

## Original article

# A Comparison between Quantitative Gated Myocardial Perfusion Scintigraphy and Strain Echocardiography as Indicators of Ventricular Functions in Patients with Anterior Myocardial Infarction

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## Abstract

The purpose of this study is to compare the strain echocardiographic and scintigraphic parameters for evaluating of the left ventricular (LV) functions in patients with anterior myocardial infarction (MI). Fifty-four patients (male/female: 36/18; mean age  $62 \pm 13$  years) with anterior MI were prospectively enrolled. All patients were performed gated myocardial perfusion scintigraphy gated single-photon emission computed tomography (GSPECT) and echocardiography (EC). GSPECT data were processed and analyzed using 4D-MSPECT (4DM, Invia Medical Imaging Solutions, Ann Arbor, MI, USA). The echocardiographic strain (S) and strain rate (SR) values were calculated. The results obtained by these techniques were compared each other. A total of 918 segments of LV wall were evaluated. In all patients, 385 segments were automatically scored as normokinetic, 206 as hypokinetic, 122 as akinetic, 205 as dyskinetic and 300 as normal thickening, 348 as decrease thickening and 270 as no thickening. The means of S and SR values in thickening and motion score groups according to GSPECT were statistically different from each other ( $P < 0.001$ ). There was a negative significant correlation between LV wall thickening sum score and S and SR and between LV wall motion sum score and S and SR ( $P < 0.001$ ). There was a good correlation between GSPECT and echocardiographic LV-ejection fraction ( $r = 0.7$ ,  $P < 0.001$ ). GSPECT and strain EC are similar in quantitative grading of the severity of regional and global myocardial dysfunction in patients with anterior MI and these techniques provide valuable diagnostic information.

**Keywords:** Left ventricular function, myocardial infarction, myocardial scintigraphy, strain echocardiography

## Introduction

Left ventricular (LV) functional parameters are useful diagnostic and prognostic indicators in the appropriate management of patients with myocardial infarction (MI).<sup>[1,2]</sup> Quantitation of regional and global

motion and thickening of LV might be helpful in the assessment and follow-up of patients with myocardial dysfunction and in evaluating the efficacy of therapeutic interventions, whether medical or invasive therapy in these patients.<sup>[3-5]</sup> Echocardiographic, magnetic resonance imaging (MRI), and scintigraphic studies have revealed that regional and global myocardial motion and wall thickening can be quantitatively assessed using these techniques.<sup>[6-8]</sup>

Echocardiography (EC) is the most commonly used imaging modality for evaluating LV functions. However, it is subjective and experience-dependent. However, strain (S) and strain rate (SR) EC analyses are sensitive

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and quantifiable methods for the evaluation of regional and global LV functions as well. Many published research shown that myocardial contractility may be objectively assessed using S and SR-EC.<sup>[9,10]</sup>

On the other hand, the use of electrocardiographic gating during the acquisition of myocardial perfusion scintigraphy gated single-photon emission computed tomography (GSPECT) has become possible to simultaneously assess LV perfusion, function and volumes.<sup>[11]</sup> In the previous studies has been shown that quantitative grading of the severity of regional myocardial dysfunction by GSPECT, is feasible, accurate and reproducible a technique.<sup>[12,13]</sup>

The purpose of this study is to compare the strain echocardiographic and scintigraphic parameters for the LV's functions in patients with anterior MI and to evaluate the availability of strain EC by comparing the GSPECT.

## **Materials and Methods**

### **Study population**

Fifty-four patients with subacute anterior wall MI had  $\geq 70\%$  stenosis in the left anterior descending (LAD) artery were prospectively enrolled in the study. Diagnosis of MI was established according the 3<sup>rd</sup> universal definition of MI criteria.<sup>[14]</sup> In all patients, EC was performed within 1-5 days after MI. The patients underwent nitrate-enhanced rest GSPECT with technetium-99m methoxy isobutyl isonitrile (<sup>99m</sup>Tc-MIBI) program before percutaneous coronary intervention.

The exclusion criteria included the following: Patients who had received thrombolytic treatment or who had primary percutaneous coronary intervention in the early terms of MI, or angina at rest, or heart failure as defined by the New York Heart Association Class III or IV criteria, cardiogenic shock, any mechanical complications (as acute ischemic mitral regurgitation, ventricular septal rupture, and free wall rupture) after MI, history of coronary artery disease, other myocardial wall infarctions except anterior MI, cardiac muscle disease, bundle branch block or atrial fibrillation, hemodynamic instability, or permanent pacemaker. Patients with poor EC window were also excluded. This study was approved by the Local Ethics Committee. All patients were informed about the study, and their written consent forms were obtained.

