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Changes in myocardial oxidative metabolism after biventricular pacing as evaluated by [^{11}C]acetate positron emission tomography

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A 70-year-old woman with dilated cardiomyopathy and recurrent severe heart failure was admitted for biventricular pacing (BVP), which was recently reported to have clinical efficacy for severe heart failure with intraventricular conduction delay. An electrocardiogram showed complete left bundle branch block, and the QRS interval was markedly prolonged at 195 msec. Echocardiogram showed marked dilatation, diffuse hypokinesis and dyssynchrony of the left ventricle, and grade III mitral valve regurgitation. The patient underwent implantation of an atriobiventricular pacemaker and three pacing leads transvenously. The QRS interval shortened to 165 msec immediately after the BVP therapy, and improvements in echocardiographic parameters were seen at 5 months after BVP therapy. Myocardial oxidative metabolism was assessed by the monoexponential clearance rate of [^{11}C]acetate (Kmono) as measured by positron emission tomography (PET), and myocardial efficiency was assessed by the work metabolic index (WMI) at 1 and 5 months after the BVP therapy. The PET images obtained 5 months after BVP therapy showed a decrease in the clearance of [^{11}C]acetate compared with that obtained 1 month after BVP therapy. The Kmono of the whole left ventricle decreased from 0.051 at 1 month to 0.038 min^{-1} at 5 months after BVP therapy, and that of the septum, anterior wall, lateral wall and posterior wall also decreased. The WMI increased from 4.2×10^6 to 6.8×10^6 mmHg·ml/m^2. These results suggest that BVP improved left ventricular function without increasing myocardial oxidative metabolism, resulting in improved myocardial efficiency, and that BVP may improve the long-term prognosis of heart failure patients with ventricular dyssynchrony. [^{11}C]acetate PET is a useful method of evaluating global and regional myocardial oxidative metabolism in patients who have undergone BVP therapy.

Key words: [^{11}C]acetate, positron emission tomography, myocardial oxidative metabolism, biventricular pacing

INTRODUCTION

DESPITE RECENT ADVANCES in pharmacological treatment, the prognosis of patients with chronic heart failure remains poor. Nonpharmacological therapies such as heart transplantation are considered only in the later stages of the disease. Recently, the clinical efficacy of biventricular pacing (BVP) has been reported in patients with severe heart failure and intraventricular conduction delay.[1–3]

We present a case of dilated cardiomyopathy and recurrent severe heart failure who underwent BVP, and evaluated myocardial oxidative metabolism using [^{11}C] acetate positron emission tomography (PET) at 1 and 5 months after BVP therapy.

CASE REPORT

A 70-year-old woman with dilated cardiomyopathy and recurrent severe heart failure was admitted to our hospital for implantation of an atriobiventricular pacemaker. The

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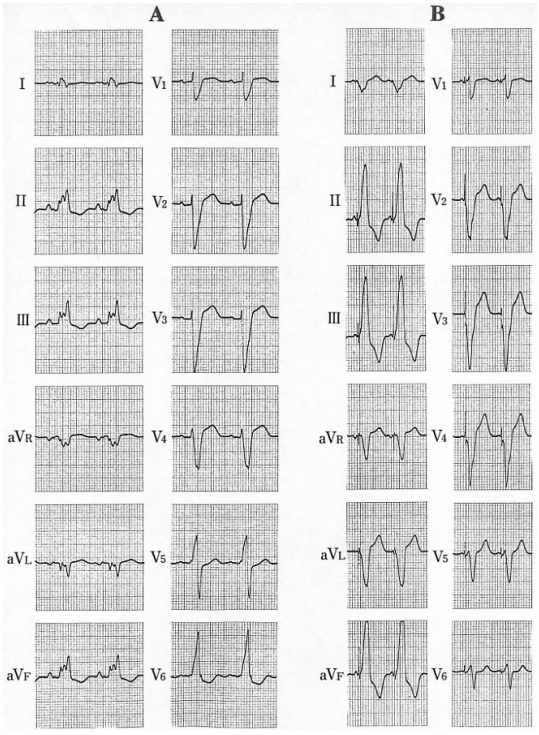

Fig. 1 Electrocardiograms. (A) Electrocardiogram obtained at admission. QRS interval = 195 msec. (B) Electrocardiogram obtained immediately after the BVP therapy. QRS interval = 165 msec.

