Dual-Chamber Pacing in Hypertrophic Obstructive Cardiomyopathy
—— A Comparison of Acute and Chronic Effects ——

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This study describes the acute and chronic effects of dual-chamber (DDD) pacing in 14 consecutive patients with hypertrophic obstructive cardiomyopathy (HOCM), whose symptoms were refractory to drug therapy. Although left ventricular (LV) outflow tract pressure gradients diminished from 106±47 to 62±33 mmHg (p<0.001) by temporary pacing, the residual pressure gradients were >30 mmHg in the majority of those with concomitant reductions in cardiac output. The DDD pacing was judged as insufficient by the acute study in the majority of patients. A dual-chamber pacemaker was, however, implanted in 11 patients, and the chronic pacing effects were evaluated. All symptoms (syncope, fainting, palpitation and dyspnea) subsided within 1 month. Left ventricular outflow tract pressure gradients diminished from 99±56 to 21±13 mmHg (p<0.004) at 1 week after, and to 17±12 mmHg (p<0.002) at 1 year after the implantation, as measured by Doppler echocardiography. Echocardiogram showed disappearance of the systolic anterior motion of the mitral valve, and significant regression of the septal hypertrophy (from 18.5±4.3 to 15.7±4.1 mm, p<0.04). There was no significant correlation between the acute and chronic pacing effects in the reduction of the pressure gradients or symptomatic improvement. These results suggest that DDD pacemaker implantation is an effective treatment without any serious risks for patients with drug-refractory HOCM. The chronic-pacing effect in the reduction of the pressure gradient, the regression of hypertrophy and symptomatic improvement cannot be predicted by the assessment of temporary DDD pacing. (Jpn Circ J 1999; 63: 971–975)

Key Words: Hypertrophic obstructive cardiomyopathy (HOCM); Dual-chamber (DDD) pacing; Acute effect; Chronic effect

Management of patients with drug-refractory, symptomatic hypertrophic obstructive cardiomyopathy (HOCM) is a challenging problem. Septal myotomy/myectomy and mitral valve replacement have been performed for 3 decades, but these surgical treatments carry significant mortality, and the postoperative prognoses are not always favorable. Anticoagulation must be continued permanently after mitral valve replacement, and symptomatic deterioration and aortic regurgitation have been reported in patients after myotomy/myectomy.

Recently, atrioventricular (AV) sequential pacing with a short AV delay has been proposed as a therapeutic method for patients with drug-refractory HOCM, and some investigators have reported favorable results from therapeutic dual-chamber (DDD) pacemaker implantation. However, the guidelines for the indication of pacemaker implantation in these patients have not been established yet. The purpose of the present study was to evaluate whether the chronic effects of DDD pacing with a short AV delay can be predicted from the temporary AV sequential pacing in these patients, and to report follow-up data of symptoms and echocardiographic findings.

Methods

Patient Population

Fourteen consecutive patients with drug-refractory HOCM (Table 1) were enrolled (9 men and 5 women; mean age 53±13 years). All patients were shown to have septal hypertrophy with a significant left ventricular (LV) outflow tract (LVOT) pressure gradient at rest. They complained of dyspnea or palpitations on mild exercise, in spite of medication with sufficient doses of ß-blockers or verapamil. Thirteen patients had apparent episodes of syncope on daily exercise and another patient had some episodes of near fainting. The patients with provocative-type HOCM were not included in this study.

Temporary DDD Pacing Study

After obtaining written informed consent, 12 of the 14 patients underwent temporary AV sequential pacing with a short AV delay. Cardiac catheterization was performed in the fasting state, and all cardiac medications were withheld 24h prior to the procedures. DDD pacing was done with catheter electrodes positioned at the high, right atrium (RA) and right ventricular (RV) apex during cardiac catheterization. The ventricular electrode was introduced into the RV
apex with the consideration of permanent pacemaker implantation. Pressure tracings at the LV apex and aorta were recorded simultaneously using a fluid-filled system and/or catheter tip manometers. Temporary pacing was performed with VDD mode, and the AV delay was set up with conditions that produced the minimum LVOT pressure gradients. Cardiac output was measured with the thermodilution method before and during appropriate pacing after stabilization for at least 5 min. The effects of the temporary pacing were evaluated with the changes in the pressure gradient and cardiac index.

