

Evaluation of cardiac resynchronization therapy in drug-resistant dilated-phase hypertrophic cardiomyopathy by means of Tc-99m sestamibi ECG-gated SPECT

Shinro MATSUO,* Yuichi SATO,** Ichiro NAKAE,* Daisuke MASUDA,*
Naoya MATSUMOTO** and Minoru HORIE*

**Department of Cardiovascular and Respiratory Medicine, Shiga University of Medical Science*

***Department of Cardiology, Nihon University School of Medicine*

This case describes a 65-year-old male with drug-resistant heart failure. Cardiac resynchronization therapy was performed. We evaluated cardiac function with volume curve differentiation software (VCDiff) from QGS data with Tc-99m sestamibi. Left ventricular parameters during atrial-right ventricular pacing were left ventricular ejection fraction (LVEF) 30%, end-diastolic volume (EDV) 156 ml, end-systolic volume (ESV) 108 ml and peak filling rate 1.12 (EDV/sec). And during dual chamber pacing, those were LVEF 35%, EDV 145 ml and ESV 95 ml and PFR 1.58 (EDV/sec). And during atrial-left ventricular pacing, those were LVEF 36%, EDV 152 ml, ESV 97 ml and peak filling rate (PFR) 1.35 (EDV/sec). Cardiac resynchronization therapy may improve cardiac function as well as dyssynchrony, which could be evaluated non-invasively and accurately by ECG-gated SPECT.

Key words: quantitative gated SPECT (QGS), cardiac resynchronization therapy, cardiac function

INTRODUCTION

RECENTLY CARDIAC RESYNCHRONIZATION THERAPY (CRT) has been introduced as adjuvant treatment in patients with severe congestive heart failure and bundle branch block. It acutely reduced pulmonary capillary wedge pressure and increased cardiac output.^{1–3} We describe a heart failure patient treated with CRT, whose cardiac functions were evaluated by technetium-99m sestamibi (^{99m}Tc-MIBI) electrocardiography-gated single-photon emission computed tomography (SPECT).

CASE PRESENTATION

A 65-year-old male with dyspnea and New York Heart Association (NYHA) functional class III heart failure was

admitted to our hospital for treatment of heart failure. Eighteen years ago, he had been diagnosed with hypertrophic cardiomyopathy and been treated with digoxin, trichlormethiazide, spironolactone, bisoprolol, fumarate, perindopril, pimobendan, and warfarin. However, severe heart failure recurred several times, requiring admission. Three years ago he had a pacemaker implanted (DDIR mode) because of atrial fibrillation with severe bradycardia. On physical examination, his blood pressure was 118/60, temperature was 36.5°C, pulse rate was 60 per minute and regular. There were pretibial edema and venous distension. A chest X-ray showed pulmonary congestion. He had NYHA functional class III heart failure. Cardiothoracic ratio of the chest X-ray was 69.0% (Fig. 1). An electrocardiogram showed left bundle branch block type and the QRS interval was markedly prolonged at 224 ms (Fig. 1). Echocardiography showed marked dilatation (end-diastolic diameter: 60 mm), diffuse hypokinesis (EF, ejection fraction: 30%), and dyssynchrony of left ventricle. Moderate mitral regurgitation was observed by Doppler echocardiography (Fig. 2). The plasma level of brain natriuretic peptide (BNP) was markedly elevated at 829 pg/dl. Medical therapy was started with a diuretic,

Received May 29, 2006, revision accepted August 17, 2006.

For reprint contact: Shinro Matsuo, M.D., Department of Cardiovascular and Respiratory Medicine, Shiga University of Medical Science, Tukiowa-cho, Seta, Otsu, Shiga 520–2192, JAPAN.

E-mail: smatsuo@belle.shiga-med.ac.jp



Fig. 1 ECG and chest X-ray before and after cardiac resynchronization therapy.



