



# Left ventricular ejection fraction, end-systolic and end-diastolic volume values in female with normal gated myocardial perfusion spect: The comparison with 4DM-SPECT and Siemens Icon®-QGS

## Normal gated miyokardiyal perfüzyon spect'e sahip kadın hastalarda sol ventrikül ejeksiyon fraksiyonu ve volüm değerleri: 4DM-SPECT ve Siemens Icon®-QGS ile karşılaştırma

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### Abstract

**Introduction:** Gated myocardial perfusion SPECT (g-MPS) is an important method in the diagnosis of coronary artery disease (CAD). Left ventricular ejection fraction (LVEF), end-systolic volume (ESV) and end-diastolic volume (EDV) are required parameters for evaluation of cardiac performance. Our aim is to compare LVEF and volume values and to determine normal limits in patients with normal myocardial perfusion using two (4D-MSPECT ve SIEMENS ICON® QGS) computer software programs.

**Methods:** One hundred nine females were included study with the suspicion of CAD but their g-MPS was reported as normal between October 2004 and February 2007. Single day rest-stress g-MPS protocol was applied. Modified Bruce protocol was done for effort test with treadmill performance or dobutamine injection for pharmacological effort. Reconstruction was performed via Butterworth filtration without attenuation correction. LVEF, ESV and EDV were calculated.

**Results:** The mean rest (REF) and stress (SEF) ejection fraction values between 4DM and QGS algorithms had significant differences statistically ( $\Delta$ REF[4DM-QGS]=9.5;  $\Delta$ SEF[4DM-QGS]=8.9;  $p<0.05$ ). Wide Blandt Alman limits (BAL) were detected among the results (BAL: [4DM-REF]-[QGS-REF]=26.4-(-7.8),  $R=0.61$   $p<0.05$ ; 4DM-SEF-QGS-SEF: 27.7-(-10.1),  $R=0.54$ ;  $p=0.000$ ). Significant differences ( $p<0.05$ ) were found beside the strong correlation coefficient values ( $r=0.81-0.93$ ) in the volumes.

**Discussion and Conclusion:** There were significant differences in the averages between the two g-MPS software program in LVEF and volume values so they should not be used in place of each other at the follow-up of patients.

**Keywords:** End diastolic volume; end systolic volume; gated myocardial perfusion SPECT; left ventricle ejection fraction; QGS; 4DM.

### Özet

**Amaç:** Koroner arter hastalığı (KAH) teşhisinde gated miyokard perfüzyon SPECT (g-MPS) sık kullanılan bir yöntemdir. Kardiak performansın değerlendirmesinde sol ventrikül ejeksiyon fraksiyonu (SVEF), sistol ve diastol sonu volüm en önemli parametrelerdir. Amacımız sol ventrikül ejeksiyon fraksiyonu ve volüm değerlerini normal miyokardiyal perfüzyon ve fonksiyona sahip kadın hastalarda iki g-MPS bilgisayar yazılım programı (4D-MSPECT ve SIEMENS ICON® QGS) ile karşılaştırarak normal sınırlarını belirlemektir.

**Gereç ve Yöntem:** Çalışmaya KAH şüphesi nedeniyle Ekim 2004-Şubat 2007 tarihleri arasında g-MPS uygulanmış ve sonuçları normal raporlanmış 109 kadın (54±10 yıl) hasta alındı. Tc-99m MIBI kullanılarak tek gün rest-stres g-MPS protokolü uygulandı. Modifiye Bruce protokolü ile hastalara treadmillde veya dobutamin ile efor testi yapıldı. Atenüasyon düzeltmesi yapılmadan "butterworth filtresi" aracılığıyla, rekonstrüksiyon yapıldı. 4DM ve QGS algoritmeleri yardımıyla sol ventrikül % EF, end diastolik volüm (EDV; ml), end sistolik volüm (ESV; ml) değerleri hesaplandı.

