**Midterm Benefits of Left Univentricular Pacing in Patients With Congestive Heart Failure**

Jean-Jacques Blanc, MD; Valérie Bertault-Valls, MD; Marjaneh Fatemi, MD; Martine Gilard, MD; Pierre-Yves Pennec, MD; Yves Etienne, MD

**Background**—Resynchronization therapy by simultaneous pacing of the right and left ventricles has gained wide acceptance as a useful treatment for patients with severe congestive heart failure. Several short-term hemodynamic studies in humans and animals failed to demonstrate any benefit of biventricular pacing over left univentricular pacing, but long-term studies on this pacing mode are lacking. The objective of this study was to assess the outcome over a 1-year period of patients paced exclusively in the left ventricle.

**Methods and Results**—Clinical, angiographic, echocardiographic, and ergometric data were collected at baseline and after 12 months in 22 patients (age, 69.3 ± 6.5 years) with NYHA class III or IV (10 patients), sinus rhythm, left bundle-branch block, and no bradycardia indication for pacing. After 12 months, compared with baseline values, NYHA class improved significantly by 40% (P < 0.0001), 6-minute walk distance by 30% (P = 0.01), peak VO₂ by 26% (P = 0.01), left ventricular end-diastolic diameter by 5% (P = 0.02), ejection fraction by 22% (P = 0.07), mitral regurgitation area by 40% (P < 0.01), and norepinephrine level by 37% (P = 0.04).

**Conclusions**—In patients with severe congestive heart failure, sinus rhythm, and left bundle-branch block despite optimal pharmacological treatment, left univentricular pacing is feasible and results in significant midterm benefit in exercise tolerance and left ventricular function. (Circulation. 2004;109:1741-1744.)

**Key Words:** heart failure ■ pacing ■ prognosis

Despite recent advances in drug treatment, congestive heart failure (CHF) remains a major healthcare problem associated with a poor quality of life and a high mortality rate, reaching ≈ 50% at 1 year in NYHA class IV patients. Recently, in patients with wide QRS complexes and severe CHF despite optimal pharmacological treatment, biventricular (BIV) permanent pacing has been demonstrated to result in significant improvement in quality of life. This treatment was initially based on the hypothesis that improvement in cardiac function was the consequence of restored simultaneous contractions of right and left ventricular (LV) cavities. However, many arguments have been developed to support the concept that LV univentricular (UNI) pacing by reversing the intraventricular dyssynchrony is sufficient to improve LV function to the same extent as BIV pacing. These data, based initially on short-term hemodynamic studies, were supported by experimental data. Nevertheless, although clinical improvement during permanent BIV pacing has been assessed in randomized prospective observational series, very few results are available on permanent UNI LV pacing. Furthermore, these results were based on a limited number of patients or included a very short-term follow-up. In a comparative nonrandomized trial, Touiza et al described a trend toward improvement in a limited series of patients with severe CHF and left bundle-branch block (LBBB) during LV pacing; this improvement at 6 months was almost identical to that in patients with BIV. In the present study, our aim was to report the 1-year outcome of patients with CHF and sinus rhythm with a conducted LBBB-pattern QRS who were exclusively LV paced.

**Methods**

**Study Population**

This prospective observational study was conducted on consecutive patients admitted to our department for severe CHF, LBBB, and no bradycardia indication for pacing. Selection criteria included age < 80 years, sinus rhythm, LBBB pattern (QRS duration > 140 ms), and stable NYHA class III or IV for ≥ 6 weeks despite a tailored optimal pharmacological treatment. Until 1999, only patients who demonstrated significant improvement during acute hemodynamic evaluation were implanted with a permanent pacemaker (4 patients enrolled in the present series; 3 others were not improved during short-term evaluation and were not implanted), but after that date (18 patients), this criterion was no longer required. Exclusion criteria were permanent atrial fibrillation, recent myocardial infarction or cardiac surgery (< 6 months), life expectancy of < 1 year for diseases other than CHF, and eligibility for heart transplantation.
Study Protocol
After informed consent was obtained, patients were evaluated at baseline (within 2 weeks before implantation); at 1, 6, and 12 months; and every 6 months thereafter. For the purpose of this study, only data observed at baseline and at 12 months were analyzed. Patient evaluation included physical examination, 12-lead ECG, cardiothoracic ratio, echocardiogram, radionuclide angiography, 6-minute walk distance, determination of peak oxygen consumption (peak VO₂) when feasible (7 patients in NYHA class IV were unable to perform this test), and norepinephrine blood level. Ischemic or nonischemic nature of the cardiomyopathy was diagnosed in every patient by coronary angiography.