Fig. 2 Four-chamber view of echocardiography before and after cardiac resynchronization therapy. Moderate amount of mitral regurgitation was observed by Doppler echocardiography and mitral regurgitation diminished significantly after the therapy. Pre; pre CRT, Post; post CRT.

atrial natriuretic peptide agent and nitrates. A right heart catheterization showed a mean pulmonary capillary wedge pressure of 18 mmHg. Left ventricular end-diastolic pressure was 18 mmHg. Cardiac output was 3.8 l/min and cardiac index was 2.1 l/(min × m²). He was diagnosed with dilated-phase hypertrophic cardiomyopathy. We decided to place a biventricular system due to the depressed ventricular function and wide QRS interval. Therefore, he was treated with implantation of a biventricular pacemaker (Medtronic, USA). Echo-cardiography revealed that the mitral regurgitation diminished significantly (Fig. 2). He underwent rest ^{99m}Tc-MIBI cardiac scintigraphy for evaluation of cardiac function and viability. The patient's cardiac functions were measured at three different pacing modes; right ventricular (RV) pacing, dual chamber pacing with capture of the ventricles, and left ventricular (LV) pacing. Alterations in pacing mode were done 5 min before the acquisition of the SPECT images. Rest ^{99m}Tc-MIBI imaging was performed during

biventricular pacing (Fig. 3). At resting condition, the patient received ^{99m}Tc-MIBI at a dose of 740 MBq intravenously. A three-headed rotating gamma camera (GCA-9300 A/DI, Toshiba Medical, Japan) equipped with a high-resolution collimator and a medical image processor GMS-5500 U/DI (Toshiba Corporation, Tokyo) was employed for image processing. For gating, 16 frames per cardiac cycle with a re-fixed RR interval and a 15% window were used. Repeated acquisition in the same protocol was performed during RV pacing. And the pacing mode was changed to LV pacing, and the image acquisition was repeated. The myocardial SPETC image was divided into 13 segments.⁴ A 4-point scoring system by visual interpretation (3, normal; 2, mildly reduced; 1, severely reduced; 0, no activity) was used.⁴ The total perfusion score of ^{99m}Tc-MIBI images was calculated as the sum of the scores for all 13 segments.⁴ The dyssynchrony index (DSI) was defined as the difference in the number of frames showing the maximum systolic move-

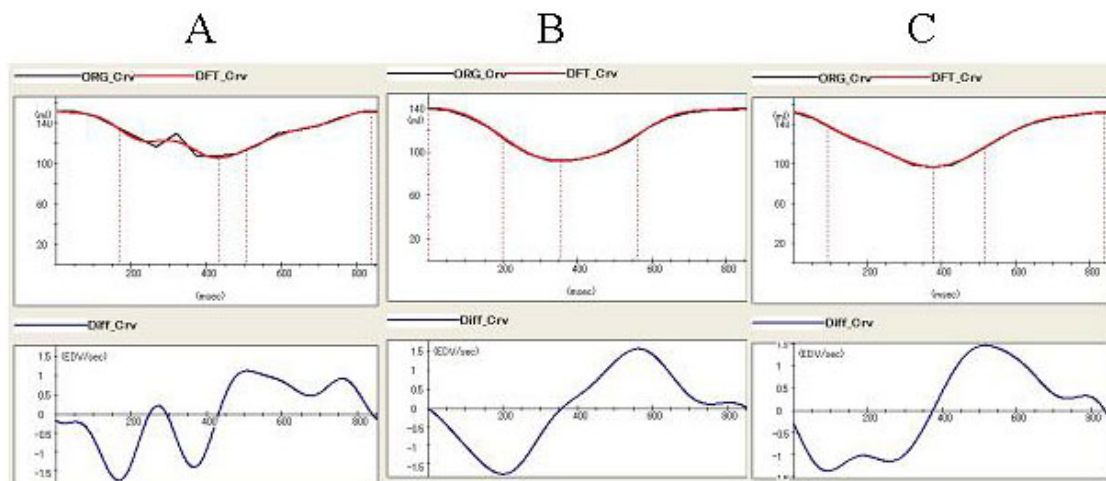


Fig. 3 Volume curve of left ventricle obtained from left ventricular functional images of Tc-99m sestamibi gated SPECT. A; Right ventricular pacing, B: Left ventricular pacing, C; Dual chamber pacing.

