ORIGINAL ARTICLE

The agreement of left ventricular function parameters between ^{99m}Tc-tetrofosmin gated myocardial SPECT and gated myocardial MRI

Yasuyoshi Kuroiwa · Shigeki Nagamachi · Tosiaki Miyati · Kennichirou Yamaguchi · Ryuichi Nishii · Noriyuki Kuga · Toshiya Azuma · Hideo Arita · Masaji Maeda · Shozo Tamura · Keiichi Kawai

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Abstract

Objective The aim is to compare and evaluate the agreement of quantification of left ventricular functional parameters obtained by two different methods, ^{99m}Tc-tetrofosmin gated myocardial perfusion SPECT (MPS) and cardiac magnetic resonance imaging (CMR).

Methods Ten healthy male volunteers participated. Gated MPS data were acquired using 32 frames, which were also combined into 16- and 8-frame data set for the investigation. Gated CMR data were acquired using 8, 16 and 32-frame for the different sets. All examinations were conducted in resting and at exercise conditions. Quantitative measurements of end-diastolic volume (EDV), end-systolic volume (ESV), left ventricular ejection fraction (LVEF), peak ejection rate (PER), peak filling rate (PFR) and time to peak filling (TTPF) were done for each study,

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Y. Kuroiwa · M. Maeda Department of Radiological Technology, Koga General Hospital, Miyazaki, Japan

Y. Kuroiwa · T. Miyati · K. Kawai Division of Health Sciences, Graduate School of Medical Science, Kanazawa University, Kanazawa, Ishikawa, Japan

S. Nagamachi (⊠) · K. Yamaguchi · R. Nishii · N. Kuga · T. Azuma · H. Arita · S. Tamura
Department of Radiology, School of Medicine,
Miyazaki University, 5200 Kihara, Kiyotake, Miyazaki,
Miyazaki 889-1692, Japan
e-mail: snagama@med.miyazaki-u.ac.jp

K. Kawai

Department of Radiology, Faculty of Medical Sciences, University of Fukui, Fukui, Japan respectively. Finally, we evaluated the concordance of parameters between gated MPS and gated CMR by % difference and Bland–Altman plot analysis.

Results LVEF showed favorable concordance in both rest and exercise conditions (% differences were around 10%). PER, PFR and TTPF also showed good concordances in rest conditions, under 32-frame gated collections particularly (% differences were around 10%). In exercise conditions, although the concordances were relatively good, certain variances were noted (% differences were around 20–25%). Regarding left ventricular volumes, the concordance were worse in both conditions (% differences were around 30–40%).

Conclusions In quantifying of left ventricular function parameter, gated CMR provides similar quantitative values comparing with gated MPS except for ventricular volumes in rest conditions. In contrast, there were certain variations except for LVEF in exercised examinations. When we follow patients by the same cardiac parameters with CMR and MPS, using parameters across the two modalities proved to be possible under rest condition. However, it is limited at exercise condition.

Keywords Left ventricular function parameters · Gated MPS · Gated CMR · The agreement

Introduction

Measurement of left ventricular systolic function (SFx) as assessed by left ventricular (LV) volumes and ejection fraction (EF) is a powerful and reliable method for the prediction of long-term prognosis in various heart diseases [1–4]. In addition, left ventricular diastolic dysfunction (DFx) is usually recognized earlier than abnormalities of other parameters in many cardiac diseases, including coronary artery disease (CAD), congestive heart failure (CHF), hypertrophic cardiomyopathy, valvular heart disease, diabetes mellitus, and hypertension [5–10]. Therefore, assessing left ventricular diastolic function is also important in determining the effective treatment strategy.

Conventionally, echocardiography, conventional planar equilibrium radionuclide angiography (ERNA), and cardiac-gated blood-pool scintigraphy (GBPS) have been widely used for the evaluation of DFx [11–13]. In recent years, in addition to myocardial perfusion analysis, gated myocardial SPECT (MPS) is widely used assessing SFx, DFx, end-diastolic volume (EDV) and end-systolic volume (ESV) [10, 14–20]. It has also worth for determining prognosis [2].

As an alternative method, cardiac MRI (CMR) examination has become a convenient procedure to diagnose cardiovascular disease with the improvement of imaging techniques and the speed of data processing of image operations [20–26]. It has excellent temporal resolution and also helps to visualize coronary arteries, myocardial perfusion and myocardial viability [27–32]. In addition, because CMR does not rely on geometric assumptions of left ventricular shape, it has been used as the standard of reference for validation of gate MPS in assessment of cardiac volumes and function [33–35]. Thus, CMR will be more frequently used as an important method by routine practice like gated MPS. Therefore, it is extremely

Table 1 The % differences between gated SPECT and gated MRI

important to evaluate the compatibility of quantitative parameter across both methods, MPS and CMR. However, a few studies addressed how values of left ventricular function parameters obtained by the two different modalities are concordant with each other [36–38].

