NUCL SCI TECH (2017) 28:6
DOI 10.1007/s41365-016-0156-9

Accuracy of left ventricular function from electrocardiography-gated myocardial perfusion SPECT by MyoMetrix in Chinese

Yang-Chun Chen[1] · Ruo-Zhu Dai[2] · Ke-Lian Zhang[2] · Yong-Da Dong[2] · Hui-Lin Zhuo[2] · Qing-Mu Wang[3]

Received: 24 December 2015 / Revised: 11 April 2016 / Accepted: 15 April 2016 / Published online: 30 November 2016

Abstract This work was to determine threshold values for accurate measurements of left ventricular end-diastolic volume (EDV), end-systolic volume (ESV), and ejection fraction (EF) from electrocardiography-gated myocardial perfusion imaging (MPI) in Chinese, and these data were compared with those of echocardiography. A total of 110 patients with definite or suspected coronary artery disease were referred for both gated MPI and echocardiography within 1 week. The EDV, ESV, and EF automatically measured by MyoMetrix and echocardiography were analyzed using Bland–Altman plot correlation and paired t test. The results showed that these parameters quantified by MyoMetrix software were correlated, moderately to highly, with those on echocardiography (ρ, $r \geq 0.75$, $P < 0.01$). However, the EF was not significantly correlated, with post-exercise MPI ESV of <15 mL or resting MPI ESV of <20 mL. At or above this ESV value, EF was underestimated by MyoMetrix ($t \geq 4.60$, $P < 0.01$). In a word, a small ESV was underestimated by MyoMetrix, which could lead to EF overestimation. On the contrary, a normal or large ESV was overestimated by MyoMetrix, which led to EF underestimation.

Keywords Myocardial perfusion imaging · Left ventricular function · Software

This study was supported by the Natural Science Foundation of Fujian Province (No. 2015J01516).

✉ Ruo-Zhu Dai
dairzcn@126.com

[1] Department of Nuclear Medicine, Quanzhou No.1 Hospital Affiliated to Fujian Medical University, Quanzhou 362000, China

[2] Department of Cardiology, Quanzhou No.1 Hospital Affiliated to Fujian Medical University, Quanzhou 362000, China

[3] Department of Ultrasound, Quanzhou No.1 Hospital Affiliated to Fujian Medical University, Quanzhou 362000, China

1 Introduction

Electrocardiography (ECG)-gated myocardial perfusion imaging (MPI) by single photon emission computed tomography (SPECT) is the main clinical force in the identification of ischemic myocardium. It provides not only perfusion data, but also left ventricular (LV) end-diastolic volume (EDV), end-systolic volume (ESV), and ejection fraction (EF). LV volumes and EF are important diagnostic and prognostic information for patients with heart disease. As the normal gated MPI database is established on the basis of Western patients, we investigate in this paper the accuracy and repeatability of the parameters gained by gated MPI from Chinese patients. The methods to gain the data include angiography, echocardiography, magnetic resonance imaging (MRI), equilibrium radionuclide ventriculography (ERV), and positron emission tomography (PET). Many studies [1–6] compared the gated MPI by SPECT with the other methods in LV volumes and functional measurements. There were moderate to high correlations among the results of different methods; however, large discrepancies in patients with small LV [2, 7] were investigated. Unfortunately, there was no determined cut-off value of LV volume for evaluating LV volume and function accuracy, especially for Chinese. Here we aimed at answering this question.

2 Materials and methods

2.1 Population

From January 2014 to July 2015, patients with definite or suspected coronary artery disease (CAD) who were referred for ^{99m}Tc sestamibi (^{99m}Tc-MIBI) perfusion imaging with a protocol of 2-day rest/exercise, rest only, or exercise only, and resting echocardiography within a 1-week period were included. Exclusion criteria were irregular heart rate and myocardial infarction. This retrospective study was approved by our hospital ethics committee without patients' informed consent.

A total of 110 patients (59.8 ± 12.8 years; 30 women, 80 men) were included in this study. Their weight, height, and body mass index (BMI) were recorded. The patients whose LV EF <50% measured by echocardiography were defined as heart failure, while the rest were normal heart function. Two-day rest/exercise MPI ($n = 50$), resting MPI ($n = 46$), or exercise MPI ($n = 14$) were followed by the participants.

