Assessment of Left Ventricular Systolic and Diastolic Function Using ECG-Gated Technetium-99m Tetrofosmin Myocardial Perfusion SPECT

Comparison With Ultrasound Echocardiography

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SUMMARY

Because left ventricular (LV) diastolic dysfunction is frequently the earliest indicator of LV dysfunction in patients with heart failure, the estimation of LV diastolic function is very important. On the other hand, electrocardiography (ECG)-gated technetium (Tc) -99m tetrofosmin single-photon emission computed tomography (SPECT) has been reported to be a useful method for evaluation of LV function. The objective of this study was to examine the usefulness of ECG-gated Tc-99m tetrofosmin SPECT in terms of estimation of cardiac diastolic function. Consecutive 145 patients underwent an ECG-gated Tc-99m tetrofosmin SPECT to estimate systolic and diastolic LV function, and were compared with those evaluated by ultrasound echocardiography (UCG). LV end-diastolic volume, LV end-systolic volume, and LV ejection fraction values obtained by quantitative gated SPECT (QGS) showed significant positive linear correlations with those obtained by UCG. All 145 patients were classified into 3 groups according to diastolic function estimated by UCG. The first-third mean filling rate (1/3 MFR) and peak filling rate (PFR) that revealed the LV diastolic function of the group B (normal systolic function and mild diastolic dysfunction) patients (1.01 ± 0.35 , 1.85 ± 0.57) were both significantly lower than those of the group A (normal systolic and diastolic function) patients (1.43 ± 0.37 , 2.43 ± 0.56). The 1/3 MFR and PFR of the group C (moderate ~ severe systolic and diastolic dysfunction) patients (0.47 ± 0.34 , 0.92 ± 0.62) were also significantly lower than those of the group A and B patients. QGS may be a useful method for the evaluation of cardiac systolic and diastolic function, especially in patients with normal systolic function and diastolic dysfunction. (Int Heart J 2013; 54: 212-215)

Key words: Cardiac function, QGS, First-third mean filling rate, Peak filling rate

Previous studies have demonstrated that cardiac systolic (left ventricular (LV) ejection fraction (EF)) and diastolic (mitral inflow velocity pattern and/or mitral deceleration time, and/or pulmonary vein inflow velocity pattern) functions evaluated by ultrasound echocardiography (UCG) were predictors of the clinical outcome.^{1,2)} On the other hand, previous studies have also demonstrated that approximately 50% of patients with heart failure present with a normal LV systolic function.³⁾ LV diastolic dysfunction is frequently the earliest indicator of LV dysfunction in patients with heart failure. Therefore, the estimation of LV diastolic function is very important. Recently, electrocardiography (ECG)-gated technetium (Tc)-99m tetrofosmin single-photon emission computed tomography (SPECT) has been reported to be a useful method for evaluation of LV systolic and diastolic functions.^{4,5)} The purpose of the present study was, therefore, to examine the usefulness of ECG-gated Tc-99m tetrofosmin SPECT in terms of estimation of cardiac function, especially, LV diastolic function. In order to examine this, we compared cardiac systolic

and diastolic functions evaluated by ECG-gated Tc-99m tetrofosmin SPECT with those evaluated by UCG.

METHODS

Study subjects: The study population consisted of 145 consecutive patients (33-84 years old; mean age, 66.5 ± 13.5 years) who underwent an ECG gated Tc-99m tetrofosmin SPECT from July 2010 to June 2012 in our hospital (Table I). Thirty-four patients with cerebrovascular disease underwent screening for coronary artery disease and to evaluate cardiac function, while 18 patients with a brain tumor underwent the procedure as a cardiovascular screening before an operation.

All the enrolled patients provided written informed consent, and the study protocol was based on the regulations of the hospital ethics committee. All 145 patients underwent a complete two-dimensional and Doppler UCG examination within 2 days before or after SPECT examination. Patients who met

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Table I. Clinical Backgrounds of the Study Patients

Characteristics	Value
<i>n</i>	145
Age (years)	66.5 ± 13.5
Gender, male (%)	81 (55.9%)
Clinical diagnosis	
Heart disease	
Coronary artery disease	
Acute myocardial infarction	3 (2.1%)
Old myocardial infarction	5 (3.4%)
Angina pectoris (suspected)	77 (53.1%)
Ischemic cardiomyopathy	5 (3.4%)
Dilated cardiomyopathy	3 (2.1%)
Brain disease	
Brain tumor	18 (12.4%)
Cerebrovascular disease	34 (23.4%)

Values are mean ± SD or *n* (%).

the following exclusion criteria were not enrolled: 1) atrial fibrillation and intraventricular conduction disturbance, including complete atrioventricular block, 2) clinically significant congenital heart disease, 3) cardiac hypertrophy with or without hypertension (wall thickness over 14 mm on echocardiography), and 4) moderate or severe mitral stenosis and aortic stenosis.