To our knowledge, the current study is the first research comparing the left ventricular function parameters including diastolic function parameter (DFx) by two different modalities, MPS and CMR, directly at both rest and exercise. The purpose is to evaluate the concordance of left ventricular parameters including DFx obtained by MPS and CMR in healthy normal volunteers. In addition, we evaluated how much error ranges we should take into account in the follow-up with functional parameters across the two different modalities.

Materials and methods

Subjects

This investigation complied with the tenets of the Declaration of Helsinki promulgated in 1964 and was approved by the Institutional Review Board. Ten healthy volunteers (ten men, mean age, 30.4 ± 4.2 years) participated in the study. None had a history of hypertension, diabetes, valvular disease, or other cardiac diseases. All volunteers were recruited and provided written informed consent. The

Frame	Rest			Exercise			
	Gated SPECT	Gated MRI	Difference (%)	Gated SPECT	Gated MRI	Difference (%)	
8	92.0 ± 24.0	127.4 ± 15.0	28.3 ± 17.8	82.2 ± 22.4	114.5 ± 15.7	40.1 ± 29.0	
16	92.0 ± 21.0	122.4 ± 20.1	27.6 ± 14.7	84.6 ± 25.3	109.6 ± 14.8	38.6 ± 26.2	
32	95.5 ± 26.9	118.8 ± 16.0	25.0 ± 14.2	86.6 ± 24.7	105.7 ± 11.1	34.5 ± 19.5	
8	38.6 ± 18.1	58.0 ± 12.7	36.9 ± 18.7	31.8 ± 14.1	35.1 ± 15.7	31.1 ± 15.9	
16	32.9 ± 11.6	51.4 ± 12.3	39.7 ± 17.5	29.4 ± 14.1	30.9 ± 13.6	26.3 ± 22.8	
32	30.9 ± 15.6	48.7 ± 9.5	42.2 ± 18.7	27.0 ± 13.4	27.0 ± 10.5	24.2 ± 18.3	
8	59.6 ± 8.5	54.7 ± 7.0	8.2 ± 5.2	62.8 ± 9.1	60.6 ± 6.7	8.5 ± 6.6	
16	65.0 ± 5.6	58.2 ± 6.1	11.5 ± 7.4	66.7 ± 8.8	65.2 ± 6.3	11.0 ± 8.6	
32	68.9 ± 7.3	59.0 ± 5.4	13.3 ± 5.1	70.3 ± 9.1	67.9 ± 4.6	11.5 ± 7.8	
8	2.7 ± 0.6	3.0 ± 0.5	17.3 ± 10.2	3.4 ± 1.0	3.9 ± 0.7	21.7 ± 12.4	
16	3.1 ± 0.5	3.5 ± 0.4	16.3 ± 12.4	3.7 ± 0.9	4.2 ± 0.6	25.5 ± 11.6	
32	3.5 ± 0.6	3.7 ± 0.4	11.7 ± 7.7	4.1 ± 1.1	4.1 ± 0.4	21.1 ± 15.8	
8	2.4 ± 0.6	2.6 ± 0.6	20.7 ± 16.8	3.4 ± 1.2	3.4 ± 1.0	17.5 ± 13.6	
16	2.9 ± 0.9	3.1 ± 0.5	18.6 ± 15.2	3.5 ± 0.9	3.7 ± 0.8	23.0 ± 10.5	
32	3.1 ± 0.8	3.0 ± 0.6	11.5 ± 8.9	4.5 ± 1.4	4.0 ± 1.0	21.4 ± 16.3	
8	168.2 ± 29.9	145.9 ± 24.5	17.7 ± 14.2	149.5 ± 43.0	154.4 ± 19.4	24.2 ± 11.9	
16	153.3 ± 20.0	145.2 ± 25.1	20.1 ± 7.1	148.2 ± 56.3	135.4 ± 35.7	35.0 ± 12.3	