2.2 SPECT imaging protocols

The ^{99m}Tc-MIBI (740 MBq) was injected at rest or during ≥85% of maximal age-predicted heart rate achieved on an upright bicycle. Patients drank 250 mL of milk 30 min later. Supine eight-frame ECG-gated MPI SPECT images were acquired 1 h post-exercise or 2 h post-injection at rest. The images were gained on a dual-detector gamma camera (Infinia 4, GE Healthcare) with low-energy, high-resolution collimators using 60 projections over 180° from the right anterior oblique 45° to the left posterior oblique 45° at 20 s per projection. The energy window was set at 126–154 keV, and a 64 × 64 matrix, zoom 1.3 was used. Patient's average heart rates during data acquisition were recorded. Images were reconstructed with MyoMetrix software (GE Healthcare) handled by a single experienced nuclear medicine physician. The projection data were prefiltered using a Butterworth filter (critical frequency, 0.4 cycles per pixel; power, 10) and reconstructed by filtered back-projection with scatter correction. The EDV, ESV, and EF of LV were automatically computed by MyoMetrix code [6, 8].

2.3 Echocardiographic measurements

A single experienced cardiologist blinded to the patient group assignments performed all the echocardiographic studies using an ultrasound system (iE Elite, Philips Medical Solutions) equipped with an S5-1 transducer. The images were obtained from the parasternal and apical positions using two-dimensional, M-mode, and Doppler echocardiographic techniques in the left lateral decubitus position. In each patient, EDV, ESV, and EF were measured using two-dimensional echocardiography in two- and four-chamber apical views by the modified Simpson's method [1]. The echocardiographic data were averaged from three measurement cycles.

2.4 Statistical analysis

The normal data distribution, t test, Chi-square test, and correlation coefficient calculation were performed as appropriate. The data are presented as value (interquartile range) since they were not normally distributed. Linear regression analysis was performed to calculate Pearson's correlations between gated MPI and echocardiographic LV function parameters. The cutoff value of ESV was 10, 15, 20, 25, or 30 mL. Two-tailed values of $P < 0.05$ were considered statistically significant.

3 Results

Forty-three heart failure patients and 67 normal heart function patients were included in this study. Their clinical characteristics are shown in Table 1. The heart failure rate was almost 50% (39/80) in male patients, which was significantly higher than female (4/30) ($P < 0.01$), while the age, weight, and BMI did not differ significantly between the heart failure and normal groups. As we know, the resting heart rate, EDV, ESV of heart failure patients were significantly larger than those whose heart function was normal ($P < 0.01$). However, no difference in the post-exercise heart rate was found between heart failure and normal groups (Table 2). And the resting and post-exercise heart rates did not differ significantly ($t < 1.50$, $P > 0.05$).

The Bland–Altman plots (Fig. 1) showed good correlation between gated MPI and echocardiographic EDV, ESV, and EF. The differences in EDV (5/96), ESV (6/96), and EF (5/96) between the gated resting MPI and

Table 1 Clinical characteristics of patients

Patients	EF <50%	EF ≥50%	P
Female	4	26	
Male	39	41	<0.01*
Age (years)	61.2 ± 14.3	59.1 ± 11.8	>0.05 ($t = 0.47$)
Weight (kg)	69.3 ± 12.5	66.2 ± 10.1	>0.05 ($t = 1.19$)
Height (m)	1.67 ± 0.05	1.64 ± 0.07	0.02 ($t = 2.37$)
BMI (kg m^{-2})	24.9 ± 4.5	24.8 ± 3.4	0.99 ($t = 0.01$)

* Using Fisher's exact test

echocardiography over 2SD (standard deviation) from the total mean difference are shown in Fig. 1a. The differences in EDV (4/64), ESV (6/64), and EF (3/64) between the gated post-exercise MPI and echocardiography, over 2SD from the total mean difference, are shown in Fig. 1b. The discrepancy of EDV and ESV extended as the volume increased; however, the EF discrepancy did not show this feature.