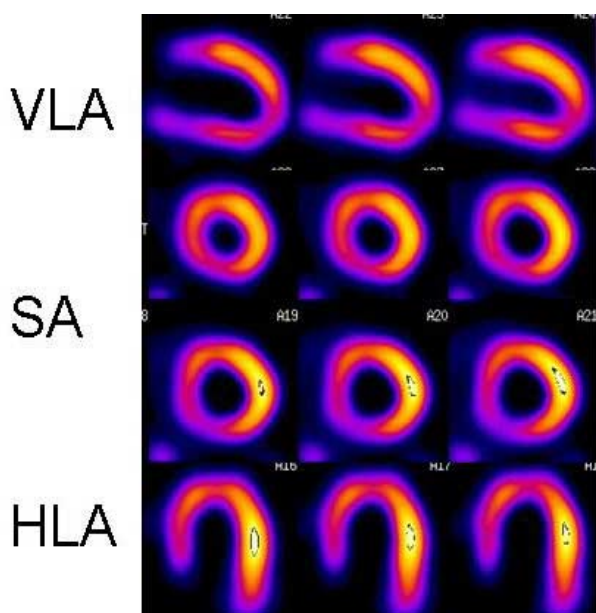


Fig. 4 SPECT images of a 65-year-old patient with dilated phase hypertrophic cardiomyopathy. Slightly hypo-perfused myocardium in inferior segment and apical portion of left ventricle, with large amount of segments of viability, were observed.

ment of the LV septal and lateral walls.⁵ In data analysis, the volume curve differentiation software (VCDiff; Daiichi Radioisotope Laboratories, Ltd. Tokyo, Japan) combined with QGS program was applied to process short-axis tomograms to determine left ventricular ejection fraction (LVEF), end-systolic and end-diastolic volume (ESV, EDV), and peak filling rate (PFR).⁴⁻⁷ Left ventricular parameters during RV pacing were LVEF 28%, EDV 141 ml and ESV 101 ml. And during dual chamber pacing,

Table 1 Clinical parameters before and after CRT

Parameters	before CRT	After 6 M	After 12 M
BNP, pg/ml	829	603	386
Systolic BP, mmHg	106	110	112
Diastolic BP, mmHg	70	68	70
LVDd, mm	60	58	60
LVDs, mm	51.4	45.3	44.3
LVEF, mm	30	43.6	50.5
%FS	14.0	21.9	26.2
LAD, mm	57	54	54
NYHA class	III	I	I

CRT: cardiac resynchronization therapy, BNP: brain natriuretic peptide, BP: blood pressure, LVDd: left ventricular end-diastolic diameter, LVDs: left ventricular end-systolic diameter, %FS: percent fractional shortening. LAD: left atrial diameter. NYHA class: New York Heart Association functional class

those were LVEF 31%, EDV 142 ml and ESV 98 ml (Fig. 3). And during LV pacing, those were LVEF 32%, EDV 148 ml and ESV 100 ml. We evaluated his cardiac diastolic function using the VCDiff software. Filling fraction during the first third of diastole were 14.8%, 31.0%, and 49.5% during RV pacing, LV pacing, dual-chamber pacing, respectively. Peak filling rates were 1.12 ml/s (EDV/s) during RV pacing, 1.35 ml/s (EDV/s) during LV pacing, and 1.58 ml/s (EDV/s) during dual-chamber pacing (Fig. 3). SPECT images showed slightly hypo-perfused myocardium in the inferior segment and apical portion of the left ventricle, with large amount of segments of viability (Fig. 4). Myocardial perfusion score of SPECT images was unchanged before and after CRT (before CRT; 33, after CRT; 33). The DSI before CRT was 4, and changed to 0 after CRT. After 4 weeks of biventricular pacing along with conventional heart failure

therapy, his NYHA functional class improved from III to I, and partial LV reverse remodeling was achieved (Table 1). An electrocardiogram with CRT showed the QRS interval was markedly improved at 172 ms (Fig. 1). After treatment with CRT, the patient has been uneventful for two years.