32	150.4 ± 27.4	149.7 ± 40.1	10.6 ± 4.2	137.9 ± 60.5	139.0 ± 48.5	26.9 ± 17.4	
	Frame 8 16 32 8 16 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	FrameRest $\overline{\text{Gated SPECT}}$ 892.0 ± 24.01692.0 ± 21.03295.5 ± 26.9838.6 ± 18.11632.9 ± 11.63230.9 ± 15.6859.6 ± 8.51665.0 ± 5.63268.9 ± 7.382.7 ± 0.6163.1 ± 0.5323.5 ± 0.682.4 ± 0.6162.9 ± 0.9323.1 ± 0.88168.2 ± 29.916153.3 ± 20.032150.4 ± 27.4	FrameRestGated SPECTGated MRI8 92.0 ± 24.0 127.4 ± 15.0 16 92.0 ± 21.0 122.4 ± 20.1 32 95.5 ± 26.9 118.8 ± 16.0 8 38.6 ± 18.1 58.0 ± 12.7 16 32.9 ± 11.6 51.4 ± 12.3 32 30.9 ± 15.6 48.7 ± 9.5 8 59.6 ± 8.5 54.7 ± 7.0 16 65.0 ± 5.6 58.2 ± 6.1 32 68.9 ± 7.3 59.0 ± 5.4 8 2.7 ± 0.6 3.0 ± 0.5 16 3.1 ± 0.5 3.5 ± 0.4 32 3.5 ± 0.6 3.7 ± 0.4 8 2.4 ± 0.6 2.6 ± 0.6 16 2.9 ± 0.9 3.1 ± 0.5 32 3.1 ± 0.8 3.0 ± 0.6 8 168.2 ± 29.9 145.9 ± 24.5 16 153.3 ± 20.0 145.2 ± 25.1 32 150.4 ± 27.4 149.7 ± 40.1	FrameRestGated SPECTGated MRIDifference (%)892.0 \pm 24.0127.4 \pm 15.028.3 \pm 17.81692.0 \pm 21.0122.4 \pm 20.127.6 \pm 14.73295.5 \pm 26.9118.8 \pm 16.025.0 \pm 14.2838.6 \pm 18.158.0 \pm 12.736.9 \pm 18.71632.9 \pm 11.651.4 \pm 12.339.7 \pm 17.53230.9 \pm 15.648.7 \pm 9.542.2 \pm 18.7859.6 \pm 8.554.7 \pm 7.08.2 \pm 5.21665.0 \pm 5.658.2 \pm 6.111.5 \pm 7.43268.9 \pm 7.359.0 \pm 5.413.3 \pm 5.182.7 \pm 0.63.0 \pm 0.517.3 \pm 10.2163.1 \pm 0.53.5 \pm 0.416.3 \pm 12.4323.5 \pm 0.63.7 \pm 0.411.7 \pm 7.782.4 \pm 0.62.6 \pm 0.620.7 \pm 16.8162.9 \pm 0.93.1 \pm 0.518.6 \pm 15.2323.1 \pm 0.83.0 \pm 0.611.5 \pm 8.98168.2 \pm 29.9145.9 \pm 24.517.7 \pm 14.216153.3 \pm 20.0145.2 \pm 25.120.1 \pm 7.132150.4 \pm 27.4149.7 \pm 40.110.6 \pm 4.2	FrameRestExerciseGated SPECTGated MRIDifference (%)Gated SPECT892.0 \pm 24.0127.4 \pm 15.028.3 \pm 17.882.2 \pm 22.41692.0 \pm 21.0122.4 \pm 20.127.6 \pm 14.784.6 \pm 25.33295.5 \pm 26.9118.8 \pm 16.025.0 \pm 14.286.6 \pm 24.7838.6 \pm 18.158.0 \pm 12.736.9 \pm 18.731.8 \pm 14.11632.9 \pm 11.651.4 \pm 12.339.7 \pm 17.529.4 \pm 14.13230.9 \pm 15.648.7 \pm 9.542.2 \pm 18.727.0 \pm 13.4859.6 \pm 8.554.7 \pm 7.08.2 \pm 5.262.8 \pm 9.11665.0 \pm 5.658.2 \pm 6.111.5 \pm 7.466.7 \pm 8.83268.9 \pm 7.359.0 \pm 5.413.3 \pm 5.170.3 \pm 9.182.7 \pm 0.63.0 \pm 0.517.3 \pm 10.23.4 \pm 1.0163.1 \pm 0.53.5 \pm 0.416.3 \pm 12.43.7 \pm 0.9323.5 \pm 0.63.7 \pm 0.411.7 \pm 7.74.1 \pm 1.182.4 \pm 0.62.6 \pm 0.620.7 \pm 