Table 2 LV function parameters and heart rate measured by MyoMetrix based on gated MPI

Items	EF <50%	EF ≥50%	*P*
Heart rate (bpm)			
At rest	82.2 ± 19.5	69.1 ± 11.5	<0.01 ($t = 3.81$)
P.E.	78.5 ± 13.6	72.9 ± 13.2	>0.05 ($t = 1.64$)
EDV (mL)			
At rest	189.2 ± 70.3	93.0 ± 37.3	<0.01 ($t = 9.16$)
P.E.	200.3 ± 69.9	91.2 ± 34.0	<0.01 ($t = 9.62$)
ESV (mL)			
At rest	145.2 ± 64.1	32.6 ± 19.5	<0.01 ($t = 12.3$)
P.E.	155.5 ± 64.7	31.2 ± 18.7	<0.01 ($t = 11.7$)
EF (%)			
At rest	25.7 ± 9.6	66.3 ± 9.0	<0.01 ($t = -18.4$)
P.E.	24.7 ± 9.7	67.0 ± 8.4	<0.01 ($t = -15.3$)

bpm beat per minute

P.E. post-exercise

Table 3 shows moderate to high correlations between the gated MPI and echocardiographic EDV, ESV, and EF, with the correlation coefficients of 0.75–0.95 ($P < 0.01$). The ESV obtained from post-exercise MPI ≥15 mL, EF calculated from post-exercise MPI and echocardiography was highly correlated ($r = 0.95$, $P < 0.01$), and the linear regression equation was $y = 0.92x + 7.8$ (Table 3; Fig. 2). EF obtained from MPI and echocardiography are shown as x and y in the linear regression equation. However, they were not significantly correlated when ESV <15 mL; post-exercise EF was obviously smaller than echocardiographic EF ($t = 4.60$, $P < 0.01$) when ESV ≥15 mL, but they did not differ greatly ($t = 1.68$, $P = 0.12$) when ESV <15 mL.

As ESV gained from resting MPI was ≥20 mL, EF calculated by resting MPI and echocardiography was moderately correlated ($r = 0.89$, $P < 0.01$); the linear regression equation was $y = 0.84x + 12.2$ (Table 3; Fig. 3). However, they did not correlated significantly when ESV was <20 mL; the resting EF was significantly smaller than echocardiographic EF ($t = 5.60$, $P < 0.01$) as ESV ≥ 20 mL, but was significantly larger than echocardiographic EF ($t = 2.82$, $P = 0.01$) at ESV <20 mL.

The post-exercise ESV was significantly smaller than echocardiography when post-exercise ESV was <15 mL