Table 1 Clinical parameters before and 1 and 5 months after BVP therapy

Parameters	before BVP	1 month after BVP	5 months after BVP
BNP, pg/m*l*	> 2000	1350	972
HR, bpm	70	66	64
Systolic BP, mmHg	86	90	88
Diastolic BP, mmHg	56	58	52
LVDd, mm	83	82	79
LVDs, mm	79	77	73
LVEF, %	10	12	17
SVI, m*l*/m^2	31	36	46
MR grade	III	II	II
Kmono, min^{-1}		0.051	0.038
WMI, mmHg × m*l*/m^2		4.2×10^6	6.8×10^6

BVP: biventricular pacing, BNP: brain natriuretic peptide, HR: heart rate, BP: blood pressure, LVDd: left ventricular end-diastolic diameter, LVDs: left ventricular end-systolic diameter, LVEF: left ventricular ejection fraction, SVI: stroke volume index, MR: mitral regurgitation, WMI: work metabolic index

patient had been diagnosed as having nonischemic dilated cardiomyopathy at the age of 65 years, and was being treated with an angiotensin II receptor blocker, diuretics (furosemide and spironolactone) and a beta-blocker.

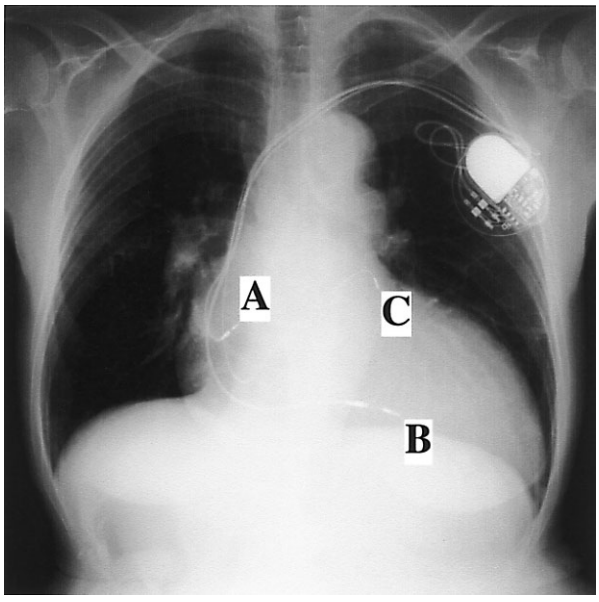

Fig. 2 Chest roentgenogram obtained immediately after the BVP therapy. A, right atrial lead; B, right ventricular lead; C, left ventricular lead that had been placed into a distal cardiac vein by way of the coronary sinus.

However, severe heart failure recurred several times. On admission, the patient was in New York Heart Association (NYHA) class IV. An electrocardiogram showed normal sinus rhythm and complete left bundle branch block, and the QRS interval was markedly prolonged at 195 msec (Fig. 1A). An echocardiogram showed marked dilatation (end-diastolic diameter: 83 mm), diffuse hypokinesis (ejection fraction: 10%), and dyssynchrony of the left ventricle, and grade III mitral valve regurgitation. The plasma level of brain natriuretic peptide (BNP) was markedly elevated at over 2,000 pg/m*l*.

The patient underwent implantation of an atriobiventricular pacemaker (KappaDR731, Medtronic, Minneapolis, USA) and three pacing leads, i.e., a right atrial lead, a right ventricular lead, and a left ventricular lead that was placed into a distal cardiac vein by way of the coronary sinus through a guiding catheter (Fig. 2). Immediately after the BVP therapy, acute hemodynamic effects including elevation of systolic blood pressure (86→98 mmHg), decrease in pulmonary wedge pressure (27→20 mmHg) and increase in cardiac output (2.3→3.0 *l*/min), were observed, and the QRS interval shortened to 165 msec (Fig. 1B). Five months after the BVP therapy, echocardiographic measurements and the BNP level had improved as shown in Table 1, and the patient was in NYHA class III.

We used [^{11}C]acetate PET imaging to evaluate myocardial oxidative metabolism. PET examinations were performed 1 and 5 months after the BVP therapy. PET imaging could not be performed before BVP because of the poor general status of the patient. The patient was

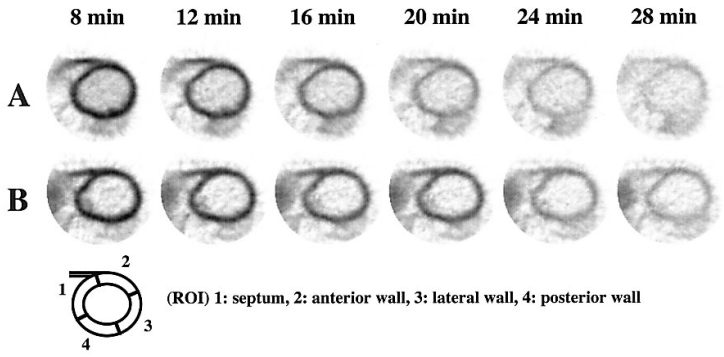

Fig. 3 Serial [^{11}C]acetate positron emission tomograms obtained every 4 min. (A) At 1 month after the BVP therapy. (B) At 5 months after the BVP therapy.

