

The impacts of severe perfusion defects, akinetic/dyskinetic segments, and viable myocardium on the accuracy of volumes and LVEF measured by gated ^{99m}Tc -MIBI SPECT and gated ^{18}F -FDG PET in patients with left ventricular aneurysm: cardiac magnetic resonance imaging as the reference

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Received Apr 1, 2014; accepted Aug 4, 2014

doi:10.1007/s12350-014-9978-1

Background. To compare the accuracy of end-diastolic and end-systolic volumes (EDV, ESV) and LV ejection fraction (LVEF) measured by both GSPECT and GPET, using cardiac magnetic resonance imaging (CMR) as a reference. Furthermore, the impacts of severe perfusion defects, akinetic/dyskinetic segments, and residual viable myocardium on the accuracy of LV functional parameters were investigated.

Methods. Ninety-six consecutive patients with LV aneurysm and LV dysfunction (LVEF $32 \pm 9\%$) diagnosed by CMR were studied with GSPECT and GPET. EDV, ESV, and LVEF were calculated using QGS software.

Results. Correlations of volumes were excellent (r 0.81-0.86) and correlation of LVEF was moderate (r 0.65-0.76) between GSPECT vs CMR and between GPET vs CMR. Compared with CMR, ESV was overestimated by GSPECT ($P < .01$) and underestimated by GPET ($P < .0001$); EDV was underestimated by GPET ($P < .001$); LVEF was underestimated by GSPECT but overestimated by GPET (both $P < .001$). Multivariate regression analysis revealed that the number of segments with severe perfusion defects ($P < .001$) was the only independent factor

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1071-3581/\$34.00

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which was correlated to the EDV difference between GSPECT and CMR, the number of akinetic/dyskinetic segments with absent wall thickening (WT) was the only independent factor which was significantly correlated to the differences of ESV and LVEF measurements between GSPECT vs CMR and between GPET vs CMR ($P < .0001$), respectively. Neither the mismatch score nor the segments with viable myocardium were correlated to the differences of LV volumes and LVEF measurements between different imaging modalities.

Conclusions. In LV aneurysm patients, LV volumes and LVEF measured by both GSPECT and GPET imaging correlated well with those determined by CMR, but should not be interchangeable in individual patients. The accuracy of LVEF measured by GSPECT and GPET was affected by the akinetic/dyskinetic segments with absent WT. (J Nucl Cardiol 2014;21:1230–44.)

Key Words: Aneurysm • gated ^{99m}Tc -sestamibi SPECT • gated ^{18}F -FDG PET • cardiovascular MRI • ejection fraction

INTRODUCTION

Patients with left ventricular (LV) aneurysm usually have severe LV remodeling and LV dysfunction, which may result in a poor prognosis if treated medically only.¹⁻⁴ An accurate assessment of global LV function, myocardial perfusion and viability in patients with LV aneurysm (LVA) is crucial for management and cardiac risk stratification. The clinical value of ^{99m}Tc -sestamibi (MIBI) SPECT and ^{18}F -fluorodeoxyglucose (^{18}F -FDG) PET for assessing myocardial viability in LVA patients has been demonstrated previously.^{4,5} However, at that time, gated acquisition was not routinely performed in both SPECT and PET studies, while LV function was analyzed by echocardiography.

Nowadays, electrocardiography gated myocardial perfusion SPECT (GSPECT) combined with automated quantitative algorithms enables the simultaneous assessment of myocardial perfusion and LV function, and its value has been extensively validated in patients with coronary artery disease (CAD)⁶⁻⁸ and further investigated in patients with myocardial infarction (MI).⁹⁻¹⁴ Although severe perfusion defects (SPD) and akinetic/dyskinetic segments were assumed to affect the accuracy of LV volumes and LV ejection fraction (LVEF) measured by GSPECT, there is no previous investigation systematically demonstrated that these two factors were correlated to the differences of LV volumes and LVEF measurements by GSPECT and the other imaging modalities.⁹⁻¹⁴ Therefore, the value of GSPECT in LVA patients remains to be established.¹⁵ In addition, compared with SPECT imaging modality, PET imaging system has a higher temporal and spatial resolution, and gated acquisition is routinely performed for viability assessment and thus can simultaneously assess LV function. Several earlier studies have demonstrated that the value of gated PET (GPET) analyzing LV function compared with different imaging modalities in patients with CAD.¹⁶⁻²¹ Yet, the value of GPET for assessing LV function in LVA patients compared with cardiac magnetic resonance imaging (CMR) as gold standard remains to be defined. Finally,

it was well known that dysfunctional but viable myocardium often shows preserved uptake of ^{18}F -FDG in perfusion defects, GPET may provide more accurate LV functional parameters compared with that assessed by GSPECT. However, no previous study thoroughly compared the accuracy of LV volumes and LVEF measured by GSPECT and GPET, and little information has become available whether GSPECT and GPET-derived functional parameters are interchangeable.^{22,23}

Therefore, we aimed to compare the accuracy of LV end-diastolic and end-systolic volumes (EDV, ESV) and LVEF from ^{99m}Tc -MIBI GSPECT and ^{18}F -FDG GPET in LVA patients, using CMR as a gold standard. Additionally, we analyzed the impacts of SPD, the residual viable myocardium, and the number of akinetic/dyskinetic segments on the accuracy of LV volumes and LVEF measured by both GSPECT and GPET.

METHODS

Patient Population

Patients with LVA documented by MRI were recruited retrospectively from a study population referred to the Fu Wai Hospital between September 2009 and February 2012 for routinely scheduled myocardial viability assessment with ^{99m}Tc -sestamibi GSPECT rest perfusion imaging and ^{18}F -FDG GPET/CT metabolic imaging, using a 2-day protocol. All patients were examined with CMR within a 2-week period (median 4 days) and they were in a stable state and none of them had any cardiac events or additional therapeutic intervention between PET, SPECT, and CMR examinations. Patients with severe arrhythmia, rheumatic valvular disease, dilated cardiomyopathy, previous LVA resection surgery, metal fragments, and implanted ferromagnetic devices were excluded. Further, patients with impaired SPECT or PET imaging quality (very low activity) were also excluded ($n = 6$). Accordingly, the finally study population consisted of 96 patients (88 males and 8 females; mean age 57 ± 10 years, mean LVEF $32 \pm 9\%$ by CMR). All patients had a history of at least one previous MI. The clinical characteristics are summarized in Table 1. The study protocol

Table 1. Clinical characteristics (n = 96)

Characteristic	Values
Age (years)	57 ± 10
Male gender, n (%)	88 (92)
Coronary risk factors	
Current and previous smokers, n (%)	76 (79)
Hypertension, n (%)	48 (50)
Diabetes, n (%)	27 (28)
Hyperlipidemia, n (%)	62 (65)
New York Heart Association class III-IV, n (%)	20 (21)
Coronary angiography	n = 68
One-vessel disease, n (%)	23 (34)
Two-vessel disease, n (%)	17 (25)
Three-vessel disease, n (%)	28 (41)

Data are number (with percentage in parentheses) or mean ± SD.

was approved by the ethics committee of the Cardiovascular Institute and Fu Wai Hospital.

