in the simultaneous BiV, sequential BiV, and LV pacing groups, respectively; *P* = 0.06, χ² test). When all groups were combined, 28% of patients had a marked (≥25%) reduction in LVESV. The simultaneous BiV pacing group had significantly more patients with a marked reduction (≥25%) in LVESV (40%, 24%, and 20% in the simultaneous BiV, sequential BiV, and LV pacing groups, respectively; *P* = 0.001, χ² test). The distribution of change in LV volumes and EF at 6 months among the 3 pacing groups is shown in the Figure.

**LV Systolic Function**

Systolic function was assessed by stroke volume, cardiac output, LVEF, MR dP/dt, and myocardial performance index (Table 3). All groups had a statistically significant increase in stroke volume and LVEF at 6 months. When all groups were combined, the mean LVEF increased by 6.7 ± 7.9 absolute units (median, 6.7 units), and 34% of patients had a marked (≥10 unit) increase in LVEF by 6 months. With each group separated, 42% of the simultaneous BiV pacing group, 33% of the sequential BiV pacing group, and 25% of the LV pacing group had a marked improvement in LVEF after 6 months (*P* = 0.05, χ² test). MR dP/dt also improved significantly within in all groups.

**LV Diastolic Function and Valvular Regurgitation**

With mitral inflow velocities, LV pacing was the only pacing modality that did not lead to a decrease in peak E-wave velocity. Sequential BiV pacing resulted in the greatest decrease in peak E velocity and E/A ratio compared with LV pacing (Table 4). These changes likely suggest a reduction in LV filling pressures with BiV pacing and/or an improvement in MR severity. The MR severity improved at 6 months in the simultaneous BiV and sequential BiV groups but not in the LV pacing group (Table 5). With each group separated, 27% of the simultaneous BiV pacing group, 32% of the sequential BiV pacing group, and 23% of the LV pacing group had an improvement in their MR severity by at least 1 grade. It was observed that 18% of patients in the LV pacing group
had worsened MR at 6 months compared with 5% in the simultaneous BiV pacing group and 3% in the sequential BiV pacing group ($P=0.004$ for comparison across groups based on a $\chi^2$ test).

### Echocardiographic Changes in Relation to the Origin of HF
Patients with nonischemic cardiomyopathy had a greater improvement after CRT compared with patients with ischemic cardiomyopathy. When 6-month data from all 3 pacing arms were pooled to compare patients with nonischemic and ischemic cardiomyopathy, the mean percent change in LVEDV was $-10.4\pm18.8$ versus $-1.2\pm18.5$ ($P<0.001$); the mean percent change in LVESV was $-20.1\pm22.9$ versus $-7.8\pm22.4$ ($P<0.001$); and the mean absolute improvement in LVEF was $8.7\pm8.5$ versus $5.6\pm7.3$ ($P=0.002$) for nonischemic versus ischemic origin, respectively. Although the simultaneous BiV group had a nonsignificantly larger percentage of patients with nonischemic cardiomyopathy, there was a trend toward greater improvement with simultaneous BiV pacing that was evident in patients with both ischemic and nonischemic cardiomyopathy when each group was analyzed separately. Furthermore, a multivariate analysis demonstrated that the trend favoring simultaneous BiV pacing after 6 months of CRT remained unchanged and was independent of HF origin.

### Discussion
The present study measured the benefits of 3 different CRT pacing modes on a background of optimal medical therapy for advanced HF. This is the first prospective randomized trial designed to compare simultaneous BiV pacing, sequential BiV pacing, and LV pacing. Despite having features of advanced cardiomyopathy, all groups exhibited a reduction in ventricular size, evidenced by a highly statistically significant reduction in LV end-diastolic dimension and LVESV. Overall, simultaneous BiV pacing was associated with a trend toward a greater reduction in ventricular size. Although CRT has been recognized for its ability to improve symptoms rapidly, its effect on ventricular volumes is equally important. Yu et al$^{11}$ have shown that even a 10% reduction in LVESV is a more powerful predictor of survival than is clinical improvement. The results from the DECREASE-HF trial showed an even greater improvement in LVESV. We observed that 40% of
patients treated with simultaneous BiV had a ≥25% improvement in LVESV.

Systolic function improved in all groups, as evidenced by the increase in stroke volume, LVEF, MR dP/dt, and myocardial performance index. There was a trend toward greater improvement in LV systolic function with simultaneous BiV pacing.

