Positron Emission Tomographic Demonstration of Myocardial Oxidative Metabolism in a Case of Left Ventricular Restoration After Cardiac Resynchronization Therapy

Kenji Kitaizumi, MD; Kazushi Yukiiri, MD; Hisashi Masugata, MD*; Kaori Shinomiya, MD; Minako Ohara, MD; Hiroyuki Takekami, MD; Yasuyoshi Iwado, MD; Junji Yoshida, MD; Takahisa Noma, MD; Koji Ohmori, MD; Yoichi Yamashita, MD**; Taiko Horii, MD***; Shoich Senda, MD*; Masakazu Kohno, MD

A 65-year-old man with a history of coronary artery bypass grafting was admitted because of severe heart failure. Echocardiography showed diffuse severe hypokinesis of the left ventricle (ejection fraction 25%) and severe mitral regurgitation caused by tethering of the leaflet secondary to left ventricular (LV) dilation. He underwent mitral valve anuloplasty and LV papillary muscle imbrication. Postoperative aortic valve doppler flow showed that all bypass arteries and grafts were free of ostial stenosis and other stenotic lesions on the proximal right coronary artery, left anterior descending branch and circumflex branch were detected by emergency coronary angiography and he underwent coronary artery bypass grafting with anastomosis of the left internal thoracic artery to the obtuse marginal branch and the left anterior descending branch and saphenous vein to the right coronary artery. In May 2006, he was re-admitted because of cardiac failure after therapy for a gastric ulcer, when he did not improve despite treatment with catecholamines, diuretics and vasodilation in another hospital. On admission, auscultation revealed a widespread coarse crackle in the lung fields and a systolic, blowing murmur (Levine III/VI) at the cardiac apex. Laboratory tests indicated multiple organ failure: increased brain natriuretic peptide (BNP: 9,500 pg/ml), total bilirubin (5.5 mg/dl), direct bilirubin (4.1 mg/dl), glutamate oxaloacetate transaminase (243 U/L), glutamate pyruvate transaminase (540 U/L), blood urea nitrogen (62.5 mg/dl) and creatinine (2.57 mg/dl), decreased hemoglobin 9.0 g/dl, increased aspartate transaminase (540 U/L), total protein (5.5 mg/dl), direct protein (4.1 mg/dl), serum albumin (3.7 g/dl), increased platelet count (54,000/μl).

Case Report

A 65-year-old man with acute inferior myocardial infarction was admitted in January, 2006. Left coronary arterial obstruction and other stenotic lesions on the proximal right coronary artery, left anterior descending branch and circumflex branch were detected by emergency coronary angiography and he underwent coronary artery bypass grafting with anastomosis of the left internal thoracic artery to the obtuse marginal branch and the left anterior descending branch and saphenous vein to the right coronary artery. In May 2006, he was re-admitted because of cardiac failure after therapy for a gastric ulcer, when he did not improve despite treatment with catecholamines, diuretics and vasodilation in another hospital. On admission, auscultation revealed a widespread coarse crackle in the lung fields and a systolic, blowing murmur (Levine III/VI) at the cardiac apex. Laboratory tests indicated multiple organ failure: increased brain natriuretic peptide (BNP: 9,500 pg/ml), total bilirubin (5.5 mg/dl), direct bilirubin (4.1 mg/dl), glutamate oxaloacetate transaminase (243 U/L), glutamate pyruvate transaminase (540 U/L), blood urea nitrogen (62.5 mg/dl) and creatinine (2.57 mg/dl), decreased hemoglobin 9.0 g/dl) and platelet count (54,000/μl). ECG showed negative T waves in leads II, III, and aVF and QRS duration of 130 ms. Echocardiography showed dilatation of the LV, with an end-diastolic diameter of 68 mm, and severe mitral regurgitation because of tethering of the leaflet. The LV wall motion showed diffuse hypokinesis and the ejection fraction was 25%. Dyssynchrony in the LV wall was observed and the septal-to-posterior wall motion delay was more than 130 ms on M-mode echocardiography. Coronary angiography showed that all bypass arteries and grafts were free of stenosis. After reducing the infusion of catecholamines, heart failure worsened, so mitral valve anuloplasty and LV papil-
PET for Evaluating Efficacy of CRT

Fig 1. The 12-lead ECG and M-mode echocardiography before cardiac resynchronization therapy. SPWMD, septal-to-posterior wall motion delay.

Fig 2. The 12-lead ECG and M-mode echocardiography after cardiac resynchronization therapy.

Fig 3. Measurement of myocardial oxygen metabolism by $^{11}$C-acetate positron emission tomography. Clearance rate of $^{11}$C-acetate (A) during cessation of biventricular pacing (CRT Off) and (B) during biventricular pacing (CRT On). CRT, cardiac resynchronization therapy.
lary muscle imbrication were performed to reduce the mitral regurgitation. Preoperative 18F-Fluorodeoxyglucose PET was performed during insulin clamp to assess the LV, which was found to be preserved in its entirety, so volume reduction surgery, such as a Dor operation or a septal ante-rior ventricular exclusion operation (SAVE), was not performed.