16.83.4 \pm 1.2162.9 \pm 0.93.1 \pm 0.518.6 \pm 15.23.5 \pm 0.9323.1 \pm 0.83.0 \pm 0.611.5 \pm 8.94.5 \pm 1.48168.2 \pm 29.9145.9 \pm 24.517.7 \pm 14.2149.5 \pm 43.016153.3 \pm 20.0145.2 \pm 25.120.1 \pm 7.1148.2 \pm 56.332150.4 \pm 27.4149.7 \pm 40.110.6 \pm 4.2137.9 \pm 60.5 <td>FrameRestExerciseGated SPECTGated MRIDifference (%)Gated SPECTGated MRI892.0 \pm 24.0127.4 \pm 15.028.3 \pm 17.882.2 \pm 22.4114.5 \pm 15.71692.0 \pm 21.0122.4 \pm 20.127.6 \pm 14.784.6 \pm 25.3109.6 \pm 14.83295.5 \pm 26.9118.8 \pm 16.025.0 \pm 14.286.6 \pm 24.7105.7 \pm 11.1838.6 \pm 18.158.0 \pm 12.736.9 \pm 18.731.8 \pm 14.135.1 \pm 15.71632.9 \pm 11.651.4 \pm 12.339.7 \pm 17.529.4 \pm 14.130.9 \pm 13.63230.9 \pm 15.648.7 \pm 9.542.2 \pm 18.727.0 \pm 13.427.0 \pm 10.5859.6 \pm 8.554.7 \pm 7.08.2 \pm 5.262.8 \pm 9.160.6 \pm 6.71665.0 \pm 5.658.2 \pm 6.111.5 \pm 7.466.7 \pm 8.865.2 \pm 6.33268.9 \pm 7.359.0 \pm 5.413.3 \pm 5.170.3 \pm 9.167.9 \pm 4.682.7 \pm 0.63.0 \pm 0.517.3 \pm 10.23.4 \pm 1.03.9 \pm 0.7163.1 \pm 0.53.5 \pm 0.416.3 \pm 12.43.7 \pm 0.94.2 \pm 0.6323.5 \pm 0.63.7 \pm 0.411.7 \pm 7.74.1 \pm 1.14.1 \pm 0.482.4 \pm 0.62.6 \pm 0.620.7 \pm 16.83.4 \pm 1.23.4 \pm 1.0162.9 \pm 0.93.1 \pm 0.518.6 \pm 15.23.5 \pm 0.93.7 \pm 0.8323.1 \pm 0.83.0 \pm 0.611.5 \pm 8.94.5 \pm 1.44.0 \pm 1.0<!--</td--></td>	FrameRestExerciseGated SPECTGated MRIDifference (%)Gated SPECTGated MRI892.0 \pm 24.0127.4 \pm 15.028.3 \pm 17.882.2 \pm 22.4114.5 \pm 15.71692.0 \pm 21.0122.4 \pm 20.127.6 \pm 14.784.6 \pm 25.3109.6 \pm 14.83295.5 \pm 26.9118.8 \pm 16.025.0 \pm 14.286.6 \pm 24.7105.7 \pm 11.1838.6 \pm 18.158.0 \pm 12.736.9 \pm 18.731.8 \pm 14.135.1 \pm 15.71632.9 \pm 11.651.4 \pm 12.339.7 \pm 17.529.4 \pm 14.130.9 \pm 13.63230.9 \pm 15.648.7 \pm 9.542.2 \pm 18.727.0 \pm 13.427.0 \pm 10.5859.6 \pm 8.554.7 \pm 7.08.2 \pm 5.262.8 \pm 9.160.6 \pm 6.71665.0 \pm 5.658.2 \pm 6.111.5 \pm 7.466.7 \pm 8.865.2 \pm 6.33268.9 \pm 7.359.0 \pm 5.413.3 \pm 5.170.3 \pm 9.167.9 \pm 4.682.7 \pm 0.63.0 \pm 0.517.3 \pm 10.23.4 \pm 1.03.9 \pm 0.7163.1 \pm 0.53.5 \pm 0.416.3 \pm 12.43.7 \pm 0.94.2 \pm 0.6323.5 \pm 0.63.7 \pm 0.411.7 \pm 7.74.1 \pm 1.14.1 \pm 0.482.4 \pm 0.62.6 \pm 0.620.7 \pm 16.83.4 \pm 1.23.4 \pm 1.0162.9 \pm 0.93.1 \pm 0.518.6 \pm 15.23.5 \pm 0.93.7 \pm 0.8323.1 \pm 0.83.0 \pm 0.611.5 \pm 8.94.5 \pm 1.44.0 \pm 1.0 </td	