The overall improvement in LV volumes and LVEF is of a higher magnitude than has been seen in other CRT trials such as the Multicenter In Sync Randomization Clinical Evaluation (MIRACLE) study, in which the absolute median increase in LVEF was only 4.6 U compared with a median increase of 6.7 U in this trial. Some of the differences between our study and prior CRT trials may be due to the high rate of β-blocker use in our trial (>80% of patients) compared with 28% in the Multisite Stimulation in Cardiomyopathy (MUSTIC) trial, 58% in the MIRACLE study, and 67% in the more recent Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial. Without a control arm randomized to usual medical therapy without CRT, it is impossible to address the contribution of a greater penetration of β-blocker use. However, the requirement of stable doses of β-blockers and angiotensin-converting enzyme inhibitors for at least 90 days before randomization should have minimized the contribution of medical therapy to the echocardiographic changes at 6 months. By study design, the exclusion of the 11 patients who died before follow-up echocardiography also may have skewed the results to favor CRT responders. Additionally,

### TABLE 4. Diastolic Function

<table>
<thead>
<tr>
<th></th>
<th>LV Pacing</th>
<th>Sequential BiV</th>
<th>Simultaneous BiV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. Mean±SD</td>
<td>No. Mean±SD</td>
<td>No. Mean±SD</td>
</tr>
<tr>
<td>Peak E, m/s</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>91 0.82±0.28</td>
<td>96 0.83±0.27</td>
<td>90 0.79±0.28</td>
</tr>
<tr>
<td>Change at 3 mo</td>
<td>81 −0.03±0.22</td>
<td>87 −0.12±0.23</td>
<td>85 −0.08±0.25</td>
</tr>
<tr>
<td>Change at 6 mo</td>
<td>76 −0.01±0.21</td>
<td>83 −0.12±0.22</td>
<td>80 −0.08±0.26</td>
</tr>
<tr>
<td>*P</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak A, m/s</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>91 0.81±0.31</td>
<td>96 0.81±0.29</td>
<td>91 0.82±0.25</td>
</tr>
<tr>
<td>Change at 3 mo</td>
<td>80 −0.03±0.20</td>
<td>87 −0.00±0.23</td>
<td>87 −0.05±0.18</td>
</tr>
<tr>
<td>Change at 6 mo</td>
<td>75 −0.04±0.18</td>
<td>83 0.02±0.22</td>
<td>82 −0.06±0.23</td>
</tr>
<tr>
<td>*P</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E/A ratio</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>90 1.27±0.90</td>
<td>96 1.27±0.86</td>
<td>89 1.11±0.78</td>
</tr>
<tr>
<td>Change at 3 mo</td>
<td>78 0.04±0.79</td>
<td>86 −0.19±0.78</td>
<td>84 −0.05±0.71</td>
</tr>
<tr>
<td>Change at 6 mo</td>
<td>74 0.06±0.83</td>
<td>83 −0.24±0.77</td>
<td>80 −0.02±1.00</td>
</tr>
<tr>
<td>*P</td>
<td></td>
<td></td>
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</tbody>
</table>

*P value for between-group difference based on ANOVA.
\*P value for within-group change from baseline to 6 months based on a paired t test.

### TABLE 5. Valvular Regurgitation

<table>
<thead>
<tr>
<th></th>
<th>LV Pacing</th>
<th>Sequential BiV</th>
<th>Simultaneous BiV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. Mean±SD</td>
<td>No. Mean±SD</td>
<td>No. Mean±SD</td>
</tr>
<tr>
<td>TR grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>80 0.85±0.45</td>
<td>79 0.95±0.53</td>
<td>66 0.89±0.43</td>
</tr>
<tr>
<td>Change at 3 mo</td>
<td>64 −0.06±0.53</td>
<td>66 −0.11±0.36</td>
<td>60 −0.07±0.45</td>
</tr>
<tr>
<td>Change at 6 mo</td>
<td>63 −0.10±0.61</td>
<td>57 −0.12±0.57</td>
<td>52 −0.17±0.58</td>
</tr>
<tr>
<td>*P</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MR grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>99 1.22±0.69</td>
<td>104 1.26±0.62</td>
<td>100 1.07±0.70</td>
</tr>
<tr>
<td>Change at 3 mo</td>
<td>92 0.03±0.58</td>
<td>98 −0.27±0.58</td>
<td>96 −0.18±0.66</td>
</tr>
<tr>
<td>Change at 6 mo</td>
<td>87 −0.03±0.72</td>
<td>92 −0.29±0.60</td>
<td>92 −0.24±0.58</td>
</tr>
<tr>
<td>*P</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TR indicates tricuspid regurgitation.
*P value for between-group difference based on ANOVA.
\*P value for within-group change from baseline to 6 months based on a paired t test.
because the requirement of a baseline QRS duration of ≥150 ms was greater than in some other studies, the DECREASE-HF study may have selected patients with more ventricular dyssynchrony who were more likely to benefit from CRT. A QRS duration of ≥150 ms may lead to a more favorable response to LV pacing. Despite this potential bias, LV pacing was associated with much weaker overall benefits compared with the other 2 pacing modes.