**Bulgular:** 4DM ve QGS algoritmeleri arasında ortalama rest ve stres EF değerlerinde tüm hastalarda anlamlı düzeyde ( $\Delta$ REF % [4DM-QGS]=9.5;  $\Delta$ SEF [4DM-QGS]=8.9;  $p<0.05$ ) fark bulundu. Sonuçlar arasında geniş Blandt Alman limitleri (BAL) (BAL: [4DM-REF]-[QGS-REF]=26.4-(-7.8),  $R=0.61$   $p<0.05$ ; 4DM-SEF-QGS-SEF: 27.7-(-10.1),  $R=0.54$ ;  $P=0.000$ ) saptandı. Volüm ölçümlerinde güçlü korelasyon katsayı değerleri ( $r=0.81-0.93$ ) yanında anlamlı farklılıklar ( $p<0.05$ ) saptandı.

**Sonuç:** İki g-MPS yazılım programı arasında, SVEF ve hacim ölçümünde, takipte birbirinin yerine kullanımı sınırlandıran ortalamalar arası anlamlı derecede farklar saptanmıştır ( $p<0.05$ ). Takiplerin, başlangıçta kullanılan yazılım programı ile yapılması daha uygundur.

**Anahtar Sözcükler:** Diastol sonu volüm; sol ventrikül sistol sonu; gated miyokardiyal perfüzyon SPECT; sol ventrikül ejeksiyon fraksiyonu; QGS; 4DM.



Knowledge of left ventricular ejection fraction (LVEF), end systolic volume (ESV) and end diastolic volume (EDV) is the most important parameters in the measurement of cardiac performance with a prognostic value. LVEF, ESV and EDV can be calculated with many invasive and non-invasive methods currently. These methods include contrast enhanced ventriculography,<sup>[1-3]</sup> two dimensional echocardiography,<sup>[4,5]</sup> magnetic resonance imaging,<sup>[6,7]</sup> radionuclide angiography either with stabilization or first pass method, multi-gated radionuclide ventriculography,<sup>[8]</sup> gated Fluor 18 Fluorodeoxyglucose Positron Emission Tomography and g-MPS.<sup>[9-12]</sup> G-MPS has become a routine choice in myocardial perfusion studies in nuclear cardiology because of capacity of cardiac perfusion measurement as well as evaluation of left ventricular function. Our aim is to compare LVEF and volume values with two gated SPECT computer software program (4D-MSPECT vs SIEMENS ICON® QGS) in female patients with normal myocardial perfusion and determine their normal limits.

## Material and Method

One hundred nine females (mean age 54±10) were included in the study with the suspicion of CAD but whose g-MPS was reported as normal between October 2004 and February 2007. Patients with cardiac disease, breast attenuation, left bundle branch block in electrocardiography, marked ischemia, left ventricular overload pattern, Q wave or QS pattern, prominent arrhythmia at rest, typical chest pain during exercise were excluded. All patients were questioned regarding CAD risk factors. Drugs used by patients (β-blocker and calcium antagonists before 48 hours, the nitrate group before 4 hours) were stopped and all patients fasted 4 hours before work.

### Tc-99m MIBI myocardial perfusion scintigraphy

Tc-99m MIBI (296 MBq [8 mCi]) injection was performed according to one-day rest-stress MIBI protocol to all the patients. Resting gated SPECT imaging was performed 45–90 minutes after the injection. Three hours after injection, exercise test was done in 100 patients via the treadmill by using modified Bruce protocol and 9 patients by dobutamine injection for pharmacological effort. When the target heart rate was reached, the exercise or pharmacological stress was continued for at least 1 minute following the 888 MBq (24 mCi) Tc-99m MIBI injection and the test was terminated. 30–60 minutes after the administration of the myocardial perfusion agent, SPECT imaging was instructed.<sup>[13]</sup>

### Gated SPECT

A double-headed gamma camera (SIEMENS ECAM®) was used for myocardial perfusion scintigraphic studies. G-MPS operation was performed under low energy, high resolution parallel hole collimator, from 45° right antero oblique to 45° left postero oblique position. 50% window spacing R-R distance was divided into 8 equal intervals in the supine position. The images were gathered in 64×64 matrix, with counterclockwise position (64 images) in 25 second intervals when detectors

were at an angle of 90° with each other within the 1.45 magnification factor. Reconstruction was performed with filtered back projection method using Butterworth filter (order: 5.0; cut off: 0.50 cycle/pixel) without attenuation arrangement. Oblique-transverse (short axis), sagittal and coronal sections were taken. Transaxial images were evaluated for LVEF and volumes using two software programs (fully automated QGS and semi-automatic 4D-MSPECT).