Gated ^{99m}Tc-Sestamibi SPECT at Rest

Gated SPECT perfusion images were acquired over a 180° arc with a dual-head SPECT system (e.cam, Siemens Medical Systems) equipped with a low-energy, high-resolution, parallel-hole collimator 90-120 minutes after injection of ^{99m}Tc-sestamibi (925 MBq) at rest. GSPECT imaging was performed for 15 minutes with 32 views, at 25 seconds per view, using 64 × 64 matrix size with a zoom factor of 1.45. The cardiac cycle was divided into eight equal intervals with a 20% window centered over the 140 keV photo peak. Gated transaxial images were reconstructed using the Butterworth-filtered back-projection method (order 5; cutoff frequency 0.40) and displayed as short-axis and horizontal and vertical long-axis slices.

Gated ¹⁸F-FDG PET

Myocardial ¹⁸F-FDG images were obtained with a high-spatial-resolution full-ring PET scanner (Truepoint Biography 64, Siemens Healthcare, Knoxville, TN). Patients were studied with the glucose-loading method (25-50 g glucose) or a regular short-acting insulin intravenous injection according to the serum glucose level after an overnight fast.^{4,5} ¹⁸F-FDG 185 MBq (Chinese Atomic Energy Institute, Beijing, China) was administered intravenously; gated images were acquired after 1 hour for 10 minutes (3D mode), dividing the cardiac cycle into eight equal intervals and formatted into a 128 × 128 image matrix and a zoom factor of 2.0 was applied.

Analysis of SPECT and PET Images

Both non-gated and gated, SPECT and PET data sets were transferred to a Siemens e.soft workstation, transaxial SPECT

and PET images were reconstructed using the ordered-subsets expectation maximization (OSEM, 4 iterations, 8 subsets) and displayed as short-axis and horizontal and vertical long-axis slices. Both GSPECT and GPET were reprocessed by one trained observer (Tian CN), unaware of the clinical and CMR data. LV functional parameters, including EDV, ESV, and LVEF, were automatically calculated by using QGS software (version 3.1, Cedars-Sinai Medical Center, Los Angeles, CA, USA), with manual correction in case of inadequate endocardium and epicardium delineation, especially in patients with large severe perfusion defects (20% of the total study population). Regional functional parameters, which including wall motion (WM) and wall thickening (WT), were assessed automatically with the American Heart Association 17-segment model, 6-point scoring system with WM (0 = normokinesis, 1 = mild hypokinesis, 2 = moderate hypokinesis, 3 = severe hypokinesis, 4 = akinesis, and 5 = dyskinesis) and a 4-point scoring system with WT (0-3: from normal to absent WT).²⁴ An akinetic/dyskinetic segment was defined as WM score ≥ 4, or WT score = 3.

Two experienced observers (ZXL, TYQ), unaware of the clinical data and LV functional parameters, visually graded both MIBI and FDG myocardial activity with 5-point score and 17-segment model.²⁴ The segment with the highest perfusion activity was defined as normal, and the relative perfusion and metabolic activity in the residual segments were graded where 0 is normal radiotracer activity, 1 is mildly reduced activity, 2 is moderately reduced activity, 3 is severely reduced activity, and 4 is absence of activity. Severe perfusion defect (SPD) was defined as segments with absence of activity (MIBI score = 4). The mismatch score of the LV was calculated as the summed rest perfusion score minus the summed FDG score, and viability in perfusion defect was defined as a mismatch score of 1.0 or greater.

Cardiac MRI (CMR)

All patients underwent CMR on a 1.5-T system (Magnetom Avanto®, Siemens Medical Systems, Erlangen, Germany), equipped with gradient magnets with a maximum strength of 50 mT·m⁻¹, a maximum slew rate of 200 mT·m⁻¹ ms⁻¹, using an eight-element cardiac phased-array coil. An ECG-triggered, breath-hold steady-state free precession pulse cine sequence was used, with flip angle of 80°, matrix of 256 × 256 (field of view: 350-400 mm) and slice thickness of 8 mm. Each slice was acquired in a separate breath-hold cycle at the end expiration inspiration and 25 frames were acquired per cardiac cycle. All data were transferred to a separate workstation and analyzed by one physician using the commercially available MASS software (version 5.0, Medis Medical Imaging Systems, Leiden, The Netherlands). Endocardial and epicardial borders were outlined automatically with manual correction in case of inadequate anatomic delineation on both the ED and ES frames. The trabeculation and papillary muscles were included as part of LV volumes. LVEF was expressed as a percentage, which was calculated as the stroke volume divided by the EDV.

Statistical Analysis

Data were analyzed using SPSS software (version 17.0, Chicago, IL). Continuous data were expressed as mean value ± SD. Mean values of continuous variables were compared by paired Student's *t* test or by one-way ANOVA analysis. Categorical data were expressed as a percentage and the Chi square test was used. The degree of agreement was tested using the method of Bland-Altman analysis and the Bland-Altman limits were calculated using the mean of the differences ±1.96 SDs of the differences. Intraclass correlation was calculated to assess the strength of agreement between two measurements from different imaging modalities (GSPECT vs CMR, GPET vs CMR, and GSPECT vs GPET). To test the processing variability in GSPECT, GPET, and CMR, all imaging datasets were processed again by the same observer and another experienced observer for evaluation of the intra- and inter-observer reproducibility.

Factors which may correlate to the discrepancies of LV functional parameters between different imaging modalities were analyzed by the linear regression analysis. Only variables with a statistically significant association with the correlation by univariate analysis were included in the multivariate analysis, which was created by a stepwise method. Statistical significance was defined as two-sided if a *P* value <.05.

RESULTS

Mean EDV, ESV, and LVEF

Mean values of EDV, ESV, and LVEF from GSPECT, GPET, and CMR are presented in Table 2. Compared with CMR, ESV was overestimated (*P* < .01) by GSPECT, EDV and ESV were underestimated by GPET (*P* < .001), while LVEF was underestimated by GSPECT (*P* < .001) and overestimated by GPET (*P* < .001).