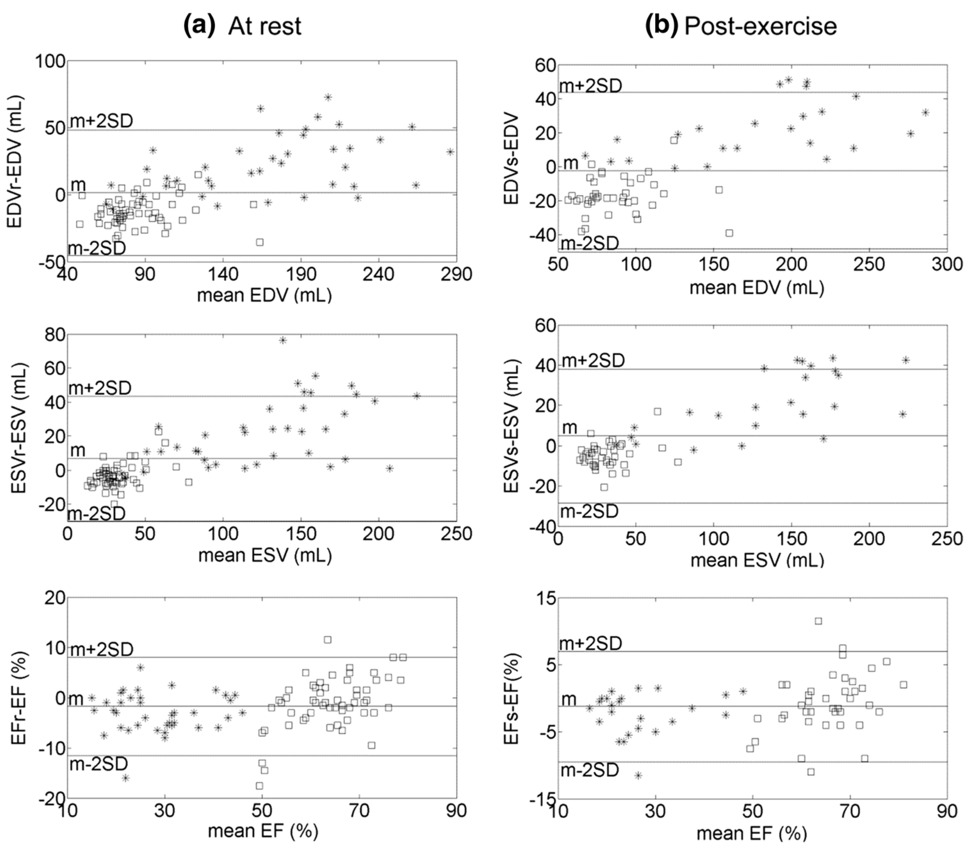

Fig. 1 Bland–Altman graphs of differences against means of gated MPI, at rest (**a**) and post-exercise (**b**), and echocardiographic EDV, ESV, and EF. Every interval value in *Y* axis is 1 SD of the differences. EDV, ESV, and EF measured by MyoMetrix are presented as EDVr, ESVr, and EFr. At EF <50% by echocardiography, the data are presented as *stars*; otherwise, they are presented as *squares*. *MPI* myocardial perfusion imaging; *EDV* end-diastolic volume; *ESV* end-systolic volume; *EF* ejection fraction

Table 3 Correlation between ECG-gated myocardial perfusion imaging and echocardiographic LV EDV, ESV, and EF

ESV by ECG-gated MPI	>0	≥10 mL	≥15 mL	≥20 mL	≥25 mL	≥30 mL
EDV–EDVr (mL)	$\rho = 0.76$	$\rho = 0.75$	$\rho = 0.77$	$\rho = 0.77$	$r = 0.78$ $y = 0.506x + 54.3$	$r = 0.77$ $y = 0.526x + 49.9$
ESV–ESVr (mL)	$\rho = 0.85$	$\rho = 0.83$	$\rho = 0.86$	$\rho = 0.87$	$\rho = 0.88$	$r = 0.86$ $y = 0.569x + 18.3$
EF–EFr (%)	$\rho = 0.86$	$\rho = 0.84$	$\rho = 0.87$	$r = 0.89$ $y = 0.84x + 12.2$	$r = 0.89$ $y = 0.884x + 10.7$	$r = 0.86$ $y = 0.887x + 10.5$
EDV–EDVs (mL)	$\rho = 0.77$	$\rho = 0.78$	$\rho = 0.79$	$\rho = 0.78$	$r = 0.83$ $y = 0.527x + 58.8$	$r = 0.82$ $y = 0.530x + 58.0$
ESV–ESVs (mL)	$\rho = 0.86$	$\rho = 0.88$	$\rho = 0.89$	$\rho = 0.88$	$r = 0.94$ $y = 0.610x + 18.8$	$r = 0.93$ $y = 0.603x + 20.2$
EF–EFs (%)	$\rho = 0.85$	$\rho = 0.87$	$r = 0.95$ $y = 0.92x + 7.8$	$r = 0.94$ $y = 0.937x + 7.3$	$r = 0.94$ $y = 0.961x + 6.6$	$r = 0.93$ $y = 0.943x + 7.0$

EDV, ESV, and EF obtained from resting MPI or post-exercise are presented as EDVr, ESVr, EFr, or EDVs, ESVs, EFs, respectively. EDV, ESV, EF obtained from MPI and echocardiography are shown as x and y in linear regression equations

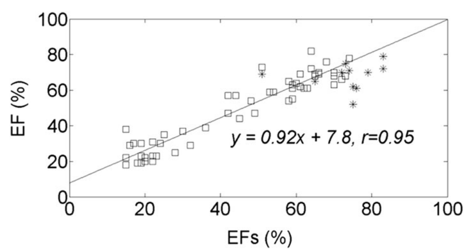

Fig. 2 Pooled correlation between post-exercise MPI EFs and echocardiographic EF. At ESV <15 mL (gained from post-exercise MPI by MyoMetrix), the data are presented as *stars*; otherwise, they are presented as *squares*

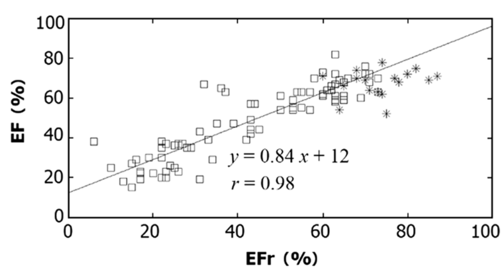

Fig. 3 Pooled correlation between resting MPI and echocardiographic EF. At ESV <20 mL (gained from resting MPI by MyoMetrix), the EF data are presented as *stars*, without significant correlation; otherwise, they are presented as *squares*, with good correlation

($t = 6.00$, $P < 0.01$) (Table 4); while ESV was ≥15 mL, it was significantly larger than that of echocardiography ($t = 3.33$, $P < 0.01$). Similarly, the resting ESV was smaller than that of echocardiography at ESV <20 mL ($t = 6.84$, $P < 0.01$) (Table 4); while at ESV ≥20 mL, it was significantly larger than that of echocardiography ($t = 4.74$, $P < 0.01$).