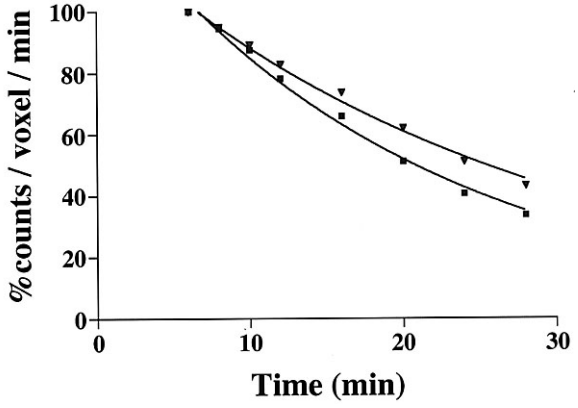

Fig. 4 Myocardial time-activity curves of the whole left ventricle after infusion of [^{11}C]acetate. ■, 1 month after BVP therapy; ▼, 5 months after BVP therapy.

positioned in a whole body PET scanner (Headtome IV, Shimadzu, Kyoto, Japan), and [^{11}C]acetate (750 MBq) was intravenously injected as a bolus. Serial PET images were acquired every 2 and 4 min for 28 min (2 min × 4, 4 min × 5). The reconstructed dynamic PET images were analyzed by applying 5 regions of interest (ROI) covering the septum, anterior wall, lateral wall, posterior wall and the whole left ventricle in a midventricular transaxial plane. The myocardial time-activity curve was fitted monoexponentially, and the monoexponential clearance rate of [^{11}C]acetate (Kmono) was determined from the initial linear part of the time-activity curve for each ROI. Moreover, myocardial efficiency was assessed using the concept of work metabolic index (WMI), where WMI = stroke volume index × systolic blood pressure × heart rate/ Kmono.[4]

The PET images obtained 5 months after the BVP therapy showed a decrease in the clearance of [^{11}C] acetate in comparison with that obtained 1 month after the BVP therapy (Fig. 3), and the Kmono of the whole left ventricle decreased from 0.051 at 1 month to 0.038 min^{-1} at 5 months after the BVP therapy (Fig. 4). As for regional oxidative metabolism, the Kmono decreased from 0.047 to 0.037 min^{-1} in the septum, from 0.044 to 0.037 min^{-1} in the anterior wall, from 0.061 to 0.041 min^{-1} in the lateral wall, and from 0.052 to 0.036 min^{-1} in the posterior wall. The WMI increased from 4.2×10^6 at 1 month to 6.8×10^6 mmHg · ml/m^2 at 5 months after the BVP therapy.

DISCUSSION

One-third of patients with chronic heart failure exhibit a prolonged QRS interval (i.e., intraventricular conduction delay) and asynchronous ventricular contraction, which further worsen left ventricular dysfunction. Recent studies suggest that atrial-synchronized biventricular pacing improves the hemodynamics, exercise tolerance and quality of life of patients with chronic heart failure by reducing ventricular asynchrony.[1–3] Therapies that increase the myocardial oxygen consumption may improve short-term hemodynamics, but are thought to worsen the long-term prognosis of patients with chronic heart failure.[5–7] However, there are few studies on the effect of BVP on myocardial oxygen consumption and oxidative metabolism. Nelson et al.[8] measured coronary blood flow and arterial-coronary sinus oxygen difference in ten patients with dilated cardiomyopathy, and reported that biventricular pacing improved systolic function without increasing myocardial oxygen consumption in contrast to dobutamine. Ukkonen et al.[9] measured Kmono using [^{11}C]acetate PET in eight patients with dilated cardiomyopathy, and reported that atriobiventricular pacing improved left ventricular function without increasing left ventricular oxygen metabolism in comparison to atrial pacing.

We measured the monoexponential clearance rate of [^{11}C]acetate (Kmono) using PET, and evaluated the changes in myocardial oxidative metabolism after BVP in a patient with advanced heart failure. The Kmono at 5 months after the BVP therapy had decreased in all regions compared with that at 1 month after the BVP therapy,

suggesting that BVP does not increase global or regional oxygen consumption in the chronic phase, while the WMI increased, suggesting that BVP improves myocardial efficiency.

In conclusion, BVP improved left ventricular function without increasing myocardial oxidative metabolism, resulting in improved myocardial efficiency in the present case. BVP may improve the long-term prognosis of heart failure patients with ventricular dyssynchrony. [^{11}C]acetate PET is a useful method of evaluating global and regional myocardial oxidative metabolism, and further PET studies are needed before and after BVP.

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