Comparison of gated myocardial perfusion SPECT, echocardiography and equilibrium radionuclide ventriculography in the evaluation of left ventricle contractility

Sol ventrikül kontraktil fonksiyonlarının değerlendirilmesinde equilibrium radyonüklid ventrikülografi, ekokardiyografi ve miyokart perfüzyon gated SPECT görüntülemenin karşılaştırılması

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ABSTRACT

Objectives: In this study, we investigated the reliability of gated myocardial perfusion single-photon emission computerized tomography (GSPECT) for the evaluation of left ventricle (LV) function. We compared left ventricle ejection fraction (LVEF) calculated with GSPECT with the values derived from planar equilibrium-gated radionuclide ventriculography (ERVG) and echocardiography (ECHO).

Study design: Forty-eight patients with suspected coronary artery disease (CAD), who were referred for evaluation of myocardial perfusion and LV function and underwent two-day 99mTc-MIBI protocol GSPECT and ERVG, were examined retrospectively. LVEF was calculated with GSPECT Myometrix software, and wall motion and thickness were calculated with QGS analysis program. In the ERVG study, LVEF values were calculated using left anterior oblique images. In the GSPECT and ERVG study, wall motion was evaluated visually and scored. LVEF values and wall motion data measured with ECHO were noted.

Results: For all cases, there was a significant correlation between LVEF values calculated by GSPECT and ERVG. Numerical LVEF values of 30 patients measured with ECHO showed no significant difference from the values measured with GSPECT. When 240 segments obtained from 48 patients were examined, the correlation between GSPECT and ERVG was 77.5% and between GSPECT and ECHO was 75.4% by visual wall motion analysis. Quantitatively calculated wall motion and thickness scores of segments visually defined as normokinetic were significantly higher than segments visually defined as having contraction defect.

Conclusion: GSPECT can be used safely in clinical practice for the evaluation of LV function. Quantitatively calculated wall motion and thickness scores are promising methods to verify the visual evaluation.

ÖZET

Amaç: Çalışmamızda, sol ventrikül (SV) fonksiyonlarının değerlendirilmesinde 'miyokart perfüzyon gated SPECT' (GSPECT) yönteminin güvenilirliği araştırıldı, GSPECT ile hesaplanan sol ventrikül ejeksiyon fraksiyonu (SVEF) ortalaması planar 'equilibrium gated radyonüklid ventrikülografi' (ERVG) ve ekokardiyografi (EKO) ile elde edilen değerlerle karşılaştırıldı.

Çalışma planı: Koroner arter hastalığı (KAH) şüphesi olan miyokart perfüzyonu ve SV fonksiyonlarının değerlendirilmesi için iki gün Tc99m-MIBI protokolü ile GSPECT ve ERVG görüntülemeleri yapılan 48 hasta geriye dönük olarak incelendi. GSPECT Myometrix yazılımı ile SVEF, Cedars-Sinai Quantitatif Gated SPECT (QGS) analiz programı ile duvar hareket ve kalınlık skorları belirlendi. ERVG görüntülemesinde sol ön oblik görüntüleri kullanılarak SVEF değerleri hesaplandı. GSPECT ve ERVG görüntülerinde; SV duvar hareketleri görsel olarak değerlendirilerek skorlandı. Olguların EKO ile belirlenen SVEF değerleri ve duvar hareket bilgileri ile karşılaştırıldı.

Bulgular: Olguların GSPECT ile hesaplanan ortalama SVEF ile ERVG verileri arasında iyi derecede korelasyon bulundu. EKO ile ölçülen nümerik SVEF değeri olan 30 olgunun; GSPECT ve EKO ile hesaplanan SVEF değerleri arasında belirgin fark olmadığı görüldü. Kırk sekiz hastadan elde edilen 240 segment incelendiğinde, görsel duvar hareketleri açısından GSPECT ile ERVG arasında %77.5 segmentte, GSPECT ile EKO arasında %75.4 segmentte uyum saptandı. Görsel olarak normokinetik segmentlerde hesaplanan hareket ve kalınlık skorları, kontraksiyon kusuru izlenen segmentlere oranla belirgin yüksek bulundu.