Examinations Protocol
Implantation and evaluations—including history, clinical, and echocardiographic data—were performed by 2 different groups of physicians. Peak VO₂ measurement was performed in the morning. After a 2-minute warm-up at level 0 on the treadmill, the workload was increased by 20-W steps every 2 minutes until occurrence of severe dyspnea or inability to continue. Doppler echocardiography was performed at every visit by the same experienced physician who systematically measured the same parameters according to the usual techniques: LV end-systolic and end-diastolic diameters, fractional shortening, and mitral regurgitation (MR) area. LV ejection fraction (LVEF) was obtained by gated radionuclide ventriculography. Norepinephrine level was determined from blood samples drawn from patients in the supine position for ≥8 hours. Analysis was performed by reverse-phase HPLC and expressed in picomoles per milliliter.

Implantation Protocol
The transvenous long guiding sheath approach for permanent LV pacing used in our center has been previously described in detail. 20, 21 Attempts were made to place the LV lead in a lateral coronary vein where the latest local electrogram was recorded relative to the QRS onset. The atrial lead was then positioned in the right atrial appendage. The AV delay was set at 100 ms and, before discharge, individually programmed through the use of echocardiographic criteria. Before discharge and at every follow-up visit, appropriate functioning of the device was carefully verified, as was the fact that ventricular capture was permanent.

Follow-Up
As previously mentioned, the different tests were performed by physicians who had not implanted the device (clinical and echocardiographic data) or who were not members of the cardiology department and not involved in the present study (determination of peak VO₂ and nuclear gated angiography). For patients who died, cause of death was determined through interviews with family members and general practitioners.

Statistical Analysis
Values are expressed as mean±SD. Statistical tests are intrapatient comparisons; the values obtained in each individual at 12 months were related to those obtained in the same patient at baseline. Comparison of parameters between baseline and end of follow-up was performed by use of Student’s t test. Changes in these parameters were considered statistically significant P<0.05.

Results
A total of 30 consecutive patients in sinus rhythm were successfully implanted with a UNI LV pacing system in our department (4 patients during the inclusion period had unsuccessful attempts to be implanted, mainly during our learning curve period), but 8 had to be excluded from the present study for following reasons: 7 patients (16%) died during the first year (5 of refractory heart failure, 2 of sudden death), and 1 refused the follow-up visits. Thus, 22 patients were eligible for the 12-month evaluation and form the study population (13 men; mean age, 69.3±6.5 years).

Pharmacological treatment was not modified during the first year. In some patients, however, the doses of diuretics were reduced because of significant clinical improvement.

Pacing Follow-Up
We did not observe any lead dislodgement after the acute phase. One slender patient developed skin erosion and required lead and generator extraction after 8 months. New leads and device were successfully implanted in the contralateral site. At the end of the 12-month follow-up period, all patients had a fully functional LV pacing system.

Evolution over the 12-month period of functional parameters is summarized in Table 2. The 6-minute walk distance increased from 324±99 to 421±111 m (30%; P=0.01). Peak VO₂ evolved from 10.8±2.3 at baseline to 13.6±1.7 mL·min⁻¹·kg⁻¹ at 12 months (26%; P=0.01). A more dramatic improvement was observed in the functional NYHA class (mean of 3.5±0.5 at baseline to 2.1±0.7 at 12 months; P<0.0001). At an individual level, 2 patients improved by 3 NYHA classes, 7 patients by 2 classes, and 9 by 1 class, whereas 4 remained unchanged. As a whole and after inclusion of the 5 patients who died of refractory CHF before the 12-month follow-up visit, 9 patients (30%) did not exhibit functional improvement, a percentage of nonre-

<table>
<thead>
<tr>
<th>TABLE 1. Main Baseline Clinical Characteristics (22 Patients)</th>
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<tbody>
<tr>
<td><strong>Sex, male/female, n</strong></td>
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<tr>
<td><strong>Mean age, y</strong></td>
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<tr>
<td><strong>Mean QRS duration, ms</strong></td>
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<tr>
<td><strong>Dilated CM, n</strong></td>
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<tr>
<td><strong>Ischemic CM, n</strong></td>
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<tr>
<td><strong>NYHA class, n</strong></td>
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<tr>
<td>III</td>
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<tr>
<td>IV</td>
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<tr>
<td><strong>Drug treatment, n (%)</strong></td>
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<tr>
<td>Diuretics</td>
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<tr>
<td>ACE inhibitors</td>
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<td>Digoxin</td>
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<td>Spironolactone</td>
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<td>β-Blockers</td>
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CM indicates cardiomyopathy; ACE, angiotensin-converting enzyme.