Data are expressed as mean \pm SD

Fig. 1 Parameters by MPS (1) and CMR (2). Each quantitative parameter was demonstrated at rest and at exercise, respectively. EDV (a), ESV (b), LVEF (c), PER (d), PFR (e) and TTPF (f). *Each bar* represents the mean \pm SD



experiments and informed consent form were approved by the Institutional Review Board of the School of Medicine of Miyazaki University.

Exercise protocol

Both multi-stage exercise MPS and CMR examinations using a bicycle ergometer were performed from 90 W and increased by 30 W every 3 min. Accepted endpoint for the exercise test was achievement of 85% of the target heart rate. All exercise MPS were done at SPECT laboratory and CMR examinations were done in the room next to the MRI room. Both gated MPS and gated CMR started within 5 min after the exercise tests completion.

Gated MPS

A dose of 600 MBq ^{99m}Tc-tetrofosmin (Nihon Mediphysics Co., Ltd., Nishinomiya, Japan) was administered intravenously at rest under fasting conditions. Forty minutes after the injection of ^{99m}Tc-tetrofosmin, electrocardiography (ECG)-gated MPS at rest images were acquired with a 2-detector 180° camera (E-cam, Siemens Medical System, USA) equipped with cardiac collimators using elliptic 360° acquisition with 46 projections at 20 s per projection and a zoom factor of 1.45 and stored in a 64×64 matrix; ECG-gated 32-frame per R–R interval SPECT data were acquired. The exercise studies were performed a few hours after the rest studies with same data acquisition protocol. A dose of 600 MBq ^{99m}Tc-tetrofosmin was intravenously injected at peak exercise, and stress lasted for another minute. The acquisition time of both rest and exercise study were 20 min.

Both MPS image reconstruction and data analysis were conducted by one well-trained technologist. The 32-frame dataset was transferred to a workstation system (Siemens Medical System, USA), where the data were combined into 8- and 16-frame gated data. The projection data were



reconstructed into tomographic trans-axial images using a filtered back-projection method with a ramp filter followed by 2-dimensional Butterworth filtering (order, 5; cut-off frequency, 0.6 cycle/pixel on a 0–1 scale) [14, 15]. Neither attenuation correction nor scatter correction was performed.

The left ventricular volume and LVEF were calculated automatically from 8, 16, and 32 frame-gated data using QGS program (Cedars-Sinai Medical Center, Los Angeles, CA, USA) [14, 15]. Then we extracted value of left ventricular volume in each phase as a text file. After these procedures, we calculated TTPF, PER and PFR using values of ventricular volume with curve differential calculus software VCDiff software (VCDiff, Version 3.1, FUJIFILM RI Pharma CO., Ltd., Tokyo, Japan) [19].

Gated CMR

Gated CMR examinations were performed within a few days of gated MPS examinations. Images were acquired with a

1.5-T whole-body MR system (Vantage: Toshiba Medical System, Tokyo, Japan) using a quadrature phased-array body coil (Torso SPEEDER coil: Toshiba Medical System. Tokyo, Japan) [39], prospective electrocardiography triggering, and breath holding. The acquisition time of both rest and exercise study were 10 min. To detect relevant changes in hemodynamic parameters during the examination, heart rate were monitored and documented. The position of the heart was determined with a localizer sequence [single-shot two-dimensional steady-state precession sequence (SSFP) [22, 39], repetition time ms/echo time ms of 3.7/1.9, flip angle of 70°, 6-mm section thickness, 360×360 field of view, 128×256 matrix], and imaging planes were adjusted to obtain standard long- and short-axis views. Subsequently, SSFP cine MR imaging was performed in the LV from the base to the apex, with 8- to 10-mm thick sections and 5-mm gap in the short-axis orientation.

In the current study, a segmented SSFP two-dimensional sequence was modified to vary temporal resolution. The

 Table 2
 The agreement range between two methods (Bland–Altman plot analysis)

Parameters	Frame	Rest-agreement range		Exercise-agreement range	
		Lower	Upper	Lower	Upper
EDV (ml)	8	-82.3	11.4	-11.2	70.0
	16	-25.0	76.3	-31.1	75.1
	32	-72.3	30.0	-38.1	70.5
ESV (ml)	8	-0.93	39.8	-19.4	26.0
	16	-6.4	43.4	-18.7	19.7
	32	-40.0	5.0	-16.1	17.9
LVEF (%)	8	-11.5	1.5	-17.1	12.8
	16	-17.6	4.0	-19.8	16.7
	32	2.0	18.0	-22.3	17.5
PER (EDV/s)	8	-0.81	1.26	-0.90	1.85
	16	-0.40	1.20	-1.10	2.30
	32	-1.02	0.66	-1.92	1.95
PFR (EDV/s)	8	-0.76	1.22	-1.66	1.66
	16	-1.39	1.69	-1.34	1.79
	32	-1.01	1.14	-3.34	2.41
TTPF (ms)	8	-94.3	49.6	-7.66	37.4
	16	-74.2	58.1	-73.4	68.0
	32	-54.6	56.0	-74.8	48.0

acquisition was segmented to acquire several lines of data per image during each cardiac cycle to keep imaging times within a reasonable breath-hold period.

To investigate the influence by number of gated frames per R–R cycles, various data were collected, where the number of frames per R–R cycle was 8, 16 and 32. Echo train length for segmented data acquisition was set to 16, which resulted in frame durations of 60 ms. The typical parameter settings were approximately 360×360 -mm field of view with 128×192 matrix. The breath-hold time for data acquisition was 14 s for the number of frames per R–R cycle of 30 ms.