Sonuç: GSPECT'in SV fonksiyonlarının değerlendirilmesi amacıyla klinik pratikte güvenle kullanılabileceği, kantitatif olarak hesaplanan duvar hareket ve kalınlık skorlarının görsel değerlendirmeyi desteklediği düşünülmektedir.

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It is important to measure left ventricle (LV) function in patients with coronary artery disease (CAD) with LV dysfunction in order to decide the appropriate treatment and predict the prognosis. Thus, the diagnostic test to be used should reveal the smallest alterations in global and regional dysfunction delicately, and it must be precise and easy to repeat. In clinic practice, two-dimensional echocardiography (ECHO) is the modality preferred by cardiologists for evaluating ventricular function. Its short procedure time, low cost and availability are the advantages of this technique; however, this test shows significant variability.[1-3] ECHO is a user-dependent modality, and in some cases, the acoustic window is limited. In order to make a precise distinction of endocardial lumen, contrast drug usage is suggested, since it is reported that the ventricular volume and ejection fraction (EF) values are correlated more with standard techniques.[4] However, use of contrast drugs is not preferred in routine clinic practice because of its burden on the procedure and cost.[5] These technical disadvantages of ECHO created the need for other non-invasive imaging techniques that will provide fast and safe detection of clinical problems. For this purpose, equilibrium-gated radionuclide ventriculography (ERVG), which is a basic nuclear medicine test for the evaluation of contractile function, is preferred because of its reproducibility.[6] Evaluation of LV function is also possible by adding gated myocardial perfusion single-photon emission computerized tomography (GSPECT) parameters to myocardial perfusion scintigraphy (MPS), which is used to show myocardial perfusion and viability.[7,8] The most important superiority of GSPECT imaging to ECHO and ERVG is its ability to reveal post-ischemic syndromes like stunned myocardium. In addition, with GSPECT imaging, it is possible to distinguish ischemic and non-ischemic cardiomyopathy.

In this study, we investigated the credibility of GSPECT parameters and its use in clinical practice for evaluating LV function.

PATIENTS AND METHODS

Our study group consisted of 48 patients with an age range of 30-78 years who were referred to our department between January 2010 and October 2010 for detection of myocardial perfusion and LV function. After local human ethical committee approval, all patients who were subjected to GSPECT using a two-day 99mTc-MIBI protocol and on a separate day planar ERVG study were examined retrospectively. Thirty of the 48 patients who had former numerical results of ECHO were grouped as Group 2.

Abbreviations:

CAD	*Coronary artery disease*
ECHO	*Echocardiography*
ERVG	*Equilibrium-gated radionuclide ventriculography*
GSPECT	*Gated myocardial perfusion single-photon emission computerized tomography*
LAO	*Left anterior oblique*
LV	*Left ventricle*
MPS	*Myocardial perfusion scintigraphy*
MRI	*Magnetic resonance imaging*
QGS	*Quantitative gated SPECT*
ROI	*Region of interests*

Gated myocardial perfusion SPECT protocol

Patient preparation and stress testing procedures

Cardiac medications that may interfere with the stress test, such as calcium channel blockers or beta-blockers, were terminated 48 hours before GSPECT imaging if there were no medical contraindications. Long-acting nitrates were interrupted 24 hours before the procedure. For pharmacological stress testing of patients, caffeine-containing beverages (coffee, tea, cola, etc.) and methylxanthine-containing medications were also avoided for at least the last 12 hours before the procedure. Taking a detailed cardiovascular medical history and baseline vital signs, patients who were suitable for exercise tests were reviewed. The treadmill exercise test was performed with the modified Bruce protocol in 44 patients. For two patients who were unable to exercise because of physical conditions, pharmacological stress was applied with dipyridamole. Dipyridamole, by intravenous administration, is a reliable substitute for exercise during GSPECT. As the intravenous form of dipyridamole was commercially unavailable, the oral form was used. When it was not possible to apply stress due to the clinical condition of two patients, images were obtained only at rest. Two-day MPS protocol was applied. When the target heart rate was reached during exercise or exercise termination criteria were observed (physical fatigue, progressive angina, dyspnea, ataxia, cyanosis, frequent ventricular arrhythmias, decrease in systolic blood pressure >20 mmHg, elevation of systolic blood pressure >250 mmHg or diastolic pressure >130 mmHg, ST-segment depression >3 mm or ST elevation >1 mm), 740 MBq (20 mCi) 99mTc-MIBI was injected. In patients undergoing pharmacological stress, 740 MBq (20 mCi) 99mTc-MIBI was injected intravenously 45 minutes after oral administration of dipyridamole 300 mg. Stress images were obtained 15-30 minutes (min) after injection. If the stress study was interpreted as abnormal, rest MPS was applied after at least 24 hours.