Ultrasound echocardiographic examination and Doppler measurements: A complete two-dimensional and Doppler UCG examination was performed. Each patient underwent Doppler examination of mitral inflow and pulmonary venous inflow. Peak velocity of early diastole (E) and peak velocity of atrial systole (A), as well as deceleration time of the E wave were measured. The ratio of the E to A waves (E/A) was calculated. The mitral inflow velocity pattern was recorded from the apical four-chamber view. Five consecutive beats were measured and averaged for each measurement. LV dimension and wall thickness were measured according to the recommendation of the American Society of Echocardiography.⁶⁾ The LVEF was estimated using Simpson's method.⁶⁾ Pulse-wave Doppler signal of the right superior pulmonary vein was also obtained according to guidelines of the American Society of Echocardiography.⁷⁾ Peak velocity of systolic forward flow (S) and diastolic forward flow (D) and pulmonary venous atrial reverse flow (AR), and AR duration time were measured. The ratio of the S to D waves (S/D) was calculated. Diastolic function was defined according to the definition described by Redfield, *et al*⁸⁾ which is as follows: normal diastolic function, $0.75 < E/A < 1.5$ and deceleration time > 140 ms and $S \geq D$; mild diastolic dysfunction, $E/A \leq 0.75$; moderate diastolic dysfunction (pseudonormal), $0.75 < E/A < 1.5$ and deceleration time > 140 ms and $S < D$ or AR duration $< A$ duration; severe diastolic dysfunction, $E/A > 1.5$ and deceleration time < 140 ms.

Quantitative gated SPECT: ECG-gated SPECT was performed at rest and during sinus rhythm by using Tc-99m tetrofosmin (740 MBq). Sixty minutes after the intravenous tracer injection, gated SPECT data were obtained for 60 seconds per projection from 60 projections during a 180-degree rotation with an ECG gating 16 frames per cardiac cycle by using a 2-headed gamma camera with a low-energy, high-resolution parallel-hole collimator a Butterworth filter (cutoff = 0.45 cycle/pixel, power factor = 10). The data were stored in a 64- by 64-word matrix nuclear medicine computer system, and no at-

Figure 1. Schema of time-volume curve and its differentiation curve obtained by 16-frame gated single-photon emission computed tomography data using a VCDiff program. 1/3 mean filling rate = average of filling rate during first-third of diastole.

tenuation or scatter correction was applied to this protocol. For data analysis, the quantitative gated SPECT (QGS) program (Cedars-Sinai Medical Center, Los Angeles, CA, USA) was applied to process short-axis tomograms to determine the LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), and LVEF. The LV volume data on each of the 16 frames by the QGS program were manually entered into the volume curve differentiation program (VCDiff, FUJIFILM RI Pharma, Co., Ltd., Tokyo) combined with the QGS program. In this program, Fourier curve fitting was performed, and cardiac parameters were automatically calculated from the time-volume curve and its differentiation curve. Peak filling rate (PFR) and first-third mean filling rate (1/3 MFR) were obtained by the VCDiff program (Figure 1), as diastolic functional parameters.^{9,10)}

Statistical analysis: All data are expressed as the mean ± SD or *n* (%). The difference in mean values between the 2 groups was compared using an unpaired *t*-test. The incidences in the 2 groups were compared using the chi-square test. To compare mean values among 3 groups, one-way analysis of variance (ANOVA) was used, and the Bonferroni approach was used for individual comparisons when a significant difference was found. Correlation between two parameters was analyzed using linear regression analysis. A *P* value less than 0.05 was considered significant.

RESULTS

Correlation of LV values between QGS and UCG: LVEDV, LVESV, and LVEF values obtained by QGS showed significant positive linear correlations with those obtained by UCG (Figure 2).

Comparison of diastolic function parameters obtained by means of QGS with those obtained by means of UCG: All 145 patients were classified into 3 groups according to diastolic function estimated by UCG (Table II). Group A consisted of 74 patients with normal diastolic function, group B 57 patients with mild diastolic dysfunction, and group C 14 patients with moderate diastolic dysfunction (pseudonormal) or severe diastolic dysfunction estimated by UCG. LVEF values obtained

Figure 2. Left ventricular end-diastolic volume (EDV, A), end-systolic volume (ESV, B), and ejection fraction (EF, C) obtained by quantitative gated single-photon emission computed tomography (QGS) showed significant positive linear correlation with that obtained by ultrasound echocardiography (UCG).

Table II. Peak Filling Rate and First-third Mean Filling Rate According to Diastolic Function Obtained by UCG