### Statistical method

The normal distribution of the data was evaluated by Kolmogorov-Smirnov or Shapiro-Wilk tests. Pearson correlation analysis for normal distribution-matched data and Spearman rank correlation analysis for non-normal distribution data were performed. Linear regression analysis was used to determine the linear relationship between the values measured in QGS and the values measured in 4DM and Bland Altman analysis was used to show the consistency between the two methods was used. The paired-t test was used for the comparison of the repeated measures with normal distribution-matched data however Wilcoxon signed rank test was used for non-normal distributions.  $p \geq 0.05$  was considered statistically insignificant and  $p < 0.05$  was considered significant. Correlation coefficients (R); weak correlation when  $R = 0.00-0.24$ , moderate correlation when  $R = 0.25-0.49$ , good correlation when  $R = 0.50-0.74$ , perfect relationship when  $R = 0.75-1.00$  was considered.

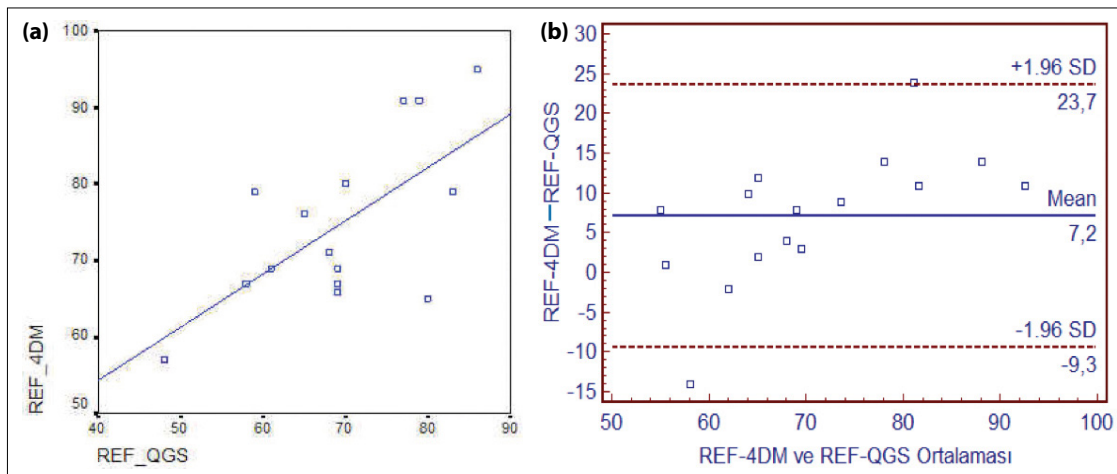
## Results

Mean±SD values of LVEF, EDV, ESV were calculated as: **QGS**: R-EF: 66.9±9.2, R-ESV: 23.6±12.9, R-EDV: 67.8±21, S-EF: 67.5±8.6, S-ESV: 21.8±11.9, S-EDV: 64±19.9, **4DM**: R-EF: 75.7±11.7, R-ESV: 17.3±12.9, R-EDV: 65.2±25.5, S-EF: 74.6±13.6, S-ESV: 16.9±13.7, S-EDV: 59.4±23.7. Mean rest EF and stress EF values between QGS and 4DM algorithms were detected significant differences in all patients ( $\Delta$  REF % [4DM-QGS]=10.1;  $\Delta$  SEF [4DM-QGS]=6.4;  $p < 0.05$ ) (Table 1).