Correlation and Regression Analysis of GSPECT Vs CMR, GPET Vs CMR, and GSPECT Vs GPET

Table 3 listed the correlation and regression analysis results. Between GSPECT and CMR, correlations of EDV (*P* < .001) and ESV (*P* < .0001) were excellent, and correlation of LVEF (*P* < .001) was good. Compared with CMR, EDV (*r* = 0.28, *P* < .01) and

ESV (*r* = 0.34, *P* = 0.001) assessed by GSPECT showed a higher trend with increasing magnitude of LV volumes. The bias in EF measurement was independent of EF magnitude (*P* > 0.05) (Figure 3 in Appendix).

Correlations of EDV (*P* < .001) and ESV (*P* < .001) were excellent and correlation of LVEF (*P* < .001) was good between GPET and CMR. Compared with CMR, no significant trend was found for estimation of EDV and ESV by GPET with increasing magnitude of LV volumes (*P* > 0.05). The Bland-Altman plot displayed a trend to overestimation of LVEF by GPET increasingly with higher LVEF (*r* = 0.26, *P* = 0.01) (Figure 4 in Appendix).

Correlations of EDV (*P* < .001) and ESV (*P* < .001) between GSPECT and GPET were excellent. Compared with GSPECT, with increasing of LV volumes, GPET showed a trend toward lower EDV (*r* = -0.36, *P* < .001) and lower ESV (*r* = -0.29, *P* < .01), respectively. Correlation of LVEF between GPET and GSPECT was good (*P* < .001). The overestimated measurement of LVEF by GPET was dependent on EF magnitude (*r* = 0.40, *P* < .001) (Figure 5 in Appendix).

Influence of SPD on the Discrepancies Between GSPECT and GPET

Patients were divided into three subgroups according to the number of segments with SPD. Group 1 (*n* = 18, 19%): ≤2 segments; Group 2 (*n* = 30, 31%): 3-4 segments (Figure 1); Group 3 (*n* = 48, 50%): ≥5 segments (Figure 2). Mean values of LV volumes and LVEF are presented in Table 4. The correlation of LVEF between GSPECT and GPET was fair in Groups 2 and 3 (*P* < .0001). In comparison with those values measured by CMR: (1) In Group 1, both EDV (*P* < .005) and ESV (*P* < .05) were mildly underestimated by GSPECT, and LVEF was overestimated by GPET (*P* < .05); (2) in Group 2, LV volumes were underestimated by GPET (*P* < .05). LVEF was slightly underestimated by GSPECT (*P* < .05) and overestimated by GPET (*P* < .05); (3) In Group 3, LV volumes were severely overestimated by GSPECT (*P* < .0001) and underestimated by GPET (*P* < .0001). LVEF was

Table 2. Mean values of EDV, ESV, and LVEF by GSPECT, GPET, and CMR

	CMR	GSPECT	GPET
EDV (mL)	193 ± 63 (71-379)	197 ± 73 (70-380)	177 ± 60 (81-360)***
ESV (mL)	135 ± 56 (43-294)	144 ± 66 (41-327)**	120 ± 57 (46-307)***
LVEF (%)	32 ± 9 (12-54)	29 ± 9 (11-49)*	35 ± 11 (11-59)***

P* < .001 vs CMR; *P* < .001 vs GSPECT; ****P* < .01 vs CMR.

Table 3. Intraclass correlation coefficient, mean bias, SEE, and 95% limits of agreement for regression analysis between different imaging modalities

	GSPECT vs CMR			GPET vs CMR			GPET vs GSPECT		
	EDV (mL)	ESV (mL)	LVEF (%)	EDV (mL)	ESV (mL)	LVEF (%)	EDV (mL)	ESV (mL)	LVEF (%)
Intraclass correlation	0.86	0.86	0.68	0.84	0.86	0.75	0.82	0.81	0.65
Mean bias	4	10	-3	-16	-14	3	-20	-24	6
SEE	36	33	8	35	30	7	41	40	9
95% limits of agreement	-67 to 75	-51 to 71	-17 to 10	-78 to 46	-67 to 38	-11 to 16	-90 to 50	-86 to 37	-7 to 19
P value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

severely underestimated by GSPECT ($P < .0001$). The difference of EDV between GSPECT and GPET in Group 3 was greater than that in Groups 2 ($P < .001$) and 1 ($P < .0001$). And the difference of ESV between GSPECT and GPET in Group 3 was greater than that in Groups 2 ($P < .01$) and 1 ($P < .0001$). However, no such difference was observed for LVEF measurement ($P > 0.05$).

Influence of Residual Myocardial Viability on the Discrepancies Between GSPECT and GPET

Patients were grouped into three subgroups according to the number of segments with viable myocardium. Group A (n = 22): ≤ 1 viable segment; Group B (n = 27): 2-3 viable segments; and Group C (n = 47): ≥ 4 viable segments. Mean values of LV volumes and LVEF are presented in Table 5. The correlations of LV volumes measurement between GSPECT and GPET were good in all the subgroups while the correlation of LVEF measurement was fair ($P < .0001$). In Group A, LVEF from GSPECT had no significant difference with that from CMR, but it was overestimated by GPET ($P < .05$). In Group B, mean LVEF measured by GPET was similar with that by CMR, whereas LVEF assessed by GSPECT was lower than that by CMR ($P < .001$). Further, in Group C, compared with CMR, LVEF was underestimated by GSPECT ($P < .001$) while overestimated by GPET ($P < .01$). In subgroups with different extent of residual viable myocardium, no significant difference was found for the biases of EDV, ESV, and LVEF measurements between GSPECT and GPET ($P > 0.05$).

Univariate and Multivariate Regression Analysis

Variables correlated with the differences of LV volumes and EF measurements are illustrated in Table 6. Univariate regression analysis showed that many factors were correlated to the differences of LV volumes and LVEF measurements between GSPECT and CMR, and few were correlated to the differences of LV functional parameters between GPET and CMR. Moreover, multivariate regression analysis identified (1) SPD ($P < .001$) was the only independent factor which was correlated to the differences of EDV measurement between GSPECT and CMR, and absent MIBI WT ($P < .001$) was the only independent factor which was correlated to the differences of ESV and LVEF measurements between GSPECT and CMR; (2) absent FDG WT was the only independent factor which was correlated to the differences of ESV and LVEF measurements

between GPET and CMR ($P < .001$). In surprise, neither the mismatch score nor the number of segments with myocardial viability was proved to be statistically significant correlated to differences of LV volumes and LVEF measurements between different imaging modalities (GSPECT vs CMR, GPET vs CMR, and GSPECT vs GPET) ($P > 0.05$).