	Group A (n = 74 patients)	Group B (n = 57 patients)	Group C (n = 14 patients)
UCG			
LVEF (%)	67.6 ± 6.5	65.8 ± 10.1	32.4 ± 8.6 ^{†*}
LVEDV (mL)	99.8 ± 25.6 [†]	85.7 ± 27.7	142.7 ± 49.6 ^{††}
LVESV (mL)	32.2 ± 9.9	29.7 ± 14.7	94.2 ± 46.0 ^{††}
E/A	1.13 ± 0.32	0.63 ± 0.08 [*]	1.41 ± 0.69 ^{††}
Deceleration time (second)	291 ± 53	261 ± 53 [*]	140 ± 51 ^{††}
S/D	1.82 ± 0.43	1.48 ± 0.46 [*]	0.70 ± 0.19 ^{††}
QGS			
LVEF (%)	68.9 ± 9.9	67.1 ± 14.0	28.8 ± 10.8 ^{††}
LVEDV (mL)	84.9 ± 26.9	73.9 ± 24.4	166.4 ± 69.3 ^{††}
LVESV (mL)	28.3 ± 16.4	26.1 ± 18.3	122.3 ± 71.3 ^{††}
PFR	2.43 ± 0.56	1.85 ± 0.57 [*]	0.92 ± 0.62 ^{††}
1/3 MFR	1.43 ± 0.37	1.01 ± 0.35 [*]	0.47 ± 0.34 ^{††}

Values are mean ± SD. A indicates atrial filling velocity; D, diastolic forward flow; E, early diastolic filling velocity; 1/3 MFR, first-third mean filling rate; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; PFR, peak filling rate; QGS, quantitative gated SPECT; S, systolic forward flow; and UCG, ultrasound echocardiography. ^{*} P < 0.05 versus Group A. [†] P < 0.05 versus Group B.

by QGS in group C patients (28.8 ± 10.8) were significantly lower than those of group A patients (68.9 ± 9.9) and group B patients (67.1 ± 14.0). However, there was no significant difference in the LVEF between the group A patients and group B patients estimated by QGS, as was the case when estimated by UCG. On the other hand, in terms of diastolic function, although there was no difference in the systolic function, the 1/3 MFR of the group B patients (1.01 ± 0.35) was significantly lower than that of the group A patients (1.43 ± 0.37). Furthermore, the 1/3 MFR of the group C patients (0.47 ± 0.34) was also significantly lower than that of the group A and group B patients. PFR of the group B patients (1.85 ± 0.57) was also significantly lower than that of the group A patients (2.43 ± 0.56). PFR of the group C patients (0.92 ± 0.62) was significantly lower than that of the group A and group B patients.

DISCUSSION

The present study has demonstrated that QGS can be a useful method for the evaluation of cardiac systolic and diasto-

lic function, especially in patients with normal systolic function and diastolic dysfunction.

Assessment of LV volume and systolic function obtained by QGS: In the present study, LVEDV, LVESV, and LVEF values obtained by QGS showed significant positive linear correlations with those obtained by UCG, as well as with those of previous studies.^{5,10)} These findings indicated that QGS could be used to assess LV volume and systolic function.

Assessment of LV diastolic function obtained by QGS: Approximately 50% of patients with heart failure present with normal LV systolic function.³⁾ Moreover, LV diastolic dysfunction is frequently the earliest indicator of LV dysfunction in patients with heart failure. Previous studies also demonstrated that even simple Doppler evidence of diastolic dysfunction is an independent risk factor for the future development of congestive heart failure and cardiac death.^{1,2)} Thus, the estimation of LV diastolic function is very important. The efficacy of LV diastolic function assessment by means of two-dimensional and Doppler UCG has been recognized.^{1,2,8)} In the present study, in terms of the estimation of cardiac function, systolic function evaluated by QGS strongly correlates with that evalu-

ated by two-dimensional and Doppler UCG. Furthermore, diastolic function parameters (1/3 MFR, PFR) evaluated by QGS in the normal diastolic function group evaluated by UCG were significantly higher than those of the mild diastolic dysfunction group and moderate ~ severe diastolic dysfunction group evaluated by UCG. Diastolic function parameters (1/3 MFR, PFR) evaluated by QGS in the mild diastolic dysfunction group evaluated by UCG were also significantly higher than those of the moderate ~ severe diastolic dysfunction group evaluated by UCG. Therefore, QGS was able to detect patients with early heart failure, or in other words, patients with normal LV systolic function and diastolic dysfunction.

ECG-gated Tc-99m tetrofosmin SPECT is a useful method for assessing myocardial viability.¹¹⁾ ECG-gated Tc-99m tetrofosmin SPECT with exercise or pharmacological stress also allows for the detection of myocardial ischemia.^{12,13)} Thus, although ECG-gated Tc-99m tetrofosmin SPECT might be a high-cost investigation, it can assess not only myocardial ischemia and viability, but also cardiac systolic and diastolic function at the same time.

Study limitations: The results from the 14 patients in group C suggested the need for a larger patient population. Further studies using a larger patient population are therefore needed to evaluate the usefulness of ECG-gated Tc-99m tetrofosmin SPECT in terms of the estimation of cardiac function, particularly diastolic function. Although the PFR and 1/3 MFR of group B were significantly lower than those of group A, the PFR and 1/3 MFR of groups A and B were relatively widely distributed and overlapped with each other. Thus, the cut-off value of diastolic dysfunction (PFR, 1/3 MFR) could not be clearly defined in the present study. Moreover, there are some methodological limitations. QGS overestimates the LVEF in patients with a small-volume heart, for example, in cases of hypertrophic cardiomyopathy or aortic stenosis. Thus, patients with cardiac hypertrophy and mitral stenosis and aortic stenosis were excluded from the present study.

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