Long-Term Left Ventricular Pacing: Assessment and Comparison With Biventricular Pacing in Patients With Severe Congestive Heart Failure
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OBJECTIVE
The purpose of this study is to report prospectively the results of six-month follow-up of permanent left ventricular (LV) based pacing in patients with severe congestive heart failure (CHF) and left bundle branch block (LBBB).

BACKGROUND
Left ventricular pacing alone has been demonstrated to result in identical improvement compared to biventricular pacing (BiV) during acute hemodynamic evaluation in patients with advanced CHF and LBBB. However, to our knowledge, the clinical outcome during permanent LV pacing alone versus BiV pacing mode has not been evaluated.

METHODS
Pacing configuration (LV or BiV) was selected according to the physician's preference. Patient evaluation was performed at baseline and at six months.

RESULTS
Thirty-three patients with advanced CHF and LBBB were included. Baseline characteristics of LV (18 patients) and BiV (15 patients) pacing groups were similar. During the six-month follow-up period, seven patients died (three BiV and four LV). In the surviving patients at 6 months, 8 of 14 patients in the LV group and 9 of 12 in the BiV group were in New York Heart Association class I or II (p = 0.39). No significant difference was observed between the two groups in terms of objective parameters except for LV end-diastolic diameter decrease (−4.4 mm in BiV group vs. −0.7 mm in LV group; p = 0.04).

CONCLUSION
At six-month follow-up, a trend toward improvement was observed in objective parameters in patients with severe CHF and LBBB following LV-based pacing. The two pacing modes (LV and BiV) were associated with almost equivalent improvement of subjective and objective parameters. (J Am Coll Cardiol 2001;38:1966–70) © 2001 by the American College of Cardiology

Congestive heart failure (CHF) is a major health care problem, associated with a high mortality rate reaching almost 50% at one year in New York Heart Association (NYHA) class IV patients (1). Moreover, the quality of life of patients with CHF remains poor despite optimal management. Some pharmacologic agents such as angiotensin-converting enzyme inhibitors, beta-blockers or spironolactone were found to improve survival in patients with CHF; others such as digoxin only ameliorate the quality of life (2). Recently, permanent cardiac pacing has been suggested as an adjuvant therapy for patients with severe CHF and wide QRS complexes (3–8). This treatment was based initially on the hypothesis that resynchronization of left and right ventricular contractions might restore left ventricular (LV) function (6,9). Left ventricular–based pacing was evaluated by several groups using uncontrolled studies and the first acute and short-term evaluations demonstrated encouraging results (3–8). Interestingly, LV pacing alone has exhibited comparable improvement to biventricular (BiV) pacing during acute hemodynamic evaluation in patients with advanced CHF and left bundle branch block (LBBB) (3–5,8). Nevertheless, clinical follow-up during permanent LV pacing is unknown. This study aimed to evaluate the six-month clinical follow-up of permanent LV pacing compared to BiV pacing in patients with CHF and LBBB.

METHODS
This prospective comparative observational study was conducted on consecutive patients with severe CHF and LBBB and no class I indication for permanent pacing. Entry in the study was decided in two steps: first, patients <80 years of age with LBBB (QRS duration >140 ms) and severe CHF were selected for hemodynamic evaluation. The ischemic or nonischemic nature of their cardiomyopathy was determined using coronary angiography. Pharmacologic treatment was considered optimal and unchanged for at least three months. The main exclusion criteria were a recent myocardial infarction (<6 months), or coronary artery bypass surgery and a limited life expectancy (<1 year) due to disease other than CHF. Potential candidates for heart transplantation were also excluded. Left ventricular or BiV pacing mode was determined according to the physician's preference (mainly BiV at the beginning of our experience).

Study protocol. Patients evaluation included the following: physical examination, electrocardiogram, blood test, echocardiography, radionuclide angiography, 6-min walk test