Reproducibility

As shown in Table 7, both intra- and inter-observer comparisons of repeated measurements of EDV, ESV, and LVEF revealed significant correlations in GSPECT, GPET, and CMR (all $P < 0.001$), indicating excellent reproducibility.

DISCUSSION

The main findings were as follows: (1) In LVA patients, LV volumes and LVEF measured by both GSPECT and GPET correlated well with those determined by CMR over a wide range, while GSPECT and GPET-derived functional parameters do not appear to be interchangeable in individual patients; (2) the number of

segments with SPD was the only independent factor which was correlated to the EDV difference between GSPECT and CMR. The number of akinetic/dyskinetic segments with absent wall thickening (WT) was the only independent factor which was significantly correlated to the differences of ESV and LVEF measurements between GSPECT vs CMR, and between GPET vs CMR, respectively. (3) In patients with small extent of SPD or without viable myocardium, LVEF by GSPECT was more accurate. In patients with large extent of SPD or moderate extent of viable myocardium, LVEF by GPET was more reliable. In patients with moderate extent of SPD or with large extent of viable myocardium, LVEF was underestimated by GSPECT and overestimated by GPET.

LV Volumes and LVEF by GSPECT, Compared with CMR

The value of GSPECT in LVA patients remains to be established.¹⁵ In addition, both SPD and akinetic/dyskinetic segments were assumed to affect the accuracy of LV volumes and LVEF measured by GSPECT. However, it has not been systematically proved, as the populations studied were not homogeneous.^{9-15,25} Chua

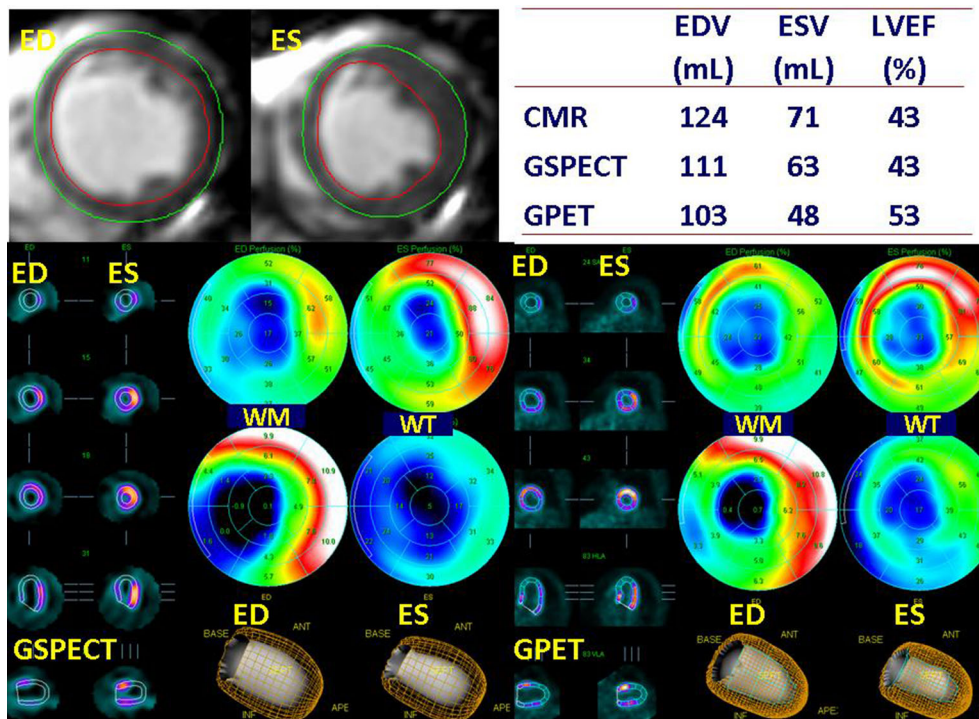


Figure 1. A 75-year-old man with history of anterior MI. Gated SPECT perfusion imaging revealed a moderate extent of severe perfusion defect and LV aneurysm involved the LV apex. The LV functional parameters from GSPECT, GPET, and CMR were displayed (upper panel).

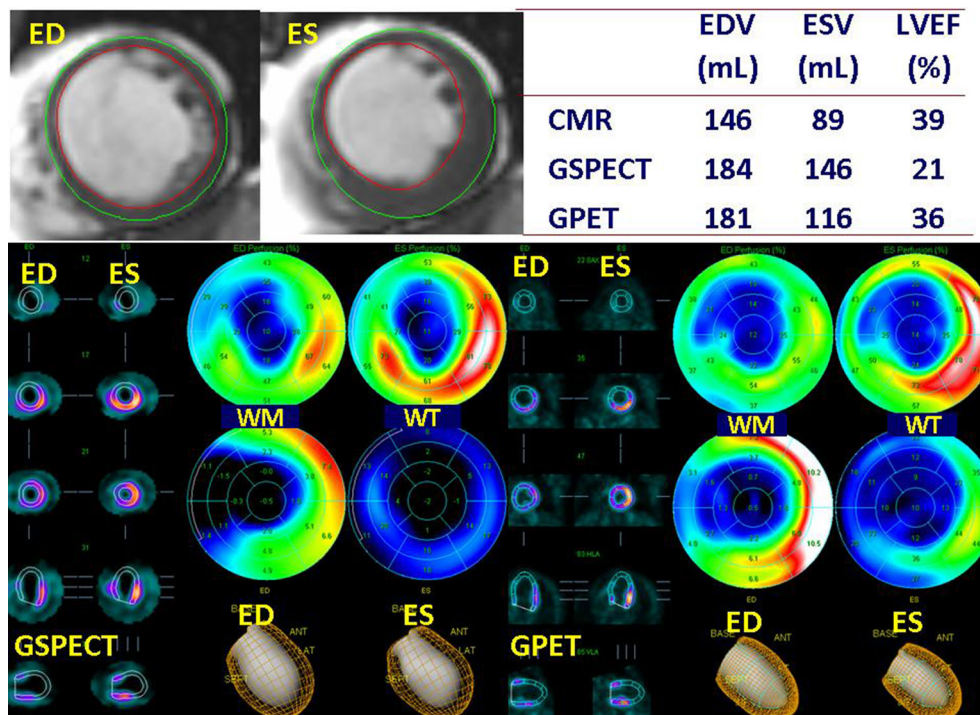


Figure 2. A 59-year-old man had a history of anterior MI. Gated SPECT perfusion imaging revealed a large extent of severe perfusion defect and LV aneurysm involved the LV apex and extended into the anterior wall. The LV functional parameters from GSPECT, GPET, and CMR were presented.