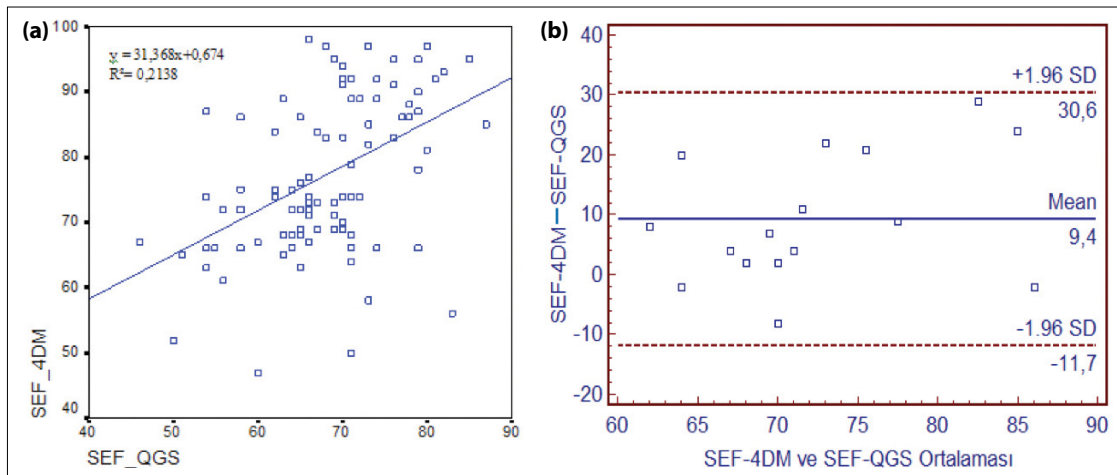
**Table 1. The comparison of QGS - 4DM SPECT results**

	Correlation		Difference between averages	
	R	p	$\Delta$	p
(REF- QGS) – (REF- 4DM)	0.56*	0.000	-10.11 <sup>†</sup>	0.000
(RESV- QGS) – (RESV- 4DM)	0.75**	0.000	6.91 <sup>††</sup>	0.000
(REDV- QGS) – (REDV- 4DM)	0.82*	0.000	1.83 <sup>†</sup>	0.070
(SEF- QGS) – (SEF- 4DM)	0.46**	0.000	-6.48 <sup>††</sup>	0.000
(SESV- QGS) – (SESV- 4DM)	0.79**	0.000	6.64 <sup>††</sup>	0.000
(SEDV- QGS) – (SEDV- 4DM)	0.91*	0.000	5.97 <sup>†</sup>	0.000

REF: Rest ejection fraction; SEF: Stress ejection fraction; RESV: Rest end systolic volume; REDV: Rest end diastolic volume; SESV: Stress end systolic volume; SEDV: Stress end diastolic volume; R: Correlation coefficient; \*: Pearson rank correlation analysis; \*\*: Spearman rank correlation analysis <sup>†</sup>: Paired-t test; <sup>††</sup>: Wilcoxon signed rank test.



**Figure 1.** Results of Linear Regression analysis (a) and Bland Altman analysis (b) obtained from the REF-4DM and REF-QGS algorithms.



**Figure 2.** Results of linear regression analysis (a) and Bland Altman analysis (b) obtained from the SEF-4DM and SEF-QGS algorithms.

Wide Blandt Altman limits (BAL) were found between the results (BAL: [4D-REF]-[QGS-REF]=23.7-(-9.3),  $R=0.56$   $p<0.05$  (Figure 1); 4D-SEF-QGS-SEF: 30.6-(-11.7),  $R=0.46$ ;  $p=0.000$ ) (Figure 2).

Significant differences ( $p<0.05$ ) were found between the two algorithms in addition to the strong correlation coefficient values ( $r=0.75-0.91$ ) in the volumetric measurements (Figure 3-6).

The mean LVEF and volume values obtained in our patient group were compared with the studies involving the normal patient group in the literature (Table 2).