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and peak oxygen consumption ($V_{O2}$) evaluation using a treadmill test with the following protocol: after a 2-min warm-up at level 0, the workload increased was proceeded by 20-W steps every 2 min until occurrence of severe dyspnea, chest pain, fatigue or inability to continue the test. Thereafter, patients underwent a hemodynamic evaluation as previously described (3). Briefly, pulmonary artery capillary wedge pressure (PCWP) and “V” wave were obtained by advancing a catheter into a distal branch of the pulmonary artery. A femoral artery catheter was used for blood pressure recordings. In patients in sinus rhythm, two bipolar catheters were positioned transvenously in the high right atrium and the right ventricular (RV) apex. A third bipolar catheter was advanced via retrograde approach through the aortic valve to pace the endocardial part of the LV lateral free wall. Pacing was performed with an atrioventricular (AV) delay of 100 ms, in order to achieve complete capture of the ventricles (pacing output of 3 V at 0.5 ms). For patients in sinus rhythm, pacing was performed in the atrial synchronous ventricular inhibited pacing (VDD) mode for 3 min before data acquisition in a random order at the RV apex alone, the left lateral free wall alone and at both sites simultaneously with the left lateral free wall being the anode and RV apex being the cathode. In patients in atrial fibrillation, the ventricular demand pacing (VVI) pacing mode was used, and the pacing rate was programmed 100 beats/min above the spontaneous mean ventricular rate.

Baseline data recorded in all patients included mean arterial blood pressure, PCWP and “V” wave amplitude (mm Hg). An immediate improvement of 20% of at least one of these hemodynamic parameters in comparison to baseline values during LV-based pacing was required for final inclusion for permanent pacing. The pacing mode, LV or BiV was left to the physician’s decision and also according to technical difficulty during implantation. Patients were aware of the possibility of having one or two leads and were informed about the clinical trial.

A transvenous approach for permanent LV-based pacing was used (10). Briefly, a “long” sheath was inserted into the coronary sinus and the pacing electrode (unipolar lead, Medtronic 4023/65 cm, Medtronic Inc., Minneapolis, Minnesota; or St Jude 1055K/75 cm, St. Jude Medical, Sylmar, California) was advanced though the long sheath into one of its branches and very preferentially in a lateral vein successfully attained in most cases. In the BiV pacing group, the RV lead (bipolar lead, St. Jude 1470T/55 cm) was placed at the apex. For patients with BiV pacing, the ventricular leads were connected to the ventricular port of a standard dual-chamber generator through a Y connector (lead extension IS-1, 3.2 mm, SYCB 53415, Sulzer Medica Ospitka, Grenzach-Wyhlen, Germany).

**Follow-up.** Clinical follow-up was performed at 1 and 6 months. At every follow-up visit, clinical parameters, 6-min walk test, echocardiography, radionuclide angiography and peak $V_{O2}$ were determined. At each visit, interrogation of the pacemaker confirmed that ventricular pacing was largely predominant (>95% of the time). Final pacemaker reprogramming was individually performed at the end of the first month using echocardiographic determination of the best AV interval (generally 100 ms).

**Statistical analysis.** Data were expressed as mean ± standard deviation or as percentage. Chi-square test was used to compare categorical variables and paired or unpaired Student t test (two-tailed) for continuous variables. Statistical significance was achieved at $p < 0.05$ level. Statistical analysis was performed using StatView 4.5 software (Abacus Concepts, Inc.).

**RESULTS**

**Study population.** Thirty-three patients fulfilled the inclusion criteria. As shown in Table 1, LV (n = 18) and BiV (n = 15) pacing groups had similar demographics characteristics. Patients included in this study presented the usual clinical parameters of advanced CHF regardless of the NYHA functional class severity (20 in class IV): the mean left ventricular ejection fraction (LVEF) was 23.4% and peak $V_{O2}$ was 11.7 ± 3.1 ml/kg per min.

### Table 1. Baseline Patient Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>LV (n = 18)</th>
<th>BiV (n = 15)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender ratio (M/F)</td>
<td>13/5</td>
<td>13/2</td>
<td>0.55</td>
</tr>
<tr>
<td>Dilated/ischemic cardiomyopathy (n)</td>
<td>12/6</td>
<td>8/7</td>
<td>0.43</td>
</tr>
<tr>
<td>Atrial fibrillation/sinus rhythm (n)</td>
<td>10/8</td>
<td>5/10</td>
<td>0.20</td>
</tr>
<tr>
<td>NYHA class III/IV (n)</td>
<td>6/12</td>
<td>7/8</td>
<td>0.43</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>69 ± 6</td>
<td>67 ± 6</td>
<td>0.46</td>
</tr>
<tr>
<td>QRS duration (ms)</td>
<td>183 ± 24</td>
<td>187 ± 37</td>
<td>0.69</td>
</tr>
<tr>
<td>LVEDD (mm)</td>
<td>72.7 ± 7.6</td>
<td>73.4 ± 7.3</td>
<td>0.81</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>24.7 ± 7.6</td>
<td>22 ± 7.1</td>
<td>0.31</td>
</tr>
<tr>
<td>MR area (cm²)</td>
<td>13.1 ± 6.0</td>
<td>10.5 ± 6.2</td>
<td>0.26</td>
</tr>
<tr>
<td>Six-min walk distance (m)</td>
<td>395 ± 109</td>
<td>412 ± 74</td>
<td>0.63</td>
</tr>
<tr>
<td>Peak $V_{O2}$ (ml/kg per min)</td>
<td>11.7 ± 3.5</td>
<td>11.7 ± 2.7</td>
<td>0.99</td>
</tr>
</tbody>
</table>