Table 4. Comparisons of LV volumes and LVEF between GPET and GSPECT in patients with different extent of severe perfusion defects

Groups	n		CMR	GSPECT	GPET	r	D	P value
Group 1	18	EDV (mL)	176 ± 64	156 ± 54*	164 ± 58	0.95	8 ± 16	<0.05
		ESV (mL)	120 ± 56	108 ± 48**	109 ± 56	0.95	1 ± 16	> 0.05
		LVEF (%)	34 ± 10	33 ± 9	37 ± 13**	0.79	5 ± 6	<0.01
Group 2	30	EDV (mL)	187 ± 67	185 ± 64	176 ± 62**	0.91	-9 ± 25	> 0.05
		ESV (mL)	127 ± 58	132 ± 61	115 ± 59**	0.87	-17 ± 26	<0.01
		LVEF (%)	34 ± 8	31 ± 9**	37 ± 10**	0.55	7 ± 7	<0.0001
Group 3	48	EDV (mL)	203 ± 60	220 ± 77***	183 ± 84***	0.75	-36 ± 41	<0.001
		ESV (mL)	144 ± 55	166 ± 69***	128 ± 67***	0.74	-35 ± 32	<0.001
		LVEF (%)	30 ± 10	26 ± 8***	32 ± 11	0.63	5 ± 5	<0.0001

r, Intraclass correlation coefficient; D, difference between GPET and GSPECT; P value, between GPET and GSPECT.
*P < 0.01 vs CMR; **P < 0.05 vs CMR; ***P < .001 vs CMR.

et al¹⁰ found that LVEF did not differ between GSPECT and radionuclide ventriculography in patients with larger MI. Manrique et al⁹ reported that underestimation of LVEF by GSPECT was not correlated to the size and severity of perfusion defects, and dyskinesia segments.

Similarly, Bax et al¹¹ revealed that in patients with ischemic cardiomyopathy, the underestimation of LV volumes by GSPECT was not correlated to the number of akinetic/dyskinetic segments, nor to the number of segments with SPD.

Table 5. Comparisons of LV volumes and LVEF between GPET and GSPECT in patients with different extent of residual viable myocardium

Groups	n		CMR	GSPECT	GPET	r	D	P value
Group A	22	EDV (mL)	191 ± 68	198 ± 77	186 ± 66	0.85	-12 ± 39	>0.05
		ESV (mL)	139 ± 65	147 ± 73	131 ± 65	0.86	-16 ± 34	<0.05
		LVEF (%)	29 ± 11	28 ± 10	32 ± 11*	0.75	4 ± 7	<0.05
Group B	27	EDV (mL)	200 ± 62	200 ± 74	177 ± 65**	0.84	-23 ± 34	<0.01
		ESV (mL)	136 ± 51	144 ± 61	119 ± 55***	0.82	-25 ± 27	<0.0001
		LVEF (%)	33 ± 8	29 ± 7***	34 ± 10	0.62	5 ± 6	<0.0001
Group C	47	EDV (mL)	199 ± 62	195 ± 72	173 ± 55**	0.80	-22 ± 35	<0.0001
		ESV (mL)	131 ± 55	143 ± 68***	116 ± 55**	0.78	-28 ± 33	<0.0001
		LVEF (%)	33 ± 10	29 ± 9***	36 ± 12***	0.63	7 ± 7	<0.0001

r, Intraclass correlation coefficient; D, differences between GPET and GSPECT; P value, between GPET and GSPECT. *P < .05 vs CMR; **P < .0001 vs CMR; ***P < .01 vs CMR.

To our best knowledge, in current study, we recruited a largest group of LVA patients with LV dysfunction, who had SPD and akinetic/dyskinetic segments. We found that measurements of LV volumes and LVEF were correlated well between GSPECT and CMR over a wide range. Further, LVEF was underestimated by GSPECT, which was consistent with earlier studies in CAD patients.^{10-15,26} The 95% of agreement limits were wide, but it was similar with a meta-analysis in CAD patients.^{27,28} In contrast to prior investigations,⁹⁻¹¹ we found that the number of segments with SPD was positively correlated to the overestimation of EDV by GSPECT, and the number of akinetic/dyskinetic segments was the only independent factor which was positively correlated to the overestimation of ESV and negatively correlated to underestimation of LVEF measurement by GSPECT. This denoted that the larger extent of SPD, the less reliable was the endocardial surface detection and EDV measurement by GSPECT, and more partial volume effects on the overestimation of ESV than EDV, and finally induced underestimation of LVEF. Further, in patients with small extent of SPD, LVEF did not differ between GSPECT and CMR, which was consistent with an earlier study.¹⁰ In patients with large extent of SPD, LV volumes were overestimated and LVEF was underestimated, which was in agreement with the study reported by Manrique et al.⁹

There are other factors which may influence LV function assessment by GSPECT, such as (1) outflow tract tissue, papillary, and trabecular muscle were included as LV volumes by CMR algorithm, and the border tracing by CMR encompasses the membranous part of the septum, while not in GSPECT. CMR should therefore indicate larger volumes; (2) the lower temporal resolution of GSPECT compared with CMR may induce

the lower LVEF.⁶ However, the differences in temporal resolution are more relevant in ventricles with good LV function than in dysfunctional enlarged ventricles. Our study with LVA patients in a small group (n = 16) revealed that mean values of EDV (186 ± 79 vs 188 ± 82 mL), ESV (136 ± 71 vs 135 ± 71 mL), and LVEF (29 ± 8% vs 31 ± 8%) did not differ (P > 0.05) between 8 vs 16 frames/cycle. It implied that the lower temporal resolution did not have much influence on the LV volumes and LVEF measurements by GSPECT in LVA patients with severe LV dysfunction; (3) LV volume measurements were affected by the reconstruction parameters, the higher cutoff value, LV volumes were more overestimated by GSPECT, but not much influence on LVEF.