### **Echocardiographic examination**

The EC was performed by Vivid 7 instruments (GE Medical Systems, Milwaukee, WI, USA), with a 2.5-MHz transducer and harmonic imaging. Echocardiographic examinations were performed with the patients

lying in the left lateral decubitus position using the recommendations of the American Society of EC.<sup>[15]</sup> Two-dimensional images were acquired at the apical four- and five-chambers and at the long axis. The LV systolic and diastolic diameters (LVS, LVD) were obtained by M-mode EC. The LV-ejection fraction (LV-EF) was calculated using the modified biplane Simpson's method.

We used the speckle tracking technical S and SR. Tissue Doppler-derived LVS longitudinal S and SR rates were obtained in two- and four-chamber apical views. Sixteen 16 segments were assessed (basal, middle, and apical segments of septum, inferior, lateral and anterior walls and basal and middle segments of anterior septum and posterior wall). Recordings were performed at the end of the expiration and involved three consecutive cycles. All EC tests were performed by two cardiology specialists.

### **Gated single-photon emission computed tomography imaging protocol**

Gated single-photon emission computed tomography images were analyzed by two experienced nuclear medicine physicians who had no knowledge of all the other data. All enrolled participants underwent a rest protocol using GSPECT with <sup>99m</sup>Tc-MIBI. Before receiving <sup>99m</sup>Tc-MIBI, patients were given 1-2 tablets of sublingual nitroglycerin (0.4 mg) 5 min apart. Finally, 740 MBq of <sup>99m</sup>Tc-MIBI were intravenously injected at rest and GSPECT study was performed 45 min later.

The GSPECT data were acquired in the supine position with the double-head GSPECT  $\gamma$ -camera (Siemens, e-Cam, Germany) equipped with a high-resolution low-energy collimator. The obtained data were projected as myocardial tomographic slices in the short axis, vertical-long axis and horizontal-long axis, views. Electrocardiogram gating was applied on the cardiac cycle, with eight frames per cardiac cycle. The GSPECT data were processed and analyzed using 4D-MSPECT (4DM, Invia Medical Imaging Solutions, Ann Arbor, MI, USA). About 20% energy window of approximately 140 keV was used to acquire the emission images. A total of 32 projections (35 s/projection) were obtained over a 180° circular orbit. The GSPECT images were reconstructed by filtered back projection method using a Butterworth filter (order 5; cut-off frequency 0.50).

The myocardium was divided into 17 segments following the American Society of Nuclear Cardiology, the American College of Cardiology and the American Heart Association Guidelines.<sup>[16]</sup> A scale of 0-4 was used for grading wall motion: (0: Normal, 1: Mildly hypokinetic, 2: Hypokinetic, 3: Akinetic, and 4: Dyskinetic), and also a scale of 0-3 for grading thickening (0: Normal, 1: Mildly decreased, 2: Moderately to severely decreased, and 3: No thickening) by automatic scores for each of the segments.<sup>[17]</sup>

Abnormal motion and thickening were defined as a score of  $\geq 2$ . Summed motion and summed thickening scores were also calculated. Furthermore, the sums of the wall motion and thickening segments, averaged over the number of segments with automatic scores, gave the wall motion and thickening score indices (wall motion score index [WMSI] and wall thickening score index [WTSI]).

### Comparing echocardiographic and scintigraphic studies

In each of apical, middle, and basal segments of all walls, S and SR values were calculated based on whether they were described as normal or abnormal according to motion and thickening scores. To compare between scintigraphic and EC images, a consensus was reached in cases of discrepancy. The asynergic segments were assigned to the appropriate coronary artery territory.