BiV = biventricular pacing; LV = left ventricular pacing alone; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; NYHA = New York Heart Association; $V_{O2}$ = oxygen consumption.
due to progressive deterioration of CHF in the other six patients. Surviving patients (n = 26) showed no significant difference in clinical characteristics when compared to the whole population (n = 33). As shown in Table 2, baseline clinical characteristics in surviving patients were identical in the two groups. The LV group included more patients with dilated cardiomyopathy (p = 0.51), whereas, atrial fibrillation was more frequently observed in the BiV pacing group (p = 0.64). The 6-min walk distance and the LV end-diastolic diameter (LVEDD) were also greater in the BiV pacing group, but the difference did not reach statistical significance (p > 0.37). After six months of permanent pacing, overall improvement from baseline was observed (Table 3) and the final values at six months were very similar in the two groups.

Comparison of benefits at 6-month follow-up in the two groups. At six months, NYHA functional class improvement was clearly observed in the two pacing groups (Table 3). In fact, eight and nine patients in the LV and BiV groups, respectively, moved to NYHA class I and II. Only three patients from each group remained in NYHA class IV. No significant difference between LV and BiV groups was observed for the NYHA functional class distribution. Mean improvements of the functional class were 1.1 and 1.3, respectively, for the LV and BiV groups (p = 0.63). The evolution of the other parameters recorded during follow-up was variable (Table 3): the LVEDD decreased more significantly in the BiV group (p = 0.04). The LVEF tended to improve more in the BiV group than in the LV group (p = 0.06); conversely, mitral regurgitation (MR) area, 6-min walk distance and peak VO2 variations remained in the same range in the two study groups. The QRS duration obtained immediately after pacemaker implantation showed a greater decrease in the BiV group than in the LV group (−19 ms vs. −1 ms, p = 0.09). Interestingly, the LVEF improvement was significantly correlated to the QRS duration diminution in the BiV group (r = 0.67, p = 0.02) but not in the LV group (r = 0.15, p = 0.66).

Safety. No significant difference in average fluoroscopic times during pacemaker implantation was observed between the LV group (36 ± 18 min) and the BiV group (39 ± 24 min; p = 0.81). Only one serious adverse event (pocket infection six months later) occurred in a patient included in the BiV pacing group, with a final favorable outcome after implantation of a new pacemaker on the other side. Lead dislodgment requiring repositioning occurred in two patients included in the LV pacing group and in one patient from the BiV pacing group.

DISCUSSION

Although all acute hemodynamic studies comparing LV pacing alone versus BiV pacing have shown equivalent (3) or even better results (4,5) with LV pacing alone, comparative long-term data are lacking in current series and only results of studies with permanent BiV pacing are reported. Two explanations could be proposed: 1) BiV was the first reported pacing mode having demonstrated long-term benefit in patients with severe CHF and long QRS duration and physicians continue to ignore the results of acute series; and 2) “resynchronization” of the two ventricles was considered, without any demonstration, as a prerequisite for improvement of the conditions of such patients. However, it is clear that from a technical, economical and perhaps safety point of view that it is easier and better to implant two rather than three leads. The absence of clear evidence for the superiority of BiV pacing led us to leave the pacing mode to the investigator’s discretion.

Rationale for the present study design. This prospective study was considered as a pilot study. The follow-up was limited to six months to allow inclusion of a sufficient number of patients due to the high mortality rate associated with NYHA class IV.

Patients included had to demonstrate a significant improvement during acute hemodynamic evaluation with either LV or BiV pacing mode. We know of no data to substantiate this attitude but, at the beginning of our experience, we believed that it was more ethical to consider LV-based pacing only in such patients. Nevertheless, this prerequisite is not a bias in the comparison of LV and BiV.
patients as they were compared after the same selection procedure and we disregarded the result of the acute evaluation regarding the choice of chronic pacing modality. Moreover, in the vast majority of cases, when hemodynamic improvement was observed, it was present with the two pacing modes.