4 Discussion

4.1 About our findings

LV EDV, ESV, and EF play major roles in the management of patients with heart disease. We have compared ECG-gated at rest and post-exercise MPI imaging and echocardiographic EDV, ESV, and EF, and confirmed that the data obtained automatically by MyoMetrix code were correlated, moderately to highly, with the echocardiography results.

When post-exercise MPI ESV was ≥15 mL, excellent Pearson's correlation ($r = 0.95$) was seen with post-exercise gated MPI and echocardiographic EF. When resting MPI ESV was ≥20 mL, good Pearson's correlation ($r = 0.89$) was seen with resting gated MPI and echocardiographic EF. However, no significant correlation was found when post-exercise MPI ESV was <15 mL or resting MPI ESV was <20 mL. Our results were similar to those of previous studies. Maret et al. [9] showed that EF gained by manual Simpson testing had good correlation versus MPI ($r = 0.80$) in 60 consecutive patients with known or suspected CAD. Hatipoglu et al. [6] observed that EF calculated by MyoMetrix had good correlation with echocardiography in 30 patients with suspected CAD ($r = 0.78$). Lipiec et al. [2] observed good correlation between gated resting MPI and echocardiographic EF ($r = 0.88$), but there were large discrepancies in patients with a small LV. Nakajima et al. [10] developed a volume-dependent edge correction algorithm to obtain an accurate ESV and EF for small hearts, but they did not compare their findings with echocardiography or MRI images. With proper ESV cutoff values, we obtained the strongest

Table 4 Characteristics of the patients with small ESV

MPI protocol	ESV (mL)	Sex	Age (years)	Number	ESV (mL)/EF (%)			
					MyoMetrix		Echocardiography	
At rest	<20	Female	59.6 ± 11.1	11/24	13.5 ± 5.1	72.9 ± 7.7	27.5 ± 8.6	68.2 ± 6.3
		Male	61.8 ± 14.2	6/72	13.2 ± 5.3	74.8 ± 7.4	31.3 ± 8.3	66.3 ± 8.4
Post-exercise	<15	Female	57.9 ± 10.6	8/16	11.4 ± 2.4	71.1 ± 9.5	30.5 ± 9.8	66.9 ± 7.4
		Male	60.7 ± 12.5	3/48	12.0 ± 2.6	79.0 ± 4.0	25.3 ± 8.5	70.3 ± 8.5

correlation between gated MPI and echocardiographic EF among the aforementioned studies.

Moderate to high correlation (ρ, $r \geq 0.75$) was observed between gated MPI and echocardiographic EDV and ESV in this study. However, the EDV difference was not significant ($t < 0.82$, $P > 0.05$), while gated MPI ESV was significantly larger than that of echocardiography ($t > 2.33$, $P < 0.03$). These were confirmed by other authors. Nakae et al. [11] found that EDV and ESV values gained from gated MPI and echocardiography were moderately correlated ($r = 0.82$, 0.85) in 60 patients with suspected or definite heart disease. Nichols et al. [1] reported gated MPI and echocardiographic EDV and ESV showed high correlation in 33 patients ($r = 0.90$, 0.94). Cwajg et al. [3] obtained a good correlation between gated MPI and echocardiographic EDV and ESV; they found that ESV data by gated MPI was similar to the echocardiography findings ($P > 0.05$), while EDV of echocardiography was significantly larger ($P < 0.01$).