### Statistical analysis

Statistical analysis was performed using SPSS 17.0 software package (version 17, SPSS Inc., Chicago, IL, USA). Parameters were expressed as mean  $\pm$  standard deviation or as a percentage. To determine the differences of S and SR values in LV wall thickening, score groups and motion score groups were assessed by analysis of ANOVA Tukey *post-hoc* test and Student's *t*-test. Statistical significance was set at  $P < 0.05$ . Pearson correlation coefficients were used to evaluate the strength of association between scintigraphic and EC parameters and expressed as  $r$ . Furthermore, to compare LV-EF among these two techniques we used the Bland-Altman analysis and paired *t*-test. In search for a diagnostic cut-off value of peak systolic S and SR values to separate normal segments from abnormal segments, a receiver operating characteristic (ROC) curve analysis was constructed, and the area under the curve (AUC) was reported, which is considered representative of the discriminatory ability of the variable cut-off. Sensitivity and specificity values of the best cut-off variables were determined using ROC curve analysis. The cut-off levels of segments were calculated using MedCalc 9.2.0.1 (MedCalc Software, Mariakerke, Belgium).

## Results

The demographic and clinical characteristics of all patients are summarized in Table 1. The mean age of patients was  $62 \pm 13$  years (18 female). All patients had LAD artery branch disease. Diabetes, hypertension, and smoking were prevalent in 44%, 37%, and 57% of enrolled patients, respectively.

No statistically significant difference was observed between EF values obtained by the EC and GSPECT ( $P = 0.7$ ) while there was a good correlation ( $r = 0.7$ ,  $P < 0.001$ ). Mean

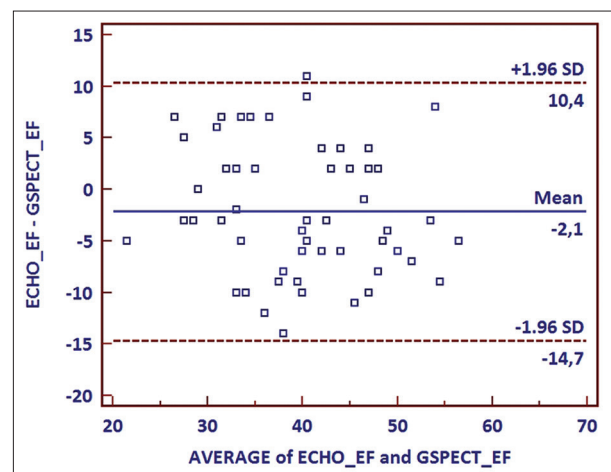
difference was  $-2.1$  and limits of agreement were  $+10.4$  and  $-14.7$  in the Bland-Altman analysis [Figure 1]. There was a negative moderate significant correlation between global S and SR in EC and LV-WMSI in GSPECT ( $r = -0.43$ ;  $r = -0.39$ ,  $P < 0.001$ , respectively) and LV-WTSI ( $r = -0.39$ ;  $r = -0.32$ ,  $P < 0.001$ , respectively). Furthermore, when correlation analysis was performed according to each of segments, it was seen that middle anteroseptal wall had the most significant correlation ( $r = -0.527$ ,  $P < 0.001$ ).

In scintigraphy examination, a total of 918 segments of LV wall were evaluated by using 4DM-SPECT. In all patients, 385 segments were automatically scored as

**Table 1: Clinical and demographic characteristics of all patients (n=54)**

Age (mean years $\pm$ SD)	62 $\pm$ 13
Female/male (n)	36/18
Hypertension n (%)	24 (44)
Diabetes n (%)	20 (37)
Smoking n (%)	31 (57)
Scintigraphy	
EF (%)	41 $\pm$ 10
EDV	134 $\pm$ 28
ESV	78 $\pm$ 24
Summed rest score	23 $\pm$ 10
Summed motion score	28 $\pm$ 15
Summed thickening score	25 $\pm$ 11
Wall motion score index	1.4 $\pm$ 1.1
Wall thickening score index	1.6 $\pm$ 0.9
Echocardiographic parameters	
EF (%)	39 $\pm$ 9
EDV (mm)	111 $\pm$ 35
ESV (mm)	69 $\pm$ 27
Left ventricular global strain value	-11.6 $\pm$ 5.5
Left ventricular global strain rate value	-0.98 $\pm$ 0.4

EF: Ejection fraction; EDV: End diastolic volume; ESV: End systolic volume; SD: Standard deviation



**Figure 1: Bland-Altman analysis for ejection fraction (EF) showed good agreement between ECHO and GSPECT**

normokinetic, 206 as hypokinetic, 122 as akinetic, 205 as dyskinetic and 300 segments as normal thickening, 348 as decrease thickening and 270 as no thickening. The means of S and SR values in thickening and motion score groups were statistically different from each other ( $P < 0.001$ ). The results are shown in Table 2.