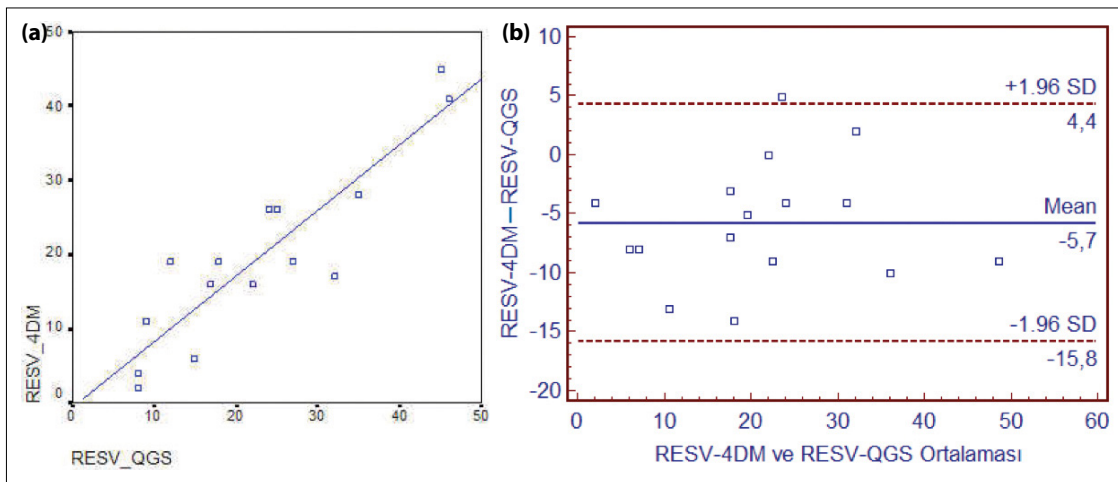
## Discussion

The knowledge of left ventricular ejection fraction (LVEF), end systolic volume (ESV) and end diastolic volumes (EDV) are important parameters as prognostic value in the measurement of cardiac performance. Nowadays, it is possible to calculate the LVEF and its volumes (ESV and EDV) with many invasive and noninvasive methods. Regional cardiac wall motion and thickening, LVEF, ESV, EDV can be analyzed with g-MPS. These combined perfusion and functional analysis approach is

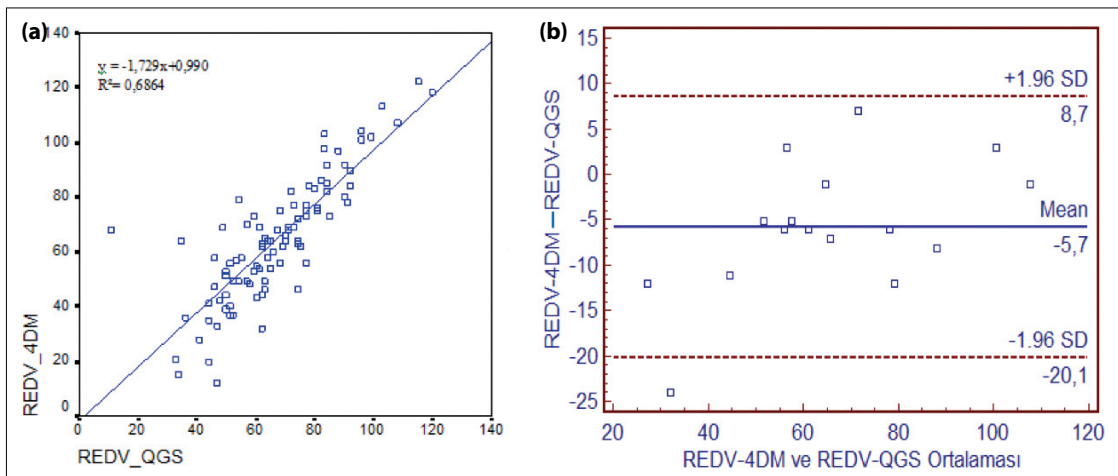
widely used with confidence and accuracy in important clinical indications such as diagnosis, preoperative risk assessment, prognosis estimation and evaluation of response to treatment.<sup>[14]</sup> For the measurement of these parameters, a lot of computer software programs were used include quantitative gated SPECT (QGS), emory cardiac toolbox (ECT), 4D-MSPECT, gated SPECT perfusion and function analysis (p FAST) and Wackers-Liu CQ quantitative analysis.<sup>[9,15-17]</sup> Knowing the normal limits have great importance to distinguish pathology in g-MPS examination.