**Comparison between the two pacing groups.** The baseline characteristics of the two groups were very close, even after exclusion of patients who died during the first six months. Patients were severely sick with a mean LVEF of <25%. The QRS duration was very long (>180 ms), especially in the BiV group. After 6 months, 7 patients had died in the study group. This high mortality rate has to be related to the NYHA class of the patients included and was certainly predictable. Of note, the mortality rate was identical in both groups and only one patient died suddenly. Due to the limited number of events, no definite conclusion regarding survival could be drawn from these data.

At six months, the functional status of the surviving patients was significantly ameliorated from baseline and was similar in both groups. Such results have already been reported during long-term studies of BiV pacing (11) but not up to now after permanent LV pacing alone. More objective parameters such as LVEDD, LVEF, peak VO2, 6-min walk distance and MR area were also improved between baseline and six months, not only in the BiV group but also in the LV group.

**Comparison of benefits in the two groups.** Although the two groups improved in most of the studied parameters between baseline and six months, improvement tended to be greater in the BiV group for LVEDD and LVEF, whereas it remained similar in the two groups for the other parameters and particularly for those exploring quality of life.

In these small groups of patients, safety was not a problem, although one patient with BiV pacing presented with a pacemaker pocket infection that required explantation of the pacing lead system and re-implantation of a new system on the other side with an excellent result.

**Hypothesis for the improvement during LV-based pacing.** It is clear from this study that although the conditions of some patients did not improve, the majority did so and sometimes very impressively. This long-term improvement occurred during BiV pacing but also during LV pacing alone in accordance with the results of acute hemodynamic studies. These results suggest that the most important phenomenon that leads to the improvement of LV function in those patients with wide QRS complexes is the LV stimulation and not the resynchronization of the two ventricles. One could argue that in patients in sinus rhythm, the QRS complex is a fusion between the impulse originating from the left lateral pacing electrode and the impulse traveling through the AV node, preferentially to the RV resulting in a “hidden” resynchronization. This hypothesis seems unlikely as: 1) the programmed AV delay is short and probably a major part of the RV was depolarized from the left, and 2) more importantly, the improvement was found to be equivalent in a previous acute study, in patients with atrial fibrillation paced either in the LV alone or in both ventricles (12). If resynchronization of the two ventricles is not the key mechanism, the beneficial effect may result from the fact that LV pacing with or without RV pacing eliminates the deleterious effects of LBBB (13). Biventricular pacing results in right bundle branch block and LV pacing alone leads to more pronounced RV conduction disturbance. Whether this induced right bundle branch block has long-term hemodynamic deleterious effects remains unknown, but acute data on hemodynamics of LBBB are not in favor of this hypothesis. The present study does not bring any definite argument to think so, although LVEDD and LVEF improved more in the BiV group than in the LV group, but their baseline value was worse in the former group.

**Study limitations.** The small number of patients included is certainly a limitation and a more extensive study is needed to confirm these data. The most obvious limitation is the absence of randomization, but the baseline values were very close in the two groups indicating that their comparison is valid. The location of the LV lead is questionable but has to satisfy many different and generally incompatible parameters such as pacing thresholds, anatomy of the tributaries of the coronary sinus, stability of the electrode and best electrophysiologic site, a concept intuitively linked to the most delayed recorded ventricular potential. Ideally, determination of the latest potential requires multiple attempts from different sites, which is time-consuming and anatomy-limited; however, new technologies may improve this research. In the present study, we attempted in every case to implant the lead in a “lateral” vein and to avoid the posterior or very anterior branches. We succeeded in the vast majority of the cases, but whether the final site was optimal remains uncertain.

**CONCLUSIONS**

This study, in agreement with previously published series, shows that permanent BiV pacing improves subjective and objective parameters at 6 months. The new data suggest that LV pacing alone achieves the same goal. Although a trend exists in favor of BiV pacing for the improvement of some parameters (poorer at baseline in this subgroup of patients), most are equivalent and the clinical status is identical in the two pacing modalities at 6 months. However, these results should be interpreted cautiously and longer follow-up may disclose significant differences in favor of BiV pacing. As there are no published series (to our knowledge) demonstrating that permanent BiV pacing is significantly better than LV pacing alone and even if this study has limitations, it gives rationale to compare in a randomized study the sophisticated BiV pacing and the more simple LV pacing in patients with CHF and LBBB.
REFERENCES