Evidence for Anti-Ischemic Effect of Dual-Chamber Pacing in Patients with the Obstructive Form of Hypertrophic Cardiomyopathy

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SUMMARY

Dual-chamber pacing reportedly improves the quality of life by reducing the frequency of anginal episodes in selected patients with the obstructive form of hypertrophic cardiomyopathy (HCM), although the underlying mechanism or coronary effect is poorly understood. We report 3 patients with obstructive HCM in whom the effects of atrial vs. dual-chamber tachypacing on systemic hemodynamics and myocardial lactate metabolism were studied. In all patients myocardial lactate production, objective evidence of myocardial ischemia, was demonstrated during atrial pacing, whereas no patient developed myocardial ischemia during dual-chamber pacing. By contrast, the responses of pressure gradient to pacing varied among the patients. These observations demonstrate for the first time that dual-chamber pacing exerted an anti-ischemic effect in obstructive HCM, which may contribute, at least partly, to the beneficial effects of chronic AV pacing on angina status and/or LV function. (Jpn Heart J 2003; 44: 587-592)

Key words: Myocardial ischemia, Coronary circulation, Lactate metabolism

PATIENTS with hypertrophic cardiomyopathy (HCM) frequently develop exercise-induced chest pain even in the absence of epicardial coronary artery disease. Angina is reportedly more frequent in those having left ventricular outflow tract (LVOFT) obstruction.1-3) Although β-blockers are the basic treatment for angina in the obstructive form of HCM, dual-chamber pacing has also been used as an option when the medical treatment fails to control symptoms.4) The European PIC (Pacing in Cardiomyopathy) randomized trial documented that ativoventricular (AV) sequential pacing improved the quality of life in selected patients with obstructive HCM.5) However, pacemaker implantation is known to have a placebo effect on symptoms,6,7) and direct evidence to demonstrate that dual-chamber pacing actually ameliorates myocardial ischemia is lacking. In this brief
communication, we report our experience of studying the effects of atrial and
dual-chamber pacing tachycardia on myocardial lactate metabolism in three
patients.

**CASE REPORTS**

The clinical backgrounds and baseline hemodynamics of the patients studied are summarized in the Table. While all patients had been on medication including metoprolol, two had exertional angina and one had easy fatigability. These patients were suspected of having LVOFT obstruction on Doppler-echocardiographic examination and underwent cardiac catheterization as a possible candidate for chronic dual-chamber pacing. Coronary angiography revealed normal epicardial coronaries in all patients. A 5F multipurpose catheter was inserted from the right brachial artery and advanced into the left ventricle. Left ventricular pressure and brachial arterial pressure were simultaneously measured and the difference was used as a surrogate of LVOFT pressure gradient. Two pacing catheters were inserted from the right femoral vein, and the tip of the catheter was placed in the right atrium and the right ventricular apex, respectively. Another 6F catheter was advanced in the coronary sinus vein to sample the blood for the determination of lactate concentrations. The lactate extraction ratio was calculated as the ratio of the arterial-coronary sinus difference in lactate concentration to arterial concentration. A negative extraction ratio (ie, lactate production) was considered to be evidence of myocardial ischemia.

Different AV delays were first tested to determine the optimal intervals that minimized LVOFT pressure gradient at the patient's own rhythm. AV sequential

| Table. Clinical Characteristics and Baseline Hemodynamics of the 3 Patients |
|-----------------------------|-------------------|-------------------|-------------------|
| Variable                    | Patient 1         | Patient 2         | Patient 3         |
| Age (y)                     | 55               | 46               | 43               |
| Sex                         | male             | female           | female           |
| Medication                  | metoprol          | metoprol         | metoprol         |
|                            | +                | +                | +                |
| Angina                      | plus              | plus             | minus            |
| Heart rate, beats/min       | 54               | 70               | 60               |
| Brachial pressure (systolic), mmHg | 144             | 84               | 121              |
| LV pressure (systolic), mmHg | 162             | 206              | 159              |
| LVEDP, mmHg                 | 11               | 15               | 20               |
| LVOFT pressure gradient, mmHg | 18              | 122              | 38               |
| Cardiac output, L/min       | 7.4              | 4.9              | 3.9              |