Imaging and data analysis

Images were obtained with a 90° dual-head gamma camera (Infinia, General Electric Medical Systems) equipped with high-resolution, low-energy parallel-hole collimators. Patients were imaged in the supine position. A 20% energy window around the 140 keV energy peak of 99mTc-MIBI was used. In a 64x64 matrix, a total of 60 projections (step & shoot mode) were acquired over 180° from 45° right anterior oblique to 45° left posterior oblique using a zoom factor of 1.33. All patients were monitored with 3-lead ECG for the GSPECT study. Images were gated at 8 frames per cardiac cycle with an R-wave trigger. Raw images were reconstructed using a filtered back-projection algorithm with a Butterworth filter.

Planar equilibrium radionuclide ventriculography

The ERVG study was performed at rest by *in vivo* labeling of red blood cells. For this, 2 mg of pyrophosphate compound was injected intravenously in 13 patients (Amerscan stannoz agen, Amersham), and 5 mg stannous pyrophosphate was injected in 35 patients. After 20 min, 740 MBq (20 mCi) 99mTc was administered intravenously to all patients. Supine imaging was performed 10 min after the injection using double-headed gamma camera (Infinia, General Electric Medical Systems) equipped with a high-resolution low-energy parallel-hole collimator. Images were obtained in the left anterior oblique (LAO) view at 45° ('best septal' for right ventricle and LV) and in the left lateral (90°) and anterior projections in order to assess the movements of the LV wall. 140 keV energy peak, ±10% energy window, with an image magnification of 1.28, was used. From each projection, data were acquired with 24 frames per cardiac cycle with ECG gating for 10 min.

Evaluation

Visual evaluation

Three-dimensional projection images of GSPECT data obtained with analysis of Myometrix (GE Healthcare) software packages, and the images from each of the three projections in the ERVG study were examined cinematically by two nuclear medicine specialists who were unaware of the clinical status of the patients. The LV was divided into five segments as four main walls and apex in both procedures. Each segment was scored as normokinetic = 1, hypokinetic = 2, akinetic = 3, or dyskinetic = 4.

Quantitative evaluation

In the GSPECT study, LVEF was calculated automatically with Myometrix software; quantitative wall motion (range, 0-10 mm) and wall thickening (in %) scores were obtained with the QGS program. These results were based on computer-derived endocardial and epicardial edges.

In the ERVG study in the LAO projection, left ventricular end diastolic and end systolic region of interests (ROI) are defined manually by the operator, and the background ROI was placed adjacent to the free wall of the ventricles automatically by the computer. LVEF was calculated from the count in the ROIs based on the equation: LVEF = (end-diastolic counts − end-systolic counts) / end-diastolic counts.

Other clinical and laboratory data

The clinical data of patients were examined, and ECHO results were modified as 1 = normal, 2 = hypokinetic, 3 = akinetic, and 4 = dyskinetic and compared on the basis of segments with GSPECT. Echocardiographic examinations of the 18 patients were defined as "normal" without a numerical value, so the remaining 30 patients with a numerical value of LVEF were grouped as Group 2.

Statistical analysis

All statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) program, version 15.0 (SPSS, Chicago, IL). The results were reported as mean±standard deviation. Spearman correlation test was used to determine the correlation between the values of LVEF obtained by the ERVG, GSPECT and ECHO studies. Strength of the correlation was determined by the value of 'r'. The correlation coefficient was defined as weak when r was <0.25, medium when $0.25 \leq r < 0.5$, powerful when $0.5 \leq r < 0.75$, and very strong when r was ≥ 0.75. Agreement between GSPECT, ERVG and ECHO for visual wall motion scores was assessed by kappa statistics. The kappa values ≤ 0.2, between 0.21 and

0.4, between 0.41 and 0.6, between 0.61 and 0.8, and ≥0.81 were considered to represent weak, medium, good, very best, and perfect agreement, respectively. Mann-Whitney and Wilcoxon tests were used to analyze the differences between the data obtained with GSPECT, ERVG and ECHO. Statistical significance was defined as $p<0.05$.