DISCUSSION

The addition of gating to routine myocardial perfusion SPECT provides accurate and reproducible information on left ventricular function. ^{99m}Tc -MIBI gated SPECT provides quantitatively global functional parameters including EDV, ESV and LVEF as well as PFR in a patient with CRT.⁴⁻⁶ Several studies^{4,7-10} compared gated SPECT with standard radionuclide techniques for the measurement of left ventricular function and found it was accurate and reproducible. The present case showed that LVEF in dual-chamber pacing was higher than in RV pacing. Furthermore the left ventricular filling was evaluated as an index of left ventricular compliance in this case. In this case, PFR during dual-chamber pacing was higher than that of right ventricular pacing in the same heart rate. This may indicate that early diastolic relaxation was improved with CRT. In previous studies, CRT was reported to improve exercise tolerance, functional class and quality of life and decrease hospitalizations due to heart failure in large trials.^{1,2} Extensive evidence has shown that CRT provides acute and long-term clinical benefits in selected patients with heart failure. Dyssynchrony can be induced by artificial pacemaker and this can itself lead to LV systolic failure.¹¹

The beneficial effects of CRT on left ventricular performance may be caused by mechanisms not associated with myocardial work in single contracting segments. Such mechanisms may include a better coordination of left ventricular segmental contraction (resynchronization), a prolongation of diastole, a reduction in the severity of mitral regurgitation, and a better atrial-ventricular synchrony. Although we have current methods of imaging ventricular asynchrony by Doppler tissue imaging, ECG-gated SPECT images provide information on dyssynchrony in an operator-independent manner and with high reproducibility.⁵ Dyssynchrony triggers regional changes in both myocardial blood flow and oxygen consumption. Nuclear studies such as gated blood pool, and positron emission tomography using ^{18}F -fluorodeoxyglucose or ^{11}C -acetate were reportedly useful in evaluating these effects of CRT.¹²⁻¹⁵ Patients who are not improved are likely to have a myocardial infarction.¹⁶ It was recently reported that acute and long-term improvement in LV performance after CRT was dependent on global myocardial viability.¹⁶⁻¹⁸ The improvement in systolic and diastolic performance after CRT would be expected only in tissue where myocyte viability is maintained. The efficacy of ECG-gated scintigraphy in patients with CRT, as

recognized in this case, is to provide such viability information as well as LV functional data and asynchrony in a single test. Further study is needed to clarify the beneficial effects of CRT by ECG-gated SPECT in a large number of patients.

CONCLUSION

Cardiac resynchronization therapy may improve both cardiac systolic and diastolic function as well as dyssynchrony, that could be evaluated non-invasively and accurately by ECG-gated cardiac scintigraphy.