In Table 4, because of the partial volume effect (PVE), a small ESV calculated by MyoMetrix (post-exercise ESV <15 mL, resting ESV <20 mL) was significantly smaller than that of echocardiography ($P < 0.01$). Almost 50% of female patients were of small ESV, while less than 10% of male patients had small ESV. This suggests a modified MPI data acquisition protocol for female patients whose heart function was normal. Hedeer et al. [8] observed that gated MPI underestimated ESV compared to cardiac MRI in 100 patients with known or suspected CAD. Nakajima et al. [10] showed that, in small hearts (ESV <20 mL), quantitative gated SPECT underestimated ESV and overestimated EF. Although ESV measured by MyoMetrix exceeded the aforementioned cutoff value, it was significantly larger than that of echocardiography ($P < 0.01$). The cause of that discrepancy of EF quantified by MyoMetrix and echocardiography could be explained by PVE. In other words, when the measured ESV was less than the aforementioned cutoff value, it was underestimated by MyoMetrix, while EF could be overestimated by MyoMetrix. Nevertheless, the obtained ESV was not less than the aforementioned cutoff value, it was overestimated by MyoMetrix, and EF was underestimated by MyoMetrix. This suggests a modification of the MyoMetrix software to increase ESV and EF measurement accuracy.

4.2 About limitations of the work

Filtering, reconstruction method, and automatic measurement software may affect the EDV, ESV, and EF results [12–14]. According to the standard protocol in our department, this effect on LV volume and function measurements was not studied. However, our results were similar to the published data from different filtering, reconstruction method, and automatic measurement software.

Another limitation of our study is that MPI and echocardiography were not performed under the same conditions. For the exercise/rest or rest/exercise with ^{99m}Tc-MIBI in 1-day protocol should be performed around 5 h, and the half-life of ^{99m}Tc is 6 h, the 1st imaging may affect the analysis of the 2nd imaging 5 h later, and may not affect 24 h later. To eliminate that confusion, we did the 2-day rest/exercise protocol. Different preload and afterload values can affect LV function, including EDV, ESV, and EF. Matsuo et al. [15] reported the post-exercise EF was smaller than resting EF in three vessels disease. However, our echocardiographic and gated MPI data, at rest or post-exercise, were moderately to highly correlated. Borges-Neto et al. [16] found an excellent correlation ($r = 0.97$, $P < 0.01$) in a rest/post-exercise study.

The third limitation in our study is the MPI imaging LV EDV, ESV, and EF measurements by a single experienced doctor, and also the echocardiographic LV EDV, ESV, and EF. We did not investigate the inter- and intra-variability of the parameter measurement. Both are common measurement. Castell-Conesa et al. [17] reported that the inter-observer variability for LV EDV, ESV, and EF measurements by MPI were 1.9, 0.5 mL, and 0.5%, respectively. Thavendiranathan et al. [18] reported the inter-observer and intra-observer variability for LV EDV, ESV, and EF measurements by echocardiography were 8.4, 5.3 mL, and 3.3%; and 16.5, 7.4 mL, and 4.0%, respectively. Therefore, the inter- and intra-variability of measurements were far less than the SDs of the parameters in this study. So the results of our study were credible.

5 Conclusion

The LV EDV, ESV, and EF values automatically measured by MyoMetrix from gated MPI, including resting or post-exercise, exhibited good to excellent correlation with those obtained on echocardiography in Chinese. However, for PVE, a small ESV was underestimated by MyoMetrix, which could lead to EF overestimation. On the contrary, a normal or large ESV was overestimated by MyoMetrix, which led to EF underestimation.

Acknowledgements The authors thank Dr. Ze-Rong Huang, Dr. Da-Gui Huang, Dr. Zhi-Wen Hong, and Dr. Yan Yang for registering the imaging data.