RESULTS

Demographic characteristics of the 48 patients (18 women [38%], 30 men [62%]) included in our study are described in Table 1.

Left ventricular ejection fraction

The mean LVEF of all cases calculated by GSPECT Myometrix software program and ERVG were 55.69±19.47 and 54.25±13.95, respectively (Table 2). LVEF values calculated using ERVG and GSPECT Myometrix software showed a very good correlation ($r=0.75$, $p<0.001$), and there was no statistically significant difference between the two methods ($p>0.05$). Mean values of LVEF calculated by GSPECT and ECHO of 30 patients (Group 2) are shown in Table 3. LVEF values measured by both methods were correlated well ($r=0.78$, $p<0.001$).

Visual evaluation of wall motion

Visual wall motion scores of 240 segments assessed by GSPECT, ERVG and ECHO according to the five-segment model are shown in Table 4. Kappa test showed significant correlation between visual wall motion scores of GSPECT, ERVG and ECHO ($p<0.05$). The concordance between GSPECT and ERVG was 77.5% (186/240) and between GSPECT and ECHO was 75.4% (181/240).

Semi-quantitative assessment of wall motion

Table 1. Clinical characterization of patients (n=48)

Parameter	Number	Percent (%)
Age	30-78	–
Mean age	56.60±9.54	–
Males	30	62
Females	18	38
History of coronary artery disease	26	54
History of myocardial infarction	19	40
History of bypass surgery	9	19
History of coronary angioplasty	8	17

Table 2. LVEF values calculated by GSPECT and ERVG (n=48)

LVEF (%)	Mean±SD	Minimum, maximum	Difference analysis
GSPECT Myometrix	55.69±19.47	15-87	p>0.05
ERVG	54.25±13.95	20-76	

ERVG: Equilibrium-gated radionuclide ventriculography; GSPECT: Gated myocardial perfusion single-photon emission computerized tomography; LVEF: Left ventricle ejection fraction.

Table 3. The mean values of LVEF calculated by GSPECT and ECHO (n=30)

LVEF (%)	GSPECT	ECHO	Difference analysis
Mean±SD	47.60±19.17	46.63±11.84	p>0.05
Minimum, maximum	15–75	25–66	

ECHO: Echocardiography; GSPECT: Gated myocardial perfusion SPECT; LVEF: Left ventricle ejection fraction.

Table 4. Segmental wall motion visually assessed by GSPECT, ERVG and ECHO

Myocardial walls	Imaging modalities	Normokinetic	Hypokinetic	Akinetic	Dyskinetic	Total
Anterior	GSPECT	31	15	2	0	48
	ERVG	34	13	1	0	
	EKO	31	15	2	–	
Lateral	GSPECT	33	13	2	0	48
	ERVG	37	10	1	0	
	EKO	37	10	1	–	
Inferior	GSPECT	28	13	7	0	48
	ERVG	37	5	6	0	
	EKO	32	13	3	–	
Septum	GSPECT	31	8	9	0	48
	ERVG	33	10	5	0	
	EKO	28	14	6	–	
Apex	GSPECT	32	4	11	1	48
	ERVG	33	6	8	1	
	EKO	35	7	5	1	
Total	GSPECT	155	53	31	1	240
	ERVG	174	44	21	1	
	ECHO	163	59	17	1	

ECHO: Echocardiography; ERVG: Equilibrium-gated radionuclide ventriculography; GSPECT: Gated myocardial perfusion SPECT.