**Permanent DDD Pacing**

Permanent DDD pacemakers were implanted in 11 patients. Among the 12 patients who underwent temporary pacing, 9 patients accepted pacemaker implantation, but the remaining 3 patients refused it. Two patients who did not undertake temporary pacing wished to have permanent pacemaker implantation, so DDD pacemakers were implanted in them. Endocardial electrodes were inserted transvenously via the left subclavian vein by the cut-down method, and positioned at the RA appendage and RV apex. The pacemakers were set up individually under Doppler echocardiographic guidance with conditions that produced the minimum LVOT pressure gradient. The pressure gradient and the echocardiographic parameters were observed before, 1 week, 6 months and 1 year after the pacemaker implantation. Because pressure gradients are known to present dynamic changes, all echocardiographic examinations were performed under the same conditions, and reap-

### Table 1 Patients' Profiles and Results of Temporary Dual-Chamber (DDD) Pacing

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age (years)</th>
<th>Sex</th>
<th>NYHA/Syncope</th>
<th>Pressures (mmHg)</th>
<th>PG (mmHg)</th>
<th>CI (L min⁻¹ m⁻²)</th>
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<tbody>
<tr>
<td></td>
<td>RA</td>
<td>PC</td>
<td>LV</td>
<td>Ao</td>
<td>Pacing off</td>
<td>Pacing on</td>
</tr>
<tr>
<td>1</td>
<td>63</td>
<td>M</td>
<td>3/+</td>
<td>16</td>
<td>175/30</td>
<td>75</td>
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<tr>
<td>2</td>
<td>60</td>
<td>M</td>
<td>3/+</td>
<td>9</td>
<td>250/16</td>
<td>164</td>
</tr>
<tr>
<td>3*</td>
<td>46</td>
<td>M</td>
<td>2/+</td>
<td>8</td>
<td>200/13</td>
<td>62</td>
</tr>
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<td>4</td>
<td>45</td>
<td>F</td>
<td>2/+</td>
<td>10</td>
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<td>70</td>
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<td>5*</td>
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<td>2/+</td>
<td>1</td>
<td>200/10</td>
<td>90</td>
</tr>
<tr>
<td>6*</td>
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<td>M</td>
<td>2/+</td>
<td>10</td>
<td>161/18</td>
<td>55</td>
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<tr>
<td>7*</td>
<td>58</td>
<td>F</td>
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<td>3</td>
<td>275/7</td>
<td>105</td>
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<td>14</td>
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<tr>
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<td>59</td>
<td>F</td>
<td>2/+</td>
<td>5</td>
<td>208/11</td>
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<tr>
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<td>M</td>
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<td>8</td>
<td>190/18</td>
<td>76</td>
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<td>M</td>
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<td>2</td>
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<td>6</td>
<td>330/10</td>
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<tr>
<td>13*</td>
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<tr>
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<td>F</td>
<td>2/+</td>
<td>4</td>
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</tbody>
</table>

| Mean±SD    | 106.1±46.8  | 61.6±32.9  | 3.09±0.77       | 2.83±0.70 |

*DDD pacemaker implanted in this study. NYHA, New York Heart Association functional class; CI, cardiac index; RA, mean right atrial; PC, mean pulmonary capillary; LV, left ventricular; Ao, aortic; PG, peak LV outflow tract pressure gradient.

**Fig 1.** Effects of temporary dual-chamber (DDD) pacing. The left ventricular outflow tract pressure gradient is significantly decreased by temporary pacing, but the residual pressure gradient is still high. The cardiac index significantly decreased by the pacing.
The effects of chronic pacing were evaluated by changes in the symptoms, pressure gradients and echocardiographic findings. Cardiac medication with β-blockers or verapamil was not changed during the follow-up period.

**Statistical Analysis**

Data are expressed as mean ± 1 SD. The paired t test was applied in the statistical analyses, and a p value <0.05 was considered significant. Bonferroni correction for multiple testing was used to analyse the effects of chronic pacing.

**Results**

**Effects of Temporary DDD Pacing**

The patients' profiles and the results of the temporary pacing are presented in Table 1. During cardiac catheterization, the heart rate did not vary in spite of ventricular pacing. The LVOT pressure gradients decreased to some extent in all patients with DDD pacing with a short AV delay (Fig 1). The reduction rate of the pressure gradient...
ranged from 18 to 81% (mean 42±20%) and a prominent pressure difference remained in most of the patients. Moreover, the cardiac index decreased in 9 patients, and the mean cardiac index decreased significantly during the pacing (Fig 1). Pulmonary capillary and RA pressures showed no significant changes during the procedures.

Effects of Chronic DDD Pacing

The results of the permanent DDD pacing are presented in Table 2. Chronic observation could not be performed in one patient who had concomitant alcoholism, because we could not locate him after discharge.