After the operation, the patient’s condition improved gradually. The plasma BNP level decreased to 750 pg/ml, but sustained ventricular tachycardia with Adams-Stokes syncope occurred and the LV ejection fraction was still as low as 30% on echocardiography. Moreover, the dysynchrony in the LV wall remained, with the long delay (>130 ms), on M-mode echocardiography (Fig 1). Although ECG showed a relatively narrow QRS of 130 ms (Fig 1), we decided to implant a biventricular pacing system with an implantable cardioverter defibrillator (In Sync III Marquis, Medtronic, MN, USA).

Although echocardiography showed disappearance of the dysynchrony after CRT, ECG revealed a QRS duration of 160 ms (Fig 2), so 11C-acetate PET was performed to evaluate the efficacy of CRT. The patient was positioned in a whole-body PET scanner (ECAT/EXACT, HR+, Siemens) and 11C-acetate (370 MBq) was injected as an intravenous bolus. The myocardial time–activity curve was fitted monoexponentially and the clearance rate of 11C-acetate (Kmono) was determined from the initial linear part of the time–activity curve. The coefficient of variation in the measurements of Kmono was 1.645% when a single doctor measured Kmono 10 times, so repeatability was considered sufficient to validate the measurements.

Cardiac efficiency was determined using the concept of work metabolic index, which is calculated as (stroke volume index) × (systolic blood pressure) × (heart rate)/Kmono, where Kmono is the monoeponential clearance rate of 11C-acetate. During CRT, the myocardial oxidative consumption in the whole LV decreased by 15%, mainly in the lateral wall, and oxygen consumption in all segments became uniform (Fig 3). We measured the stroke volume index using echocardiography, and calculated cardiac efficiency using the aforementioned equation. Heart rate, blood pressure, and stroke volume during cessation of biventricular pacing were 70 beats/min, 103/74 mmHg and 63 ml, respectively, and 70 beats/min, 113/76 mmHg and 65 ml respectively, during biventricular pacing. Therefore, cardiac efficiency with CRT improved by 33% compared to without CRT.

The patient was successfully treated with β-blockers after CRT. The daily dosage of carvedilol increased to 5 mg prior to hospital discharge and the plasma BNP level, which was 9,500 pg/ml before operation, decreased to 173 pg/ml just before discharge.

**Discussion**

The effects of CRT for patients with ischemic heart disease may differ from those with cardiomyopathy. The Multicenter InSync Randomized Clinical Evaluation (MIRACLE) revealed that both the improvement in the LV ejection fraction and the reduction in end-diastolic volume after CRT were larger in patients with non-ischemic heart disease than in those with ischemic heart disease. However, in the Cardiac Resynchronization-Heart Failure Study (CARE-HF), no clear differences between ischemic and non-ischemic heart disease regarding mortality and hospitalization because of heart failure were found. Although more evaluation is necessary, LV volume reduction surgery in addition to CRT may be needed for patients in whom large areas of the LV are unavailable.

Concerning the present case, although dyssynchrony was detected before mitral valve annuloplasty and LV papillary muscle imbrication, the QRS duration was not too long, at 130 ms. We also considered that postoperative β-blocker therapy might reduce the dyssynchrony. However, after the operation, the patient had an episode of sustained ventricular tachycardia and the LV ejection fraction was still low (30% on echocardiography), while dyssynchrony in the LV wall remained, at more than 130 ms on M-mode echocardiography. Other patients with congestive heart failure and narrow QRS duration have had dyssynchrony that improved after CRT, which our findings corroborate.

After implantation of the CRT device, we examined its efficacy using 11C-acetate PET. 11C-acetate is immediately taken up by cardiac muscle after injection and is metabolized in the tricarboxylic acid cycle after conversion to acetyl coenzyme A. Therefore, rapid myocardial turnover of 11C-acetate reflects myocardial oxidative metabolism. In this case, during CRT the regional Kmono (Fig 3) decreased in the septum (from 0.0511 to 0.0439, 14% reduction), the anterior wall (from 0.0460 to 0.0369, 20%), and the lateral wall (from 0.0520 to 0.0371, 29%). The septal/lateral ratio increased from 0.98 to 1.18 (20% increase) during CRT. Although the changes in the regional Kmono values in our case differ from the results obtained from 8 patients with dilated cardiomyopathy in a previous report, which indicated that CRT did not reduce oxidative consumption on the whole but did increase cardiac efficiency, the change in the septal/lateral ratio was similar in both.

In the present case, the myocardial oxidative consumption decreased by 15% overall and cardiac efficiency increased by 33%. The heart rate, blood pressure, and stroke volume during cessation of biventricular pacing were 70 beats/min, 103/74 mmHg and 63 ml, respectively, and 70 beats/min, 113/76 mmHg and 65 ml during biventricular pacing. The observed improvement in LV performance was somewhat less than previously reported; however, the improvement in cardiac efficiency was great, at 33%, mainly because of a reduction in myocardial oxidative consumption by CRT. Although the change in myocardial oxidative consumption by CRT may depend on the case, effective CRT should improve LV function without increasing global oxidative metabolism, resulting in improved myocardial efficiency. The difference in global LV oxidative metabolism in the present patient and the result reported by Ukkonen et al may be attributed to a difference in the effectiveness of CRT. Further examination is needed to elucidate the relationship between myocardial oxidative metabolism and the effectiveness of CRT. However, this case illustrates the usefulness of 11C-acetate PET for evaluating the efficacy of CRT in patients with severe heart failure.

**References**

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