Motion and thickness scores

Mean wall motion score of 155 (64.6%) visually normokinetic segments determined by Cedars-Sinai Quantitative perfusion-gated SPECT (QPS-QGS) software system was 8.02±2.28, while in the remaining 85 (35.4%) segments, which were defined as hypokinetic, akinetic or dyskinetic, the mean wall motion score was 4.00±2.87. When motion scores for each segment were analyzed separately, the septum had the lowest score (mean: 5.56±1.65) despite being visually normokinetic. The lateral wall had the highest score (mean: 6.12±2.29) despite contractility defects observed in visual analysis. Quantitative wall motion scores were significantly lower in segments with motion defects in the visual assessment compared to normokinetic segments ($p<0.001$) (Figure 1). Quantitative thickness score of the visually normokinetic segments was 46.26±16.93%. Wall thickness of the segments defined as hypokinetic or akinetic in visual assessment was reported as 19.49±13.37% by QGS software. There was a significant difference between

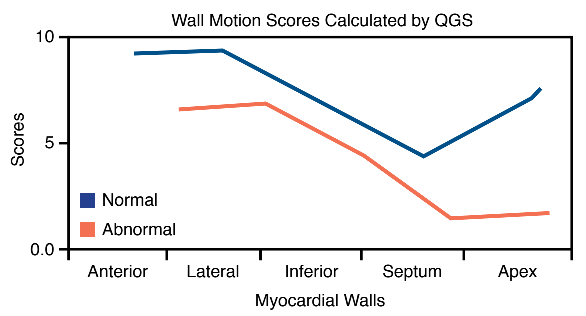

Figure 1. Wall motion scores of the segments showing normal and abnormal contractility.

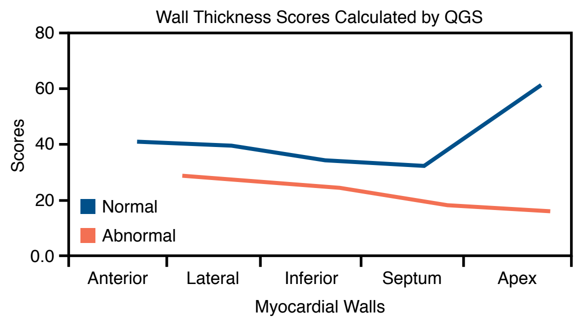

Figure 2. Wall thickness scores of the segments showing normal and abnormal contractility.

quantitative thickness scores of the segments showing normal and abnormal contraction in the visual analysis ($p<0.001$) (Figure 2).

DISCUSSION

In CAD, for the selection of an effective treatment modality, the risk of cardiac events or the probability of cardiac arrest must be identified correctly. In this sense, the prevalence and severity of perfusion defects detected by MPS are a strong indicator of prognosis.[9] Moreover, LV contractile function parameters obtained by GSPECT enhance the prognostic value of MPS.[10] LVEF value is a commonly used hemodynamic index in the evaluation of systolic function. Sharir and colleagues[11] stressed the importance of LVEF for planning the treatment in 14 patients with CAD and LV dysfunction. They reported an increase in the risk of cardiac death if stress LVEF was under 30%. In another study, the annual death rate was found lower than 1% if LVEF value was ≅ 45% even in patients with significant perfusion defects, and the annual mortality rate was reported as 9.2% when LVEF value was below 45% in patients with a moderate perfusion defect.[12] There are studies in the literature showing the similarity to a large extent between GSPECT, planar ERVG,[13,14] 2D-ECHO,[15,16] and magnetic resonance imaging (MRI)[17-19] in determining LV functional parameters. In our study, we compared the reliability of GSPECT with ERVG, which is considered the gold standard in clinical practice due to its accuracy and reproducibility, in the determination of LVEF. LVEF values of 48 patients included in this study calculated by GSPECT and ERVG showed a very good correlation. In their study, Chua and colleagues[20] similarly found good correlations between the LVEF values calculated with 99mTc-tetrofosmin GSPECT and ERVG in 62 patients with LV dysfunction and perfusion defect. However, use of different automatic software and different algorithms to create polar maps may lead to variability of the calculated values of LVEF in gated SPECT.[21] Even though the LVEF values calculated by the Cedars-Sinai Quantitative Gated SPECT and ECT software program show a good correlation,[22] due to the unique characteristics of each software program, it is not recommended to use different software programs in the follow-up of the same patient.[23] Another reason for variations in LVEF values calculated by GSPECT is the number of frames per cycle. Some studies that investigated the accuracy of GSPECT in LVEF measurement reported that the best concordance was provided by use of 32 frames per cycle with reference to ERVG.[24] The use of 16 frames instead of 8 frames in the GSPECT method causes a decrease in temporal resolution and an approximately 3.71% decrease in LVEF.[25] In patients with small hearts, end systolic volume as determined by GSPECT is lower than end diastolic volume, so LVEF can be calculated as 10% higher than normal.[26] As a result, in some cases, the measurement of LVEF with GSPECT may have a lower level of correlation with other imaging techniques.[27]