REFERENCES

1. Cazeau S, Bordachar P, Jauvert G, Lazarus A, Alonso C, Vandrell MC, et al. Echocardiographic modeling of cardiac dyssynchrony before and during multisite stimulation: a prospective study. *Pacing Clin Electrophysiol* 2003; 26 (1 Pt 2): 137-143.
2. Cazeau S, Leclercq C, Lavergne T, Walker S, Varma C, Linde C, et al. Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. *N Eng J Med* 2001; 344: 837-880.
3. Abraham WT, Fisher WG, Smith AL, Delurgio DB, Leon AR, Loh E, et al. Cardiac resynchronization in chronic heart failure. *N Eng J Med* 2002; 346: 1845-1853.
4. Matsuo S, Nakae I, Matsumoto T, Horie M. Impact of endothelial dysfunction on left ventricular remodeling after successful primary coronary angioplasty for acute myocardial infarction—analysis by quantitative ECG-gated SPECT—. *Ann Nucl Med* 2006; 20 (1): 57-62.
5. Higuchi K, Toyama T, Tada H, Naito S, Ohshima S, Kurabayashi M. Usefulness of biventricular pacing to improve cardiac symptoms, exercise capacity and sympathetic nerve activity in patients with moderate to severe chronic heart failure. *Circ J* 2006; 70 (6): 703-709.
6. Germano G, Erel J, Kiat H, Kavanagh PB, Berman DS. Quantitative LVEF and qualitative regional function from gated thallium-201 perfusion SPECT. *J Nucl Med* 1997; 38: 749-754.
7. Germano G, Kiat H, Kavanagh PB, Moriel M, Mazzanti M, Su HT, et al. Automatic quantification of ejection fraction from gated myocardial perfusion SPECT. *J Nucl Med* 1995; 36: 2138-2147.
8. Williams KA, Taillon LA. Left ventricular function in patients with coronary artery disease assessed by gated tomographic myocardial perfusion images: comparison with assessment by contrast ventriculography and first-pass radionuclide angiography. *J Am Coll Cardiol* 1996; 27: 173-181.
9. Nakae I, Matsuo S, Koh T, Mitsunami K, Horie M. Left ventricular systolic/diastolic function evaluated by quantitative ECG-gated SPECT: comparison with echocardiography and plasma BNP analysis. *Ann Nucl Med* 2005; 19 (6): 447-454.
10. Akincioglu C, Berman DS, Nishina H, Kavanagh PB, Slomka PJ, Abidov A, et al. Assessment of diastolic function using 16-frame ^{99m}Tc -sestamibi gated myocardial perfusion SPECT: normal values. *J Nucl Med* 2005; 46 (7):

- 1102–1108.
11. Freudenberger RS, Wilson AC, Lawrence-Nelson J, Hare JM, Kostis JB. Myocardial Infarction Data Acquisition System Study Group (MIDAS 9). Permanent pacing is a risk factor for the development of heart failure. *Am J Cardiol* 2005; 95 (5): 671–674.
 12. Muramatsu T, Matsumoto K, Nishimura S. Efficacy of the phase images in Fourier analysis using gated cardiac pool-SPECT for determining the indication for cardiac resynchronization therapy. *Circ J* 2005; 69 (12): 1521–1526.
 13. Nowak B, Sinha AM, Schaefer WM, Koch KC, Kaiser HJ, Hanrath P, et al. Cardiac resynchronization therapy homogenizes myocardial glucose metabolism and perfusion in dilated cardiomyopathy and left bundle branch block. *J Am Coll Cardiol* 2003; 41 (9): 1523–1528.
 14. Linder O, Sorensen J, Vogt J, Fricke E, Baller D, Horstkotte D, et al. Cardiac efficiency and oxygen consumption measured with ^{11}C -acetate PET after long-term cardiac resynchronization therapy. *J Nucl Med* 2006; 47 (3): 378–383.
 15. Araki T, Yoshida N, Tsuchiya T, Ikeda M, Namura M, Higuchi T, et al. Changes in myocardial oxidative metabolism after biventricular pacing as evaluated by [^{11}C]acetate positron emission tomography. *Ann Nucl Med* 2003; 17 (7): 605–608.
 16. Reuter S, Garrigue S, Barold SS, Jais P, Hocini M, Haissaguerre M, et al. Comparison of characteristics in responders versus nonresponders with biventricular pacing for drug-resistant congestive heart failure. *Am J Cardiol* 2002; 89 (3): 346–350.
 17. Hummel JP, Lindner JR, Belcik JT, Ferguson JD, Mangrum JM, Bergin JD, et al. Extent of myocardial viability predicts response to biventricular pacing in ischemic cardiomyopathy. *Heart Rhythm* 2005; 2 (11): 1211–1217.
 18. Matsuo S, Matsumoto T, Nakae I, Koh T, Masuda D, Takada M, et al. Prognostic value of ECG-gated thallium-201 single-photon emission tomography in patients with coronary artery disease. *Ann Nucl Med* 2004; 18 (7): 617–622.