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<th>TABLE 2. Comparison of Main Clinical and Ergometric Parameters Between Baseline and 12 Months</th>
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<tr>
<td><strong>NYHA class, n</strong></td>
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<tr>
<td>Baseline</td>
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<tr>
<td>IV</td>
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<tr>
<td>III</td>
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<tr>
<td>II</td>
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<tr>
<td>I</td>
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<tr>
<td><strong>QRS duration (n=22), ms</strong></td>
</tr>
<tr>
<td><strong>NYHA class (n=22), n</strong></td>
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<tr>
<td><strong>6-Minute walk test (n=20), m</strong></td>
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<tr>
<td><strong>Peak VO₂ (n=10), mL·min⁻¹·kg⁻¹</strong></td>
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TABLE 3. Comparison of Echocardiographic (n=21) and Angiographic (n=20) Parameters Between Baseline and 12 Months

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Basal</th>
<th>12 Months</th>
<th>P</th>
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<tbody>
<tr>
<td>LVEF, %</td>
<td>21.8 ± 7.7</td>
<td>26.6 ± 13</td>
<td>0.07</td>
</tr>
<tr>
<td>LVEDD, mm</td>
<td>76.5 ± 9.4</td>
<td>72.8 ± 10.4</td>
<td>0.02</td>
</tr>
<tr>
<td>LVESD, mm</td>
<td>68 ± 10</td>
<td>61 ± 13</td>
<td>0.002</td>
</tr>
<tr>
<td>FS, %</td>
<td>11.6 ± 3.8</td>
<td>17.3 ± 8</td>
<td>0.001</td>
</tr>
<tr>
<td>MR area, cm²</td>
<td>8.1 ± 4.5</td>
<td>4.9 ± 5.5</td>
<td>0.012</td>
</tr>
<tr>
<td>MR grade</td>
<td>1.9 ± 0.83</td>
<td>1.3 ± 0.96</td>
<td>0.007</td>
</tr>
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LVEDD indicates LV end-diastolic diameter; LVESD, LV end-systolic diameter; and FS, fractional shortening.

sponders similar to that reported in a previous series using BIV pacing. QRS duration did not decrease significantly (from 182 ± 22 to 173 ± 22 ms).

Data obtained from echocardiographic and angiographic examinations are reported in Table 3. MR area was reduced from 8.1 ± 4.5 to 4.9 ± 5.5 cm² (40%; P = 0.01), and end-systolic diameter was reduced from 68 ± 10 to 61 ± 13 mm (10%; P = 0.002). The LVEF evolved from 21.8 ± 7.7% to 26.6 ± 13% (22% improvement; P = 0.07). Cardi thoracic ratio decreased by 4.3%, from 59.1 ± 7.4% to 57.3 ± 6.3% (P = 0.07).

Norepinephrine blood levels decreased significantly between inclusion and 12 months from 2.8 ± 1.5 to 1.77 ± 0.85 pmol/mL (37%; n = 19; P = 0.04).

Discussion

This is the first study to show a significant 12-month improvement in exercise tolerance and cardiac remodeling by left UNI pacing in patients with severe CHF and LBBB.

Patient Selection

Patients included in the study were severely sick: 10 patients were in NYHA class IV, and all had a marked prolongation of QRS duration, a parameter associated with adverse outcome. Mean peak VO₂ was measured at 10.8 mL · min⁻¹ · kg⁻¹, a marker of poor quality of life and prognosis, and LV systolic function was severely altered (LVEF at 21.8%, LV end-diastolic diameter at 76.5 mm with significant MR). These patients probably had more advanced CHF than those included in randomized trials. In the Multisite Stimulation in Cardiomyopathies (MUSTIC) and Multicenter In Sync Randomized Clinical Evaluation (MIRACLE) studies, only patients with NYHA class III were recruited. Furthermore, the mean baseline peak VO₂ was measured at 14.9 mL · min⁻¹ · kg⁻¹ in the MUSTIC sinus rhythm 12-month group and at 14.0 mL · min⁻¹ · kg⁻¹ in patients included in the pacing arm of MIRACLE. This poor condition could explain the relatively high percentage of death (23%) during the first year. These patients are difficult to classify. Two patients died suddenly although they were markedly improved at their intermediate follow-up visit; we should therefore consider that they would have improved the overall results. Five patients died of intractable heart failure and therefore could be considered nonresponders. Finally, we have almost observed the “usually reported” nonresponder percentage (30%).