Acquired data were analyzed by commercially available software (AZE Virtual Place, Version 3.0, AZE, Tokyo, Japan) with separately dedicated workstation. Using a midventricular image as a reference, window level settings were done to optimize contrast between blood pool and myocardium, and they were applied to all images of slices. In all normal volunteers, high image quality with excellent contrast between blood pool and myocardium was achieved, which facilitated image segmentation. Both the end-cardiac and cardiac contours were manually drawn on end-diastolic and end-systolic short-axis images by the same radiologist. To derive LV volume serially, contours of cardiac lumen were propagated at every tomographic slice. Papillary muscles were assigned to the LV lumen and, therefore, ignored. The left ventricular volumes were thus obtained using the modified Simpson's method by summing the crosssectional areas contained by the endocardial borders of all short-axis slices included in the analysis [33]. For calculating left ventricular function parameters, we used both left ventricular volume curve obtained by CMR and the curve differential calculus software (VCDiff, Version 3.1, FUJIFILM RI Pharma CO., Ltd., Tokyo, Japan).

Data analysis

Before analyzing the concordance of quantification by two different modalities, we investigated the reproducibility of inter and intra-observers in all parameters. Namely, we calculated the % differences in each parameter by observer 1 and by observer 2, respectively. We calculated % difference of intra-observer by dividing the difference of 1st and 2nd value with 1st value. Similarly, we calculated % difference for inter-observer by dividing the difference of 1st observer's value and 2nd observer's value with 1st observer's value. Mean of ten subjects was calculated by each frame conditions for every parameter.

To evaluate the concordance of parameter's quantification by two different modalities, we calculated % difference by dividing the difference of CMR parameters and MPS parameters by MPS parameters for each corresponding parameter. We also compared the value of each parameter among three different gated conditions. Statistical analysis was conducted by Bonferroni multiple comparison test after Friedman test. Statistically, a *p* value of <0.05 was considered to be significant. Finally, the degree of data concordance between the gated MPS and gated CMR was evaluated by Bland–Altman analysis [40]. Limits of concordance were demonstrated by mean values \pm 2SD. Statistical analyses were conducted using Prism 4 (GraphPad Software Inc., San Diego, CA, USA).

Results

Physiological parameters during MPS and CMR

All examinations were performed safely and appropriately. No participants showed ST-segment depression or typical ischemic chest pain during exercise tests. The physiological parameters (mean heart rate, systolic blood pressure and diastolic blood pressure) during MPS were 70.3 ± 14.3 bpm, 116.2 ± 11.1 mmHg and 65.5 ± 8.0 mmHg in the rest study and were 91.6 ± 14.4 bpm, 140.7 ± 14.4 mmHg and 70.8 ± 8.2 mmHg in the exercise study. Similarly physiological parameters (mean heart rate, systolic blood pressure and diastolic blood pressure) during CMR were 71.2 ± 10.9 bpm, 115.3 ± 10.3 mmHg, and 67.6 ± 8.7 mmHg in

Fig. 2 Bland–Altman plots showing the agreement between gated MPS and gated CMR. EDV (a rest, b exercise), ESV (c rest, d exercise), LVEF (e rest, f exercise), PER (g rest study, h exercise), PFR (i rest, j exercise) and TTPF (k rest, l exercise)



the rest study. Similarly, they were 92.3 ± 16.7 bpm, 137.3 ± 12.8 mmHg and 68.3 ± 10.4 mmHg in the exercise study. These values did not statistically significantly differ compared with the parameters of MPS.

Left ventricular function parameters measured by MPS

None of participants showed perfusion abnormalities at gated MPS. In comparison of various left ventricular parameters among three kinds of gated conditions at rest, EDV, LVEF, PER and PFR in 8 frame-gated studies were

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significantly lower than those of 32-frame gated studies. Both LVEF and PER in 8-frame gated studies were also lower than those of 16-frame gated conditions. The value of ESV in 8-frame gated study was significantly higher than that of 32-frame gated study. No significant difference was noted for TTPF. With regard to exercise study, similar tendencies were noted. In addition, ESV in 16-frame gated conditions was significantly higher than that in 32-frame gated study. The value of PFR in 32-frame gated study was also significantly higher than that of 16-frame gated study (Table 1; Fig. 1-1).





Left ventricular function parameters measured by CMR

were noted in the exercise conditions, there was no statistical significance in PER and PFR (Table 1; Fig. 1-2).

In comparison of various left ventricular parameters among three kinds of gated condition at rest, LVEF, PER and PFR in 8 frame-gated studies were significantly lower than those of 32-frame gated studies. In addition, PER in 8 framegated study was lower than that of 16-frame gated condition. With regard to ventricular volumes, both EDV and ESV in 8-frames gated studies were significantly higher than those of 32-frame gated studies. No significant difference was noted in TTPF. Although similar tendencies

Reproducibility of quantification intra-observers and inter-observers

The reproducibility of quantification of all parameters except ventricular volumes in both methods was good, showing % differences of smaller than 5.0%. Nevertheless, % differences of ventricular volumes were smaller than 6.0% (Supplemental table 1-1, 1-2).



Percent difference (% difference) of left ventricular function parameter between MPS and CMR

The values of % difference in LVEF were about 10% in both rest and exercise study. They were from 10 to 20% for PER, PFR, and TTPF at rest. However, they tended to be higher at exercise around 20–25%. In particular, % difference of EDV and ESV was approximately 25–40% in both rest and exercise study (Table 1).