There is a limited number of studies in the literature using g-MPS to evaluate the left ventricular function in patients with normal myocardial perfusion via the different software programs.

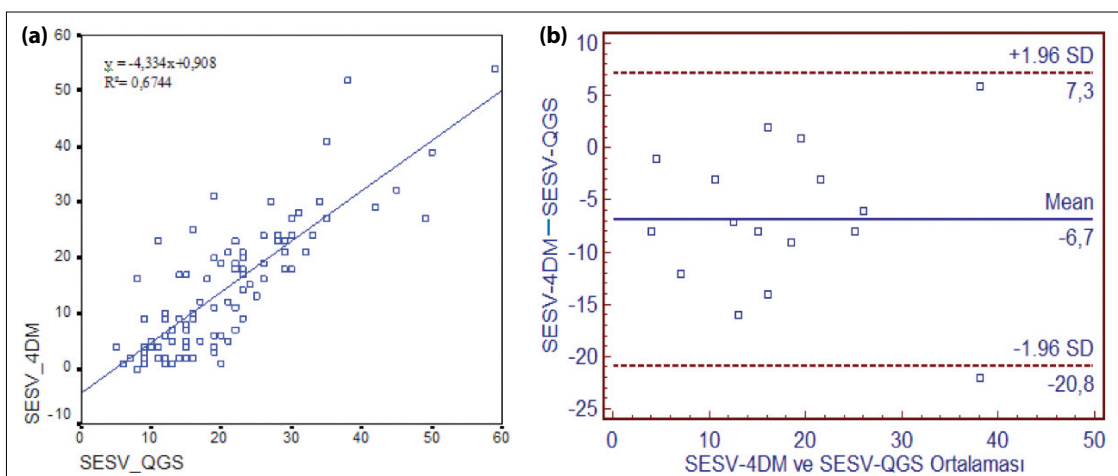
Lum et al. used QGS, 4DM and ECT (Emory Cardiac Toolbox) methods to compare LVEF and volume in 3 patients group which were small-hearted group, normal myocardial perfusion group and severe perfusion defects group.<sup>[18]</sup> In the group with normal myocardial perfusion, between QGS and 4DM;



**Figure 3.** Results of linear regression analysis (a) and Bland Altman analysis (b) obtained from RESV-4DM and RESV-QGS algorithms.



**Figure 4.** Results of linear regression analysis (a) and Bland Altman analysis (b) obtained from REDV-4DM and REDV-QGS algorithms.