LV Volumes and LVEF by GPET, Compared with CMR

Previous studies have demonstrated ¹⁸F-FDG GPET could accurately determine LV volumes and LVEF in CAD patients.¹⁶⁻²¹ But it is not well established its value of assessing LV function in patients with severe FDG defects.²⁰ Our current study with LVA patients showed that correlations of LV volumes calculated by GPET and CMR were excellent, and the correlation of LVEF was good, but LV volumes were underestimated and LVEF was overestimated by GPET. These results were in line with earlier studies in CAD patients,¹⁶⁻²¹ which did not find any correlation between underestimation of volumes by GPET with FDG defects and akinetic/dyskinetic segments. Yet, our results revealed that the number of akinetic/dyskinetic segments analyzed by absent FDG WT was the only independent predictor which was positively correlated with the underestimation of ESV and

Table 6. Variables correlated with the differences of LV volumes and EF measurements between different imaging modalities by univariate and multivariate regression analysis

	GSPECT vs CMR				GPET vs CMR			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	ΔEDV	ΔESV	ΔLVEF	ΔEDV	ΔESV	ΔLVEF	ΔEDV	ΔESV
Scar segments	0.34 *	0.29 *						
SPD	0.48 **	0.47 **		0.48 **				
Akinetic/dyskinetic segments by WM _{MIBI}	0.32 *	0.42 **	-0.29 *					
Akinetic/dyskinetic segments by WT _{MIBI}	0.42 **	0.54 **	-0.36 **	0.54 **				
Akinetic/dyskinetic segments by WM _{FDG}								
Akinetic/dyskinetic segments by WT _{FDG}							0.35 **	-0.53 **

SPD, Severe perfusion defects with MIBI score = 4; WM, wall motion; WT, wall thickening.
*P < .005; **P < .0001.

negatively correlated with the overestimation of LVEF by GPET. In other words, the larger extent of myocardium with absent WT, the less underestimation of ESV and thus, the less overestimation of LVEF was measured by GPET. Some other factors which may affect LV function assessment by GPET were similar as described in GSPECT perfusion imaging.

Effects of Residual Viable Myocardium on the Accuracy of LV Volumes and EF Measured by GSPECT and GPET

It was well known that dysfunctional but viable myocardium often shows preserved uptake of ¹⁸F-FDG in perfusion defects,^{4,5} in this kind of cases, it was assumed that exact delineation of endo- and epicardial contours by GPET may provide more accurate LV functional parameters compared with that assessed by GSPECT. However, no previous study systemically compared the accuracy of LV volumes and LVEF measured by GSPECT and GPET, and little information has become available on the differences of LV volumes and LVEF between GSPECT and GPET.^{22,23} In our current study, we found that the correlations of LV volumes measurements between GSPECT and GPET were excellent and correlation of LVEF was fair, but the Bland-Altman limits were wider. Therefore, on individual patient’s level, GSPECT and GPET-derived functional parameters (especially LV volumes) should not be interchangeable. Further, it was appreciated that the number of segments with SPD was correlated to overestimation of volumes by GSPECT, compared with that by GPET (Table 8 in Appendix). Notably, we found that the number of segments with absent FDG WT was the only independent factor, which was positively correlated to the LVEF differences between GSPECT and GPET (Table 8 in Appendix). It indicated that the more extent of akinetic/dyskinetic segments revealed by absent FDG WT, the more consistent of LVEF value measured by GSPECT and GPET. These findings were different from that in previous studies.^{22,23} Kanayama et al²³ found that LVEF did not differ between gated ¹³N-NH₃ PET and ^{99m}Tc-MIBI SPECT in CAD patients, and the extent of perfusion defects had no influence on the underestimation of LV volumes determined by GPET, compared with that measured by GSPECT.

Conversely, it was somehow surprising to observe that the extent and severity of hibernation myocardium was not correlated to the differences of LV functional parameters between GSPECT and GPET. Further subgroup analysis showed that in patients without or with a small extent of viable myocardium, LVEF measured by GSPECT was more reliable while overestimated by

Table 7. The reproducibility of LV parameters measured by GSPECT, GPET and CMR

	GPET			GSPECT			CMR		
	EDV (mL)	ESV (mL)	LVEF (%)	EDV (mL)	ESV (mL)	LVEF (%)	EDV (mL)	ESV (mL)	LVEF (%)
Inter-observer	0.96	0.98	0.93	0.94	0.97	0.89	0.98	0.98	0.98
Intra-observer	0.97	0.99	0.94	0.95	0.98	0.95	0.99	0.99	0.99

Significant correlations (*r*) between the repeated measurements revealed excellent reproducibility (all *P* < .001).

GPET, and in patients with moderate extent of viable myocardium, LVEF measured by GPET was more accurate while underestimated by GSPECT. Finally, in patients with large amount of viable myocardium, LVEF was underestimated by GSPECT and overestimated by GPET. The exact reason is not very clear. In current study, myocardial perfusion was performed by ^{99m}Tc-MIBI SPECT without attenuation correction rather by PET perfusion with N-13 ammonia or Rb-82, thus the extent and severity of hibernation myocardium could be overestimated, especially in inferior and posterior wall with mild reduced perfusion activity. But if these segments with normal regional function, they were regarded as normal myocardium. Further, it would be possible, only in patients with large extent of SPD, the differences of LV volumes measured by GSPECT and GPET were correlated to the extent of viable myocardium. However, no any trend was found even if we clarified patients into four subgroups according to the extent of SPD and extent of viable myocardium together.

Study Limitations

Our study had some limitations. Drug treatment and patient’s pathophysiological changes may have affected current observations, due to the time interval between radionuclide imaging and CMR examinations. Yet, 85% of patients were performed within 7 days, which should have widely excluded effects of confounding factors on measurements of LV function with different imaging modalities.

In conclusions, in LVA patients, LV volumes and LVEF measured by both GSPECT and GPET imaging correlated well with those determined by CMR, while the accuracy of EDV measurement by GSPECT was affected by SPD, and the accuracy of ESV and LVEF

measurements by both GSPECT and GPET was affected by the extent of akinetic/dyskinetic segments with absent WT.

NEW KNOWLEDGE GAINED

This study revealed that in routine clinical practice for viability assessment, GSPECT and GPET-derived functional parameters could not be used interchangeably on individual’s patient level, even though each has its own advantages. In patients with small extent of SPD or without viable myocardium, LVEF by GSPECT was more reliable. In patients with large extent of SPD or moderate extent of viable myocardium, LVEF by GPET was more accurate. In patients with moderate extent of SPD or with large extent of viable myocardium, LVEF was underestimated by GSPECT and overestimated by GPET.

Acknowledgments

This work was supported by the Natural Science Foundation of China (8107177 and 81130029), PUMC Youth Fund and the Fundamental Research Funds for the Central Universities (3332013105) and by a Research Grant, from Ministry of Education of the People’s Republic of China.

Disclosure

We do not have any relationship with industry and financial associations from within the past 2 years that might pose a conflict of interest in connection with the submitted article.

APPENDIX

See Figures 3, 4, and 5 and Table 8.