Strain and SR findings in patients with normal and abnormal wall motion and thickening score were shown in Tables 3 and 4. Strain and SR value in all segments were significantly lower in abnormal segments compared normal segments in the motion score groups. However, the only S values of all segments were significantly lower in abnormal segments in the thickening score groups.

Optimal threshold cut-off points of peak systolic S and SR values to separate normal segments from

abnormal segments in LV walls were determined by ROC analysis [Figure 2]. In motion score groups, apical and middle segments have the highest sensitivity (78% and 79%, respectively) and the highest specificity was obtained in middle and basal segments (80% and 78%, respectively). According to thickening score groups, while the highest sensitivity was obtained in apical segments and the highest specificity was observed in middle segments for S values (70% and 73%, respectively), no difference was found between normal and abnormal groups for SR values. The highest sensitivity and specificity levels were observed according to motion score groups in the middle segments (respectively, cut-off SR value: 1.06, 79%, AUC: 0.750; cut-off S value: 9.8, 80%, AUC: 0.766).

## Discussion

In this study, we have evaluated LV functional parameters using GSPECT and S-EC in patients with anterior MI. We demonstrated that the strain imaging EC findings were consistent with the quantitative assessment of GSPECT in these patients. There was a good correlation between regional and global quantitative GSPECT parameters and S and SR values obtained from strain EC.

Similarly to our study, other researchers compared an automated function imaging method recently developed for calculating the longitudinal peak systolic strains of regional LV walls using EC with wall thickening measured by GSPECT.<sup>[18]</sup> They reported that these techniques showed good agreement with each other.

**Table 2: Comparison of S and SR values according to motion scores and thickening scores groups**

	Motion score groups			P
	Normokinetic (n=385)	Hypokinetic (n=206)	Akinetic/ dyskinetic (n=327)	
S (%)	-13.7±5.1	-12.1±5.9	-8.3±4.1	<0.001
SR (%)	-1.16±0.5	-1.03±0.5	-0.72±0.4	<0.001
	Thickening score groups			P
	Normal (n=300)	Decrease thickening (n=348)	No thickening (n=270)	
S (%)	-13.8±5.6	-11.7±4.9	-8.8±4.6	<0.001
SR (%)	-1.13±0.5	-1.02±0.5	-0.78±0.5	<0.001

S: Strain value; SR: Strain rate value

**Table 3: S and SR values (%) in normal and abnormal left ventricular wall segments according to motion score groups**

Wall segments	Normal (mean±SD)	Abnormal (mean±SD)	P	Sensitivity (%)	Specificity (%)	Cut-off value (%)
Apical S	-7.8±3.9	-5.9±2.6	<0.001	78	38	-8.7
Apical SR	-0.59±0.4	-0.51±0.3	<0.05	77	36	-0.7
Middle S	-13.4±4.4	-9.3±3.8	<0.001	60	80	-9.8
Middle SR	-1.15±0.4	-0.79±0.4	<0.001	79	63	-1.06
Basal S	-16.2±4.2	-13.9±0.4	<0.001	54	74	-13.5
Basal SR	-1.37±0.3	-1.23±0.5	<0.05	50	78	-1.15
Total S	-13.6±5.1	-10.1±5.4	<0.001	60	75	-10.15
Total SR	-1.15±0.5	-0.86±0.5	<0.001	71	62	-1.05

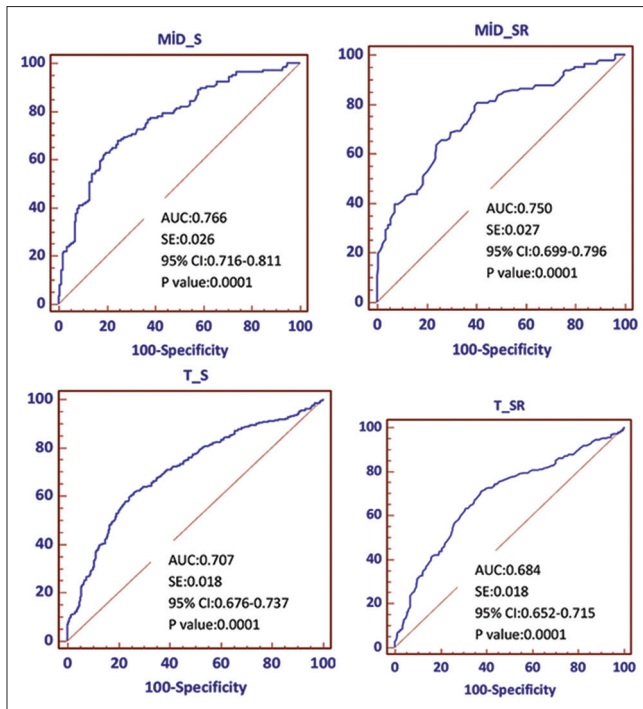
S: Strain value; SR: Strain rate value; SD: Standard deviation