Bland-Altman plot analysis

At rest condition, in TTPF, 32-frame collection showed the best agreement. In contrast, LVEF showed the best agreement range in 8-frame collection despite deviation of distribution. As for PER and PFR, no prominent differences were noted between 8-frame collection and 32-frame collection. Also in ESV and EDV, the agreement was not so different among three kinds of collection.

At exercise conditions, the agreement range tended to be wider than those in rest conditions. Although certain tendency was not noted, agreement ranges of EDV, LVEF, PER and TTPF were narrower in 8-frame gated collections. As for ESV, 32-frame collection showed the best agreement. In PFR, both 8-frame collection and 16-frame collection showed similar agreement range (Table 2; Fig. 2).



Representative case

Discussion

The representative case included a 32-year-old man in healthy condition. In the rest study, values of % difference were more than 30% in EDV and were more than 50% in ESV. In contrast, it was smaller than 10% in LVEF. In diastolic parameters, they were smaller than 25%. Similar tendencies were noted in the exercise study. Namely, values of % difference in ventricular volumes were about 30–60%. In both systolic and diastolic parameters, values of % difference were smaller than 25% (Table 3; Fig. 3).

In evaluating the agreement of left ventricular function parameters obtained by gated MPS and gated CMR, the values of LVEF showed the best concordance among all parameters. The values of % difference were around 10% in both rest and stress conditions and the agreement ranges were $\pm 10\%$ in rest and $\pm 20\%$ in stress conditions. These results were consistent with the previous report in bypass grafting patients in rest conditions by Mesquita et al. [37]. In the current study, % difference of 8-frame gated was smaller than that of 32-frame gated study (8.2 vs. 13.3) and



the agreement range was relatively narrower (-11.5 to 1.5 vs. 2 to 18%). Similar pattern was also noted under exercise condition. The following reason is speculated. In determining end-systolic point, 8-frame collection is simpler than other collection conditions, because of fewer systolic points. In 16- or 32-frame collections, the decision of end-systolic point could be relatively unstable, owing to many neighboring systolic points. Consequently, % difference in ESV calculation by 8-frame collections. Because LVEF calculation is influenced by ESV, smaller % difference in ESV calculation seemed to explain the smaller % difference in LVEF by 8-frame collection. However, 8-frame gated analysis has drawback of underestimation

[41, 42] and the phenomenon was also confirmed in our study. In considering the reliability of calculated values and also the compatibility between two different modalities, 32-frame gated study would be recommended as routine examination.

Judging from values of % differences and Bland– Altman plots analysis, the agreement of left ventricular volumes were relatively poor than other parameters. In particular for EDV, the changes of ventricular volumes following the changes of frame number showed an inverse pattern, respectively. Ventricular volumes were known to be underestimated by MPS compared to CMR [36, 43]. We confirmed similar tendency in the current study. The membranous part of the septum and the atrioventricular



valve plane do not contain myocardium and are therefore not visible in MPS images [36]. Due to such differences of depiction methods for cardiac lumen, the underestimation of left ventricle in MPS should be unavoidable. Particularly in EDV, the agreement ranges were around ± 50 ml in the current results. Although the range was smaller than previous reports [37], the agreement was not sufficient.

Both PFR and TTPF are conventional DFx parameters [10, 44, 45]. Although the agreement range was similar, value of % difference of PFR was better in 32-frame compared with 8-frame gated condition at rest study. As for

TTPF, the agreement was best in 32-frame study (% difference was 10.6 and agreement range was from -54.6 to 56.0 ms). However in exercise studies, % differences of PFR of each condition were around 20% and agreement ranges were relatively wider than those of under rest conditions. Similarly, the % differences of TTPF were around 25 to 35% and the agreement ranges got deteriorated in both 16- and 32-frame collections. We should keep in mind that concordance of diastolic parameters deteriorates at exercise.

In comparing 32-frame collection with 8-frame collection only about the agreement, there might not be major

Table 3 Parameters of representative case

Parameters	Phase	Rest			Exercise		
		SPECT	MRI	% Difference	SPECT	MRI	% Difference
EDV (ml)	8	82.3	130.7	58.8	72.2	100.0	38.5
	16	85.2	120.8	41.8	72.5	93.1	28.4
	32	89.1	115.9	30.1	71.0	90.3	27.2
ESV (ml)	8	31.1	54.3	74.6	25.8	42.9	66.3
	16	33.1	49.4	49.2	24.3	35.8	47.3
	32	32.0	46.9	46.6	17.9	24.5	36.9
LVEF (%)	8	62.2	58.3	6.3	64.2	57.0	11.2
	16	61.5	59.1	3.9	66.5	61.2	8.0
	32	63.0	59.5	5.6	75.1	68.6	8.7
PER (EDV/s)	8	2.79	3.05	9.3	5.04	4.38	13.1
	16	3.82	3.86	1.0	4.98	4.23	15.1
	32	2.77	2.94	6.1	5.41	5.12	5.4
PFR (EDV/s)	8	2.38	2.62	10.1	3.82	3.69	3.4
	16	2.51	3.11	23.9	3.75	3.93	4.8
	32	2.53	2.88	13.8	4.52	5.02	11.1
TTPF (ms)	8	124	129	4.0	171	154	9.9
	16	129	155	20.1	168	204	21.4
	32	147	134	8.8	186	187	0.5