In our study, all patients had diuretics, and 20 of 22 had angiotensin-converting enzyme inhibitors at an optimal dose. Spironolactone was prescribed in nearly half the patients, and β-blockers were given to 36%. This relatively low prescription rate was due to a lack of tolerance and to the fact that the first patients were implanted before the publication of randomized trials demonstrating the effectiveness of β-blockers in patients with severe CHF. Patients recruited in the present series were not eligible for heart transplantation mainly because of their advanced age and were offered resynchronization pacing as a last therapeutic option.

Our implantation success rate is in the range of those already reported, and our implantation and fluoroscopic times are slightly shorter. In all patients, the pacing system was adequately functioning with permanent LV pacing at the 12-month follow-up visit.

Why LV Pacing Only?

At the beginning of our experience in 1996, the rationale for pacing patients with severe CHF without bradycardia was resynchronization of right ventricular and LV contractions. For some authors, only patients with marked narrowing of QRS complexes were considered responders. However, the first published series on acute hemodynamic benefits of cardiac pacing failed to demonstrate the superiority of BIV versus UNI LV pacing. These preliminary results, confirmed by others, supported the implantation of only 1 LV lead in patients with CHF.

Present Results

All parameters evolved favorably. A placebo effect could have contributed to the improvement in some parameters such as 6-minute walk distance but certainly not others (LVEF, norepinephrine level). Furthermore, a pacemaker placebo effect is difficult to explain results 12 months after implantation of the device. The nonblinded design of the study may represent a bias. However, physicians in charge of patient evaluation during follow-up visits were not involved in the study.

Of interest is the decrease in norepinephrine levels. This parameter has been thought to be closely related to the prognosis of heart failure, and the observation of its significant favorable evolution in a limited number of patients is certainly of great value for the validity of the procedure. Despite similar effects on mechanical resynchronization, LV pacing alone may lead to worsening of electrical dispersion compared with BIV pacing, and this result could prompt argument for implantation of a combined resynchronization-defibrillator device in these high-risk patients. However, sudden death occurred in only 2 patients (markedly improved at the first intermediate visit) during the first year after implantation; this result is not in favor of a proarrhythmic effect of UNI LV pacing.

Why Is LV Pacing Effective?

Although there is no definite answer to this question, the most likely hypothesis, according to recent experimental and clinical data, is that in patients with LBBB or in animals with experimentally induced LBBB, the LV contractions are totally desynchronized. Schematically, the septal area is “akineti-" while the lateral wall is contracting normally but with a marked delay after other areas. This inhomogeneous contraction of different LV segments has deleterious consequences: induction or worsening of MR and a decrease in LVEF. Premature stimulation of the lateral LV wall resynchronizes the contractions of the septal and lateral segments of the LV, resulting
in a decrease in MR\(^9\) and an improved effectiveness of contractions.\(^{10}\) The present study shows that during long-term pacing there is reverse remodeling with a significant decrease in LV diameters. A very important finding has been reported by Nelson et al:\(^{12}\) Pacing the LV improves the strength of its contractions (dP/dt), and the consequence is a decrease in myocardial oxygen consumption. Finally, pacing the LV lateral wall results in more coordinated contractions with improved cardiac function at a lower energy cost and long-term reverse remodeling effects.

**Comparison Between UNI and BIV Pacing**

All short-term hemodynamic studies that have compared UNI LV and BIV pacing have reported either equivalent\(^9,10,12\) or even better\(^11\) results with UNI LV. Experimental data also failed to disclose any significant difference between the 2 pacing modalities.\(^{13,14}\) In patients with dilated cardiomyopathy, Fauchier et al\(^{10}\) have recently shown that only intraventricular but not interventricular desynchronization is associated with severe adverse outcomes.

The only randomized study on permanent pacing in patients with CHF and LBBB is based on a limited number of patients followed up for 4 weeks.\(^{15}\) The conclusion is that LV pacing and BIV pacing achieve the same improvement. Touiza et al.\(^{16}\) in a nonrandomized series of patients followed up during 6 months, came to a similar conclusion. In the present study, the patients followed up for 12 months remained significantly improved. Comparison between results observed at 12 months in the 35 patients included in the MUSTIC sinus rhythm group (the only published results on BIV pacing at 12 months) and the present study showed similar degrees of improvement in the 2 series.\(^3\) Finally, there are no data in the literature to exclude the possibility that UNI LV pacing could achieve results similar to those of the more expensive, fluoroscopically time-demanding, time-consuming, and complicated BIV pacing mode.

**Conclusions**

In patients with LBBB and severe CHF despite optimal pharmacological treatment, UNI LV pacing mode is feasible and results in significant midterm improvement in exercise tolerance and LV function. The present data give strong support for undertaking trials adequately designed to compare UNI LV with other more sophisticated resynchronization pacing modes in patients with severe heart failure.

**References**

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