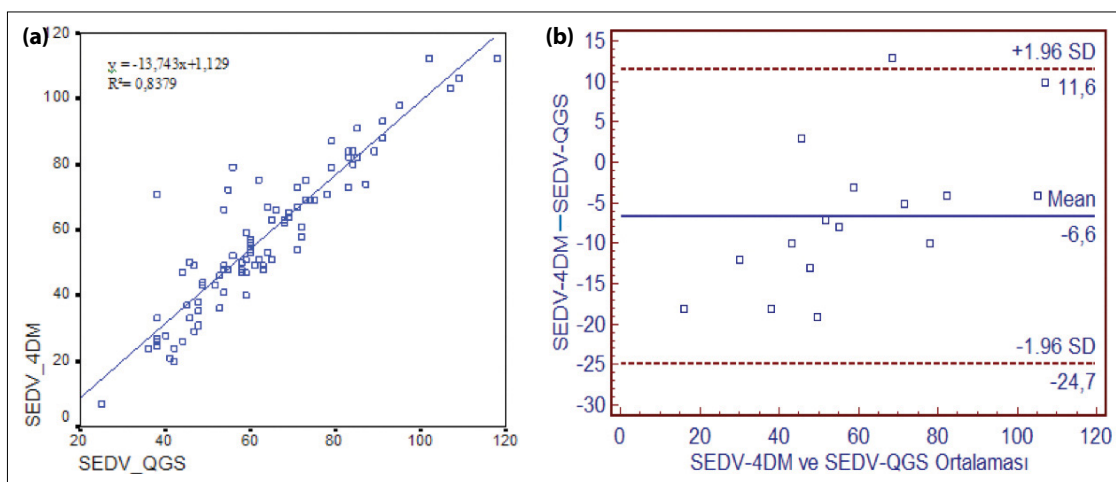


**Figure 5.** Results of linear regression analysis (a) and Bland Altman analysis (b) obtained from SESV-4DM and SESV-QGS algorithms.

QGS EF was calculated to be 5.93% less than EF calculated at 4DM ( $p < 0.001$ ). In our data, the difference between REF-4DM

and REF-QGS was 9%, and between SEF-4DM and SEF-QGS was 8.9%. Our differences between the mean values was also





**Figure 6.** Results of linear regression analysis (a) and Bland Altman analysis (b) obtained from SEDV-4DM and SEDV-QGS algorithms.

**Table 2. Comparison of mean values of LVEF and volumes with other studies**

Author	Rozanki	Ababneh	De Bondt	Akincioğlu	Nakajima	Our study	
Female (n)	100	124	59	19	149	109	109
Age (year s)	52±13	60±12	59±12	52±12	64±10	54±10	54±10
LVEF (%)	67±9	67±8	66±9	67±6	74±9	67±8	75±14
SVEDV (ml)	62±22	57±17	75±23	91±17	59±17	64±19	59±23
SVESV (ml)	21±13	19±11	27±14	31±11	17±10	21±11	17±13

LVEF: Left ventricular ejection fraction; SVEDV: Sol ventrikuler end diastolik volum, SVESV: Sol ventrikuler end sistolik volüm.

significant statistically ( $p < 0.05$ ).

Nakajima et al. compared four software programs (QGS, ECT, 4D-MSPECT and pFAST) in patients with different degrees of myocardial perfusion defects and they found good correlation between LVEF values calculated at QGS, ECT and 4DM ( $R=0.91-0.95$ ).<sup>[19]</sup> Similarly in our study, we found good correlation coefficients between the two algorithms in both the stress and rest ( $R=0.46-0.56$ ).

Schaefer WM et al. compared the results of LVEF and volume values of QGS, 4DM-SPECT and ECT methods with cardiac MR in 70 patients with known or suspected coronary artery disease.<sup>[20]</sup> In LVEF comparison, they did not find any significant difference between 4DM and MR, but found that QGS value was significantly lower than MR results. In our study, rest and stress LVEF values calculated with 4DM were significantly higher than rest and stress LVEF values calculated with QGS ( $p < 0.05$ ). Rest and stress ESD and EDV obtained in 4DM were lower than those obtained in QGS and had statistical significance ( $p < 0.05$ ).

In our study, the normal LVEF limits (QGS: REF=49%, SEF: 50%, 4DM: REF=52%, SEF: 47%) obtained from QGS and 4D-MSPECT software programs in female patients were consistent with the values given in the literature. When volume values were compared, in our patients, the EDV normal limit was 104 ml (literature normal EDV value=120 ml) and ESV value was 47

ml (literature normal ESV value=70 ml) were found lower than the literature values. The cause of that may be the difference between communities and/or the differences between the versions of the algorithms.

In conclusion, there was significant differences between the LVEF and volume values obtained from two g-MPS software programs (4D-MSPECT and QGS) which are used and accepted methods worldwide. These values differences limit their use in place of each other for the follow-up of patients. Therefore, we think that it is more reliable and accurate to keep patient's follow-up with the same program, which program had been used for diagnosis at the beginning.

**Conflict of Interest:** There are no relevant conflicts of interest to disclose.

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