difference. However, 8-frame collection has a problem in quantification. Although the values of PFR at rest obtained by either 16- or 32-frame gated MPS were almost equal to previous GBPS or MPS examinations [44, 46–48], underestimation was observed in both modalities by 8-frame collection in the current study. As stated above, using

8-frame instead of 32-frame gated SPECT data causes temporal undersampling [42]. Because PFR is denoting the maximum value of the derivative of the time–volume curve, the inaccurate determination of the end-systolic point using 8-frame gated SPECT was considered to be major causative reason of underestimation. As for value of 2

8 frame

Rest

200

DFT_Crv

400

(msec)

600

ORG_Crv

-Diff_Crv

(EDV/sec)

60 (ml)

20

3

2

1 0

-1

-2

-3

3

1.5 0

-1.5

-3

Fig. 3 continued







TTPF, it is reported to be relatively stable irrespective of age, sex, heart rate [10, 44], or numbers of gated-frame [44]. However, in the current study at rest, the value

obtained by 8-frame collection is longer than that of 32-frame collection in MPS. Such tendency was not always noted in CMR in rest condition. Nevertheless, more

400



number of frame data collections would be desired in order to obtain DFx parameters accurately by improving temporal resolution [49].

Interestingly, the value of PFR increased by around 30–40% at exercise compared to rest condition at 32-frame gating. Although normal value ranges of PFR at exercise condition had not been established, the increase rate might be related to exercise capacity [8]. However, the value at 8-frame study was lower than that of 32-frame data under exercise conditions. Therefore, the PFR value at 8-frame study was also considered to be underestimated similarly as at rest condition. As for values of TTPF at exercise condition, they were relatively shorter than those in rest condition. Although normal value ranges of TTPF at exercise condition have not been ensured either, they were around 140 ms by 32-frame gating and were approximately 150 ms by 8-frame gating. Considering quantitative accuracy and relatively good agreement, 32-frame gated condition would be recommended as routine procedure in monitoring DFx with both modalities.

One of the significant limitations in the current study is the difference of data acquisition time. Namely, CMR takes about 10 min and MPS takes about 20 min, which resulted in differences of recovery from exercised status and degree of loaded stress during imaging time. In addition, the differences in the physical conditions of volunteers between the two studies could be an additional influential factor. At the same time, because exercise test could not be carried out in MRI scanning room, there might be an individual difference in scan initiation time. Unification of the exercise protocol of CMR is desired in future. The degree of agreement will improve, if we resolve the above problems.

In SPECT data acquisition, we adopted 360° angular sampling techniques in order to reduce geometric distortion [50]. In addition, in the evaluation of detecting significant CAD in the Japanese study, 360° database showed the best diagnostic performance [51]. Although the apparent difference has not been reported between both 180° and 360° collection about an LVEF or ESV, EDV was relatively lower in 360° collection [52]. Therefore, gated SPECT data by 180° collection also may be necessary in discussing degree of the agreement with the MRI in future study.

From a clinical point of view, institutions where CMR is used in myocardial examinations will increase continuously because it can give information, such as coronary vessel stenosis, not to be evaluated with MPS [32]. Opportunities adopting each other's quantitative data as reference will also increase. Based on the current results, both SFx and DFx could be monitored jointly by CMR or MPS in rest conditions. However, in exercise conditions, we should use quantitative parameters, taking into consideration the agreement range between two methods, owing to the dissociation of image acquisition time. In future, the collection time of SPECT will be shortened by recent progression of instrument such as semiconductor detector gamma camera [53, 54]. Further study with new devices is desired to confirm the improvement of the agreement of exercise stress data between CMR and MPS.

Fig. 3 continued



Conclusion

We evaluated agreement of left ventricular function parameters obtained in MPS and CMR of healthy volunteers.

LVEF showed favorable agreement in both rest and exercise conditions. Although diastolic parameters also

showed good concordance at 32-frame gating in rest study, they showed certain differences at exercise examination. Regarding left ventricular volumes, the concordances were worse in both rest and exercise conditions.

When we follow patients by the same cardiac parameters except for ventricular volumes with CMR and MPS at

rest conditions, using parameters across the two modalities proved to be feasible. However, the use is limited at exercise condition.

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