After the pacemaker implantation, syncope or fainting disappeared in all patients. The other symptoms, such as palpitations or dyspnea on mild exercise, subsided within 1 month. The New York Heart Association (NYHA) functional class of these patients improved from 2.3±0.5 to 1.5±0.5 (p<0.05) 6 months after DDD pacing. The LVOT pressure gradient diminished from 99±56 to 21±13 mmHg (p<0.004) 1 week after implantation (Fig 2). The reduction rate of the pressure gradient at this time was 73±19%. It was significantly high in comparison with the results of temporary pacing (p<0.003). The pressure gradient was kept low during chronic pacing, and it seemed to decrease more 1 year after implantation. The echocardiogram showed disappearance of systolic anterior motion of the mitral valve. Significant regression of the hypertrophy in the interventricular septum was observed after chronic DDD pacing (Fig 2). No evidence of newly developed mitral regurgitation was observed during the follow-up period.

Comparison of Acute and Chronic Pacing Effect

In order to make clear the relationship between acute and chronic pacing effects, we compared the reduction rate of the pressure gradient calculated from the data derived from temporary and chronic DDD pacing. There was no significant correlation between them (Fig 3).

Discussion

It has been known for about 30 years that RV pacing in patients with HOCM diminishes the LVOT pressure gradient. AV sequential pacing with a short AV delay was proposed as a therapeutic method for patients with HOCM in 1984. Since then, DDD pacing in drug-refractory HOCM has been reported to improve exercise tolerance and the LVOT pressure gradient. These findings have been considered a consequence of reduced or paradoxical movement of the interventricular septum derived from RV pacing. There is, however, no method to predict the efficacy of chronic DDD pacing before pacemaker implantation. Expecting that temporary AV sequential pacing might be as effective as chronic pacing, and that therefore this method might give some guidance for pacemaker implantation, we performed an initial acute study first.

Our results showed that the LVOT pressure gradient was significantly decreased by temporary pacing, but the residual pressure gradient was still high, and the cardiac index decreased in most of the patients. These results suggested that the effects of DDD pacing were insufficient. We did not recommend permanent pacemaker implantation at first, but instead recommended myectomy. The clinical symptoms of heart failure improved with the reduction of the outflow tract pressure gradient in one patient with concomitant advanced AV block after DDD pacemaker implantation. This observation encouraged us to conduct the present study regardless of the results of the acute study.

The pressure gradient progressively diminished after chronic DDD pacing, and regression of the septal hypertrophy was also observed. These findings were in agreement with long-term results reported by Fananapazir et al. Thus, there was some discrepancy between the results of the acute and chronic pacing. It is clear that RV pacing modifies the wall motion of the septum and reduces the LVOT pressure gradient. The reduction of the pressure gradient reduces pressure overload of the LV wall and so these processes probably cause remodelling of the myocardium, and regression of the septal hypertrophy may further relieve the outflow obstruction.

Recently, Nishimura et al presented negative data for pacemaker therapy in patients with HOCM. They reported that cardiac function was affected by AV delay and therefore, the reduction in cardiac output was the result of inadequate booster effects due to short PR duration. They
concluded that the improvement in the symptoms was due to placebo effects. Our data also showed a drop in cardiac output during temporary pacing. At the same time, Nishimura et al also noticed the favorable effects of DDD pacing in decreasing the pressure gradient and relieving symptoms. Though they concluded that the improvement in the symptoms was irrelevant to the reduction in pressure gradient, we believe that the pressure gradient must be considered as an important determinant for cerebral and cardiac symptoms. Disappearance of syncope is expected with a significant reduction in the pressure gradient. In our study, syncope and fainting disappeared in all patients after pacemaker implantation. The other symptoms improved gradually during the long-term observation. This evidence can not be explained as placebo effects, and the prevention of syncope certainly improved the quality-of-life.

Drug-refractory HOCM has been treated with septal myotomy/myectomy, or mitral valve replacement. These surgical treatments are associated with significant mortality, and the postoperative prognoses are not always satisfactory. The reported mean operative mortality is 4%. Residual LV outflow obstruction, aortic regurgitation, iatrogenic ventricular septal defect and complete AV block sometimes cause problems. Recently, percutaneous transluminal septal myocardial ablation with ethanol injection has been tried as a substitute therapy for these operations. Ethanol induced septal infarction carry significant mortal-ity, and morbidity and postoperative risks, we believe that pacemaker implantation should be tried before surgical or interventional treatment, irrespective of the results of the temporary pacing study.

References