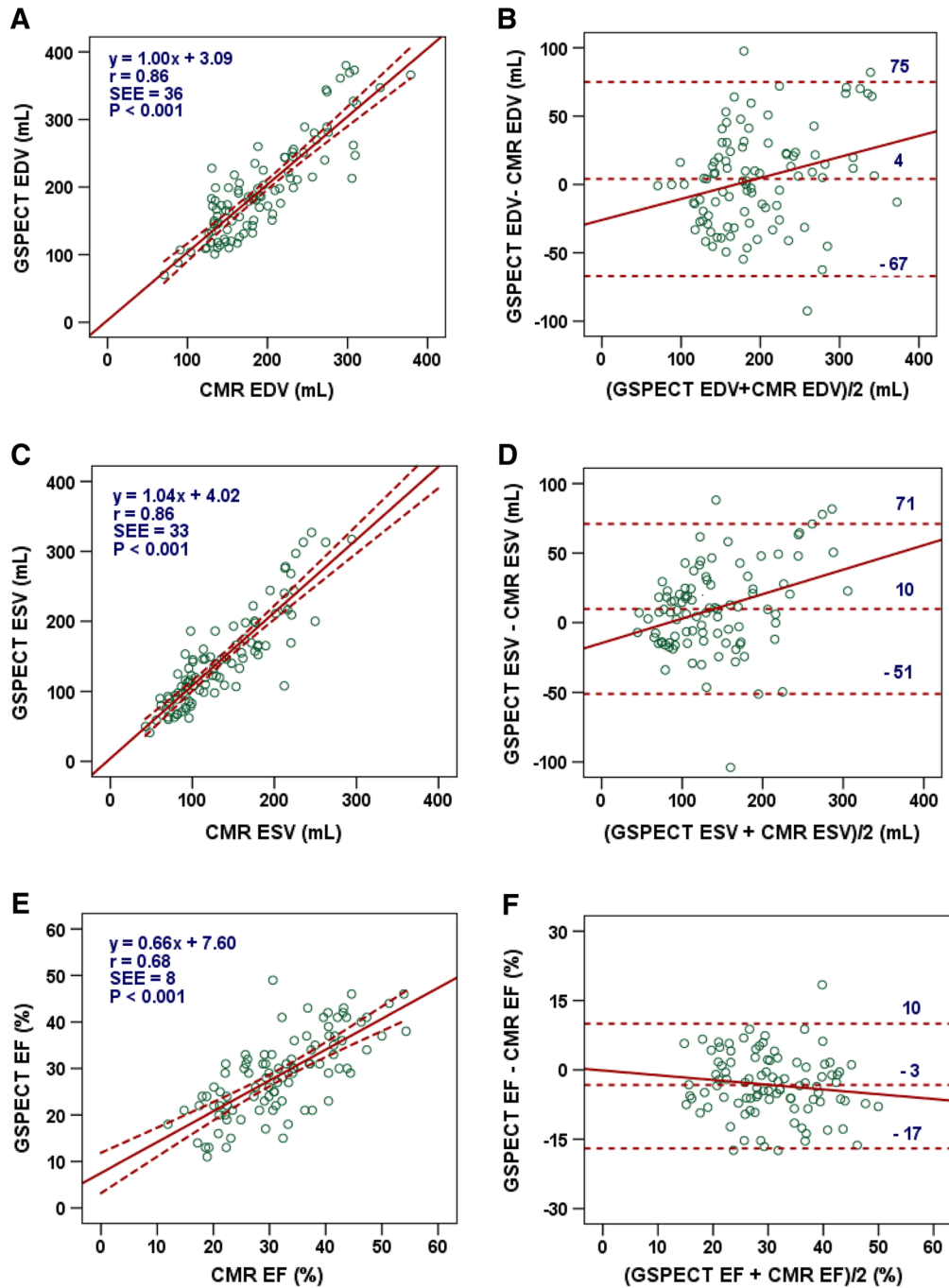


Figure 3. Correlation analysis and Bland-Altman plots of EDV (A, B), ESV (C, D), and EF (E, F) from GSPECT and CMR.