References

1. K. Nichols, D. Lefkowitz, T. Faber et al., Echocardiographic validation of gated SPECT ventricular function measurements. J. Nucl. Med. **41**, 1308–1314 (2000)
2. P. Lipiec, P. Wejner-Mik, M. Krzemińska-Pakuła et al., Gated 99mTc-MIBI SPECT for the evaluation of left ventricular ejection fraction—comparison with three dimensional echocardiography. Ann. Nucl. Med. **22**, 723–726 (2008). doi:10.1007/s12149-008-0165-9
3. E. Cwajg, J. Cwajg, Z.X. He et al., Gated myocardial perfusion tomography for the assessment of left ventricular function and volumes: comparison with echocardiography. J. Nucl. Med. **40**, 1857–1865 (1999)
4. L. Emmett, A. Ng, L. Ha et al., Comparative assessment of rest and post-exercise left ventricular volumes and left ventricular ejection fraction on gated myocardial perfusion imaging (MPI) and echocardiography in patients with transient ischaemic dilation on adenosine MPI: Myocardial stunning or subendocardial hypoperfusion? J. Nucl. Cardiol. **19**, 735–742 (2012). doi:10.1007/s12350-012-9571-4
5. Y. Yamakawa, N. Takahashi, T. Ishikawa et al., Clinical usefulness of ECG-gated FDG PET combined with 99mTc-MIBI gated SPECT for evaluating myocardial viability and function. Ann. Nucl. Med. **18**, 375–383 (2004). doi:10.1007/BF02984480
6. F. Hatipoğlu, Z. Burak, Ö. Ömür, Comparison of gated myocardial perfusion SPECT, echocardiography and equilibrium radionuclide ventriculography in the evaluation of left ventricle contractility. Turk. Kardiyol. Dern. Ars. **42**, 349–357 (2014). doi:10.5543/tkda.2014.74150
7. K. Nakajima, T. Higuchi, J. Taki et al., Accuracy of ventricular volume and ejection fraction measured by gated myocardial SPECT: comparison of 4 software programs. J. Nucl. Med. **42**, 1571–1578 (2001)
8. F. Hedeer, J. Palmer, H. Arheden et al., Gated myocardial perfusion SPECT underestimates left ventricular volumes and shows high variability compared to cardiac magnetic resonance imaging. BMC Med. Imaging **10**, 10 (2010). doi:10.1186/1471-2342-10-10
9. E. Maret, L. Brudin, L. Lindstrom et al., Computer-assisted determination of left ventricular endocardial borders reduces variability in the echocardiographic assessment of ejection fraction. Cardiovasc. Ultrasound **6**, 55 (2008). doi:10.1186/1476-7120-6-55
10. I. Nakae, H. Hayashi, T. Matsumoto et al., Clinical usefulness of a novel program “heart function view” for evaluating cardiac function from gated myocardial perfusion SPECT. Ann. Nucl. Med. **28**, 812–823 (2014). doi:10.1007/s12149-014-0875-0
11. K. Nakajima, K. Okuda, K. Nyström et al., Improved quantification of small hearts for gated myocardial perfusion imaging. Eur. J. Nucl. Med. Mol. Imaging **40**, 1163–1170 (2013). doi:10.1007/s12149-014-0875-0
12. A. Bitarafan, H. Rajabi, The effect of filtrating and reconstruction method on the left ventricular ejection fraction derived from GSPET—a statistical comparison of angiography and echocardiography. Ann. Nucl. Med. **22**, 707–713 (2008). doi:10.1007/s12149-008-0161-0
13. A.S. Hambye, A. Vervaet, A. Dobbeleir, Variability of left ventricular ejection fraction and volumes with quantitative gated SPECT: influence of algorithm, pixel size and reconstruction parameters in small and normal-sized hearts. Eur. J. Nucl. Med. Mol. Imaging **31**, 1606–1613 (2004). doi:10.1007/s00259-004-1601-2
14. K. Nakajima, J. Taki, T. Higuchi et al., Gated SPET quantification of small hearts: mathematical simulation and clinical application. Eur. J. Nucl. Med. **27**, 1372–1379 (2000). doi:10.1007/s002590000299
15. S. Matsuo, T. Matsumoto, I. Nakae et al., Prognostic value of ECG-gated thallium-201 single-photon emission tomography in patients with coronary artery disease. Ann. Nucl. Med. **18**, 617–622 (2004). doi:10.1007/BF02984584
16. S. Borges-Neto, A. Javaid, L.K. Shaw et al., Poststress measurements of left ventricular function with gated perfusion SPECT: comparison with resting measurements by using a same-day perfusion function protocol. Radiology **215**, 529–533 (2000). doi:10.1148/radiology.215.2.r00ma13529
17. J. Castell-Conesa, S. Aguadé-Bruix, A. García-Burillo et al., Reproducibility of measurements of left ventricular function with gated myocardial perfusion SPECT and comparison with blood pool radionuclide ventriculography. Rev. Esp. Cardiol. **57**, 931–938 (2004). doi:10.1016/S1885-5857(06)60471-4
18. P. Thavendiranathan, A.D. Grant, T. Negishi, J.C. Plana, Z.B. Popović, T.H. Marwick, Reproducibility of echocardiographic techniques for sequential assessment of left ventricular ejection fraction and volumes: application to patients undergoing cancer chemotherapy. J. Am. Coll. Cardiol. **61**, 77–84 (2013). doi:10.1016/j.jacc.2012.09.035