Although ECHO is the preferred method in the evaluation of ventricular function due to its lower cost and its applicability at the bedside in routine practice, for assessment of myocardial viability and the post-ischemic syndromes and distinction of ischemic and non-ischemic cardiomyopathy, emphasis has been placed on GSPECT examination. In our study, there was no statistically significant difference between the LVEF values of 30 patients calculated with ECHO and GSPECT ($p>0.05$). Similarly, Choragudi et al.[16] calculated LVEF values of 51 patients with GSPECT and 2D-ECHO and reported that the two methods showed good correlation.

In a study comparing planar ERVG and GSPECT, a very good correlation was observed between the LVEF values measured by the two methods; however, the correlation coefficient was lower in patients with large infarct areas.[20] In patients with severe perfusion defects, the determination of endocardial borders may be unclear, and the value of LVEF measured by GSPECT may be lower than actual.[28,29] In the GSPECT method, gender, myocardial perfusion defects, extra-cardiac activity, the injected dose of radioactivity, and the imaging delay are listed as factors affecting the measurement of LVEF.[30-32] Despite those limitations, LVEF values calculated with GSPECT are in good correlation[33] with the data obtained by the other techniques, but it may not be considered equivalent to those methods. Therefore, in order to obtain accurate results in the patient's follow-up, the use of the same method and software program is recommended.

In the assessment of LV function, awareness of the wall motion and systolic thickening ratio is also an important determinant. The annual risk of cardiac events in patients with normal wall motion was reported as 1.6%, while it was 6.1% in cases with wall motion deficiency.[34] Murashita et al.[35] reported that functional recovery after revascularization is more apparent in segments with a perfusion rate >50%, or wall motion score >1.5 mm and thickness score >10%.[35] In a number of studies, wall motion and contractions measured with the GSPECT method have been reported to correlate strongly with MRI and echocardiography.[17,36] In our study, there was a very good agreement between visual wall motion scores assessed by GSPECT, ERVG and ECHO. When quantitative motion scores calculated by the gated SPECT QGS program for each segment were evaluated separately, we observed a difference between myocardial walls. For example, the septum had the lowest motion score, though it had normal contraction visually. The cause of this discrepancy was explained by high intracardiac pressure on the septum and restricted mobility of the wall.[37] The motion of myocardial walls is often influenced by the neighboring regions, so especially in patients with a history of cardiac event, the assessment of wall motion becomes more difficult. In those patients, wall thickness is suggested as a valuable criterion in the evaluation of systolic functions.[17,36] In our study, when the wall thickness scores of the visually normokinetic segments were evaluated, the maximum thickness score calculated by the QGS program was at the apex due to the significant increase of the counting rate during systole. There have been many studies showing that thickness and wall motion scores calculated by gated SPECT QGS software are significantly correlated with the values obtained with MRI, but heterogeneity was observed in segmental wall motion and thickness scores in patients with normal myocardial perfusion.[17,36] Wall thickness and motion scores vary with gender, race, and the number of frames used, and it is known that there is no standard limit value.[38] It is reported that normal wall thickness decreases by 24%-68% towards the apex to base. In addition, wall thickness variations along the long axis of the ventricle and wall motion variations along the short axis of the ventricle are known to be significant.[39] In our study, in segments with abnormal motion by visual examination, quantitative wall motion and thickness scores were significantly lower than in normokinetic segments. This result is also supported by the work of the Sharir and colleagues.[39] As a result, wall thickness and wall motion scores determined by the QGS program are parameters that will be used to increase the sensitivity of the visual evaluation in patients with wall motion abnormalities.

In conclusion, we believe that GSPECT is a noninvasive and reliable method, which can concomitantly assess myocardial perfusion and function. It has gained higher diagnostic accuracy in the assessment of LV function by minimizing artifacts and by using the parameters provided with the help of various software programs.

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