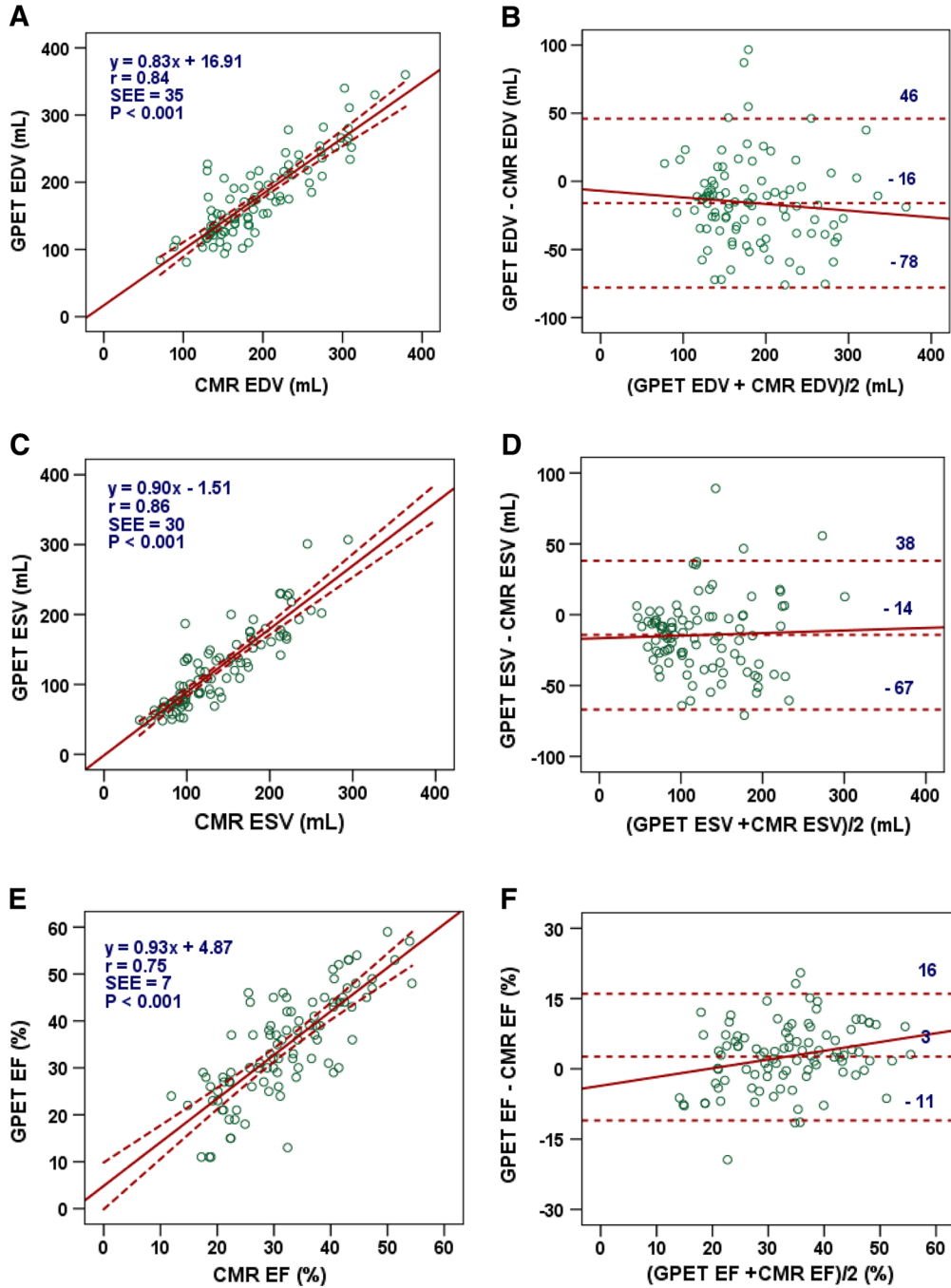


Figure 4. Correlation analysis and Bland-Altman plots of EDV (A, B), ESV (C, D), and EF (E, F) from GPET and CMR.

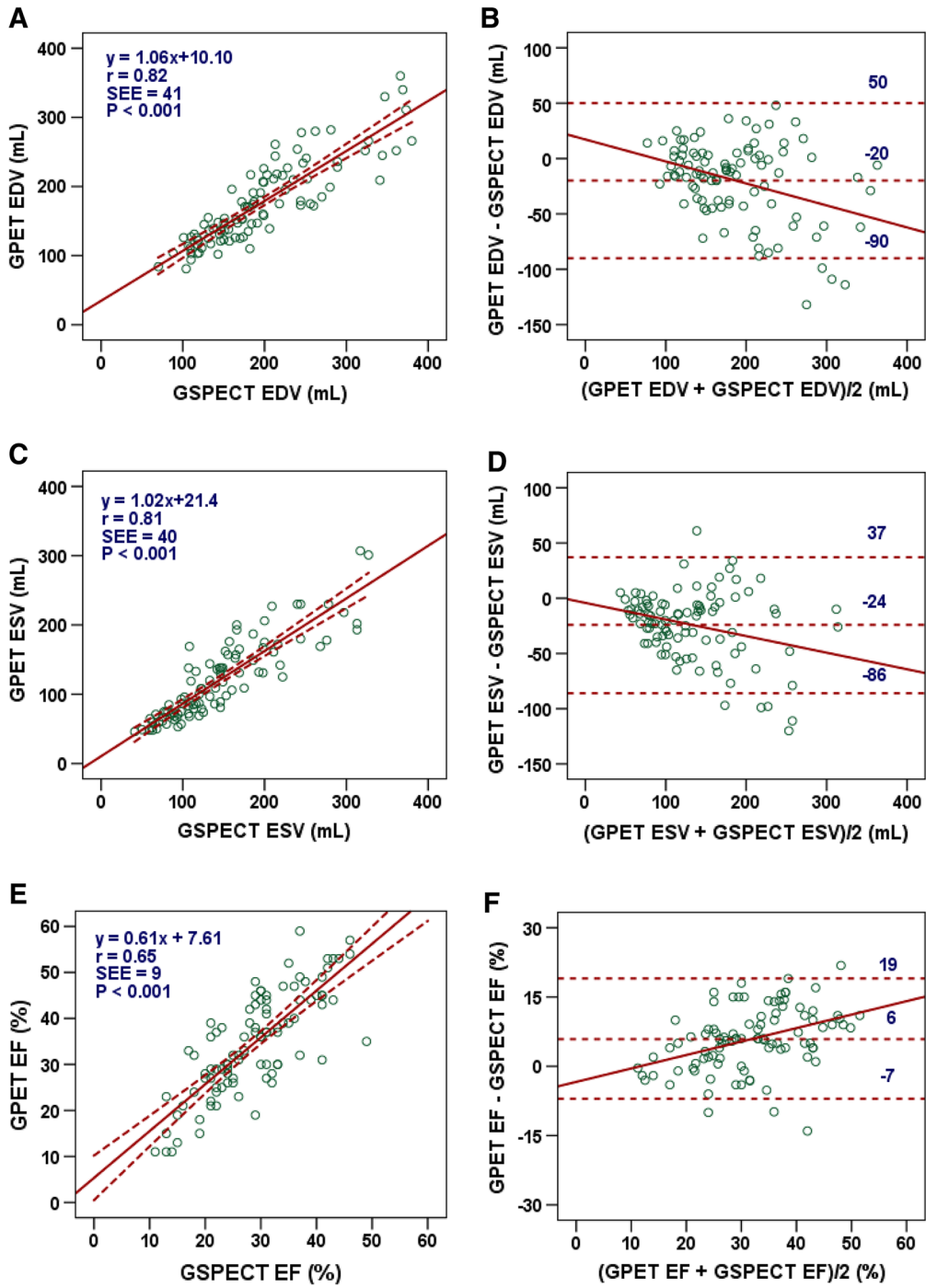


Figure 5. Correlation analysis and Bland-Altman plots of EDV (A, B), ESV (C, D), and EF (E, F) from GSPECT and GPET.

Table 8. Variables correlated with the differences of LV volumes and EF measurements between different GSPECT and GPET by univariate and multivariate regression analysis

	GSPECT vs GPET					
	Univariate analysis			Multivariate analysis		
	ΔEDV	ΔESV	ΔLVEF	ΔEDV	ΔESV	ΔLVEF
Scar segments	0.42*	0.40*				
SPD	0.61*	0.60*		0.61*	0.49*	
Akinetic/dyskinetic segments by WM _{MIBI}	0.37*	0.42*				
Akinetic/dyskinetic segments by WT _{MIBI}	0.39*	0.47*				
Segments with FDG score = 4	0.52*	0.54*				
Akinetic/dyskinetic segments by WM _{FDG}	0.29**		0.36*			
Akinetic/dyskinetic segments by WT _{FDG}			0.48*			0.48*

SPD, Severe perfusion defects with MIBI score = 4; WM, wall motion; WT, wall thickening.
P* < 0.0001; *P* < 0.005.

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