LV = left ventricular; LVEDP = left ventricular end-diastolic pressure ; LVOFT = left ventricular outflow tract.
pacing with a fixed AV delay (120 msec in two patients and 80 msec in one) was then performed at three pacing rates (100 bpm, 120 bpm, 140 bpm) for 2 minutes each. Paired blood sampling from a brachial artery and coronary sinus vein was conducted at the end of each pacing run. After heart rate and blood pressure were stabilized, atrial tachypacing (100 bpm, 120 bpm, 140 bpm for 2 minutes each) was performed in the same manner.

Serial changes in myocardial lactate metabolism at baseline and during two tachypacing runs in each patient are shown in Figure 1. AV sequential pacing up

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**Figure 1.** Changes in myocardial lactate extraction ratio (LER) during pacing. Positive LER was maintained during dual-chamber pacing (AV-pacing, open circles) in all 3 patients. By contrast, myocardial ischemia as evidenced by a negative extraction ratio was evoked during atrial pacing (A-pacing, open squares). BSL = baseline.
Figure 2. Left ventricular (LV) and brachial artery (BA) pressure tracings and ECG (V4) from Patient 1. Tracings at the pacing rate of 140 bpm are shown. Note that the pressure gradient was decreased with AV sequential pacing (AV-pace) but markedly increased with atrial pacing (A-pace).

Figure 3. Changes in peak pressure gradient (PG) at LVOFT during AV pacing (open circles) and atrial pacing (open squares).
to 140 bpm did not cause myocardial ischemia, as evidenced by the positive lactate extraction ratio. By contrast, myocardial lactate production (ie, negative extraction ratio) was demonstrated in all three patients during atrial pacing.

In contrast to the consistent changes in myocardial lactate metabolism, the hemodynamic responses to pacing varied among the patients. In patient 1, AV sequential pacing at 140 bpm decreased the LVOFT pressure gradient from 18 mmHg to 8 mmHg, while atrial pacing at the same rate increased it from 16 mmHg to 102 mmHg (Figures 2 and 3). In the remaining two patients, atrial and AV sequential pacing decreased the LVOFT gradient to an almost comparable degree (Figure 3).

**DISCUSSION**

We observed that AV sequential pacing, but not atrial pacing, ameliorated myocardial ischemia during induced tachycardia. Previous studies have documented that dual-chamber pacing improved the angina status in patients with obstructive HCM.4,5) To the best of our knowledge, our report is the first to offer direct evidence demonstrating that dual-chamber pacing prevented myocardial ischemia under the condition of increased heart rate.

Intriguingly, the improvement in myocardial lactate metabolism was not accounted for exclusively by a reduction in the LVOFT pressure gradient. For example, both atrial and AV pacing decreased the LVOFT pressure gradient to a comparable degree in patients 2 and 3, but myocardial ischemia (ie, lactate production) was prevented only when the right atrium and ventricle were sequentially paced. This finding is in accordance with earlier studies which demonstrated that an acute effect of dual-chamber pacing on the LVOFT pressure gradient did not necessarily predict long-term outcomes following pacemaker implantation.6,8) It is very likely that complex interactions among many factors other than the LVOFT gradient may also be involved in determining the balance between myocardial oxygen supply and demand. These include left ventricular end-diastolic pressure, left ventricular systolic/diastolic function, and the transmural distribution of coronary blood flow.9) Unfortunately, we did not assess these variables in our patients due to technical limitations.

In summary, we have shown that dual-chamber pacing exerted an anti-ischemic effect in obstructive HCM, which may contribute at least partly to the beneficial effects of chronic AV pacing on the angina status and/or LV function. Our observation also suggests that assessing the effect of pacing on pressure gradient alone does not necessarily predict whether dual-chamber pacing is effective
in ameliorating myocardial ischemia, and the coronary effect of pacemaker implantation may be of prognostic significance in these patients. The latter hypothesis needs to be confirmed in a future study consisting of a larger number of patients.

REFERENCES