**Study Limitations**

The present study did not test whether assessment of the acute hemodynamic response to various CRT modalities should be used to determine the optimal CRT strategy. Rather, patients were randomized equally to 1 of the 3 pacing strategies without testing the acute response to each of these modalities. Within the sequential BiV group, although the VV timing was programmed on the basis of baseline intrinsic conduction, it was not individually optimized according to the hemodynamic response. It is possible that if the CRT mode or VV timing had been adjusted on the basis of hemodynamic or echocardiographic criteria, the overall response would have been different. For example, the InSync III study recently showed that the LV stroke volume could be increased above simultaneous BiV pacing levels by using echocardiography to individually optimize the VV timing for each patient.27 However, there is no general agreement at this time on the best echocardiographic or other parameters that should be used to determine the pacing strategy and/or VV timing.

For LV pacing, it has been shown that enabling fusion of intrinsic right bundle conduction with paced LV conduction can improve systolic performance (LV dP/dt) compared with simultaneous BiV pacing.28 However, the presence of fusion was not established in our study.

Because the overwhelming majority of patients had a left bundle-branch block and a very prolonged QRS duration (≥150 ms), the present study does not address whether patients with right bundle-branch block or a QRS duration of 120 to 150 ms would have derived greater benefit from 1 CRT mode or another.

In this multicenter trial, comprehensive assessment of diastolic parameters such as pulmonary vein flow and tissue Doppler analysis was not available. However, to our knowledge, the reproducibility of tissue Doppler parameters has not previously been demonstrated in a multicenter trial.

Finally, because the follow-up echocardiograms were performed while CRT was being delivered, it is not possible to prove that reverse remodeling had taken place. However, the continued improvement in LV size between
3 and 6 months suggests that these volume changes were more likely due to structural changes at the myocardial level rather than just a temporary hemodynamic effect.

**Conclusions**

All 3 CRT pacing modes were associated with improvements in ventricular size and systolic function. Compared with the other 2 pacing modes, simultaneous CRT was associated with a greater trend toward improvement in ventricular volume. As programmed in this trial, there is no echocardiographic advantage of sequential BiV pacing compared with simultaneous BiV pacing. In contrast, LV pacing showed much weaker benefit on LV size and function and may worsen MR in a small subset of patients.

**Acknowledgment**

The authors wish to thank Patrick Yong for his assistance with the preparation of the figure.

**Sources of Funding**

The present study was sponsored by the Boston Scientific Corp, St Paul, Minn. Dr Foster and Dr De Lurgio have received research grants for this trial from Boston Scientific Corp. Dr Rao has received an unrelated research grant from Boston Scientific Corp.

**Disclosures**

Jill Schafer is an employee of Boston Scientific Corp.

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CLINICAL PERSPECTIVE
Cardiac resynchronization therapy has emerged as an important therapeutic option for patients with advanced systolic heart failure. In many patients, cardiac resynchronization therapy not only improves symptoms of heart failure but also leads to improved left ventricular size and function. Cardiac resynchronization therapy can be achieved by pacing the left ventricle alone, pacing the right and left ventricles simultaneously, or pacing the ventricles sequentially. The optimal pacing method has not been established. The Device Evaluation of CONTAK RENEWAL 2 and EASYTRAK 2: Assessment of Safety and Effectiveness in Heart Failure (DECREASE-HF) trial randomized patients to 1 of these 3 pacing modalities. The effects of these 3 pacing modalities on left ventricular size and function are presented. Although all 3 pacing modalities led to reduced left ventricular size and improved ejection fraction, there was a trend toward greater benefit in patients who received biventricular pacing. Left ventricular pacing alone was associated with more modest improvement. Patients with a nonischemic origin of heart failure derived the greatest benefit from cardiac resynchronization therapy compared with patients with ischemic heart failure. To the best of our knowledge, the present study is the largest published randomized trial comparing left ventricular, sequential biventricular, and simultaneous biventricular pacing. Although the trial was not powered to specifically compare simultaneous and sequential biventricular pacing, there was no clear advantage of sequential biventricular pacing as it was programmed in the present study. Biventricular pacing, particularly simultaneous biventricular pacing, trended toward greater improvement in left ventricular size and function.
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*Circulation*. 2007;115:2136-2144; originally published online April 9, 2007; doi: 10.1161/CIRCULATIONAHA.106.634444
*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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