**Table 4: S and SR values (%) in left ventricular wall segments according to thickening score groups**

Wall segments	Normal (mean±SD)	Abnormal (mean±SD)	P	Sensitivity (%)	Specificity (%)	Cut-off value (%)
Apical S	-8.6±4.7	-6.3±2.9	<0.05	70	51	-7.7
Apical SR	-0.59±0.3	-0.51±0.3	0.2	55	67	-0.44
Middle S	-12.8±4.5	-11.1±4.6	<0.05	50	73	-10.35
Middle SR	-1.03±0.4	-0.97±0.4	0.1	60	60	-0.96
Basal S	-15.9±4.9	-14.1±4.8	<0.05	50	67	-13.5
Basal SR	-1.34±0.4	-1.25±0.4	0.07	38	69	-1.01
Total S	-12.7±5.7	-10.9±5.3	<0.001	53	65	-10.35
Total SR	-1.04±0.5	-0.95±0.5	<0.05	56	57	-0.96

S: Strain value; SR: Strain rate value; SD: Standard deviation





**Figure 2:** ROC curves in middle (M) segments obtained highest sensitivity and specificity levels for S and SR values and in total (T) left ventricular wall segments

They found that the strain obtained by tissue Doppler imaging could accurately identify infarct-involved segments, by setting the cut-off value of  $-11\%$ . We used the same techniques of this study and our results showed good agreement with their study and other previous studies.<sup>[19,20]</sup> Eek *et al.* found both global longitudinal strain and WMSI to identify patients with MI who might benefit from urgent reperfusion therapy.<sup>[21]</sup> In patients with total and subtotal infarction of the LAD artery studied by other researchers, S and SR values obtained from EC examination were able to differentiate total occlusion.<sup>[22]</sup> These results suggest that Strain echocardiography (S-EC) and GSPECT can be applied to assess LV regional wall motion abnormalities in a noninvasive manner and provide additional information in clinical practice.

Gated single-photon emission computed tomography provides simultaneously automatic quantitative assessment of myocardial perfusion and function of LV function, infarct size and myocardial viability.<sup>[11,13]</sup> This technique is highly reproducible. It also seems to be one of the most promising and cost-effective methods for objective assessment of LV function.<sup>[23]</sup> Nitrate-enhanced GSPECT allows to identify severely hypoperfused, but still viable (hibernating) myocardium, and irreversibly fibrotic (stunning) myocardium.<sup>[3,8]</sup> Although, EC techniques used to assess LV volumes and LV function, which are observer-dependent, the GSPECT technique is nearly totally automatic. In addition to, it can be used in patients with pacemaker and renal insufficiency.

Two-dimensional EC is user-dependent, which is its most important disadvantage. S and SR as being Doppler techniques are limited by angle dependence and unsuitable in patients who have inadequate EC windows. In these patients GSPECT can be applied. In patients with adequate EC window, strain Doppler imaging from the point of view of radiation is more favorable than GSPECT. Technical problems including low count scans, gating errors, arrhythmias and patients motion during the GSPECT acquisition would affect the quality of perfusion or of function images.<sup>[24]</sup> However, automation of the image processing and quantification has made this technique simple and practical in clinical settings. Accurate quantitative analysis, affords an opportunity to eliminate observer variability and bias, provides an approach that is more generalizable to other centers than visual analysis, as it is not dependent on the expertise of the interpreter.

## Limitations

Our study population consisted only of patients with MI of the LAD artery. We included only anterior MI to ensure homogeneity within study group. Therefore significant lesions in the circumflex or the right coronary arteries may have different changes in SEC and in the scintigraphic parameters. Furthermore, we excluded patients who had additional problems such as heart failure, mechanical complications, arrhythmias, history of coronary artery disease, and hemodynamic instability. Therefore, the results of our study may be available only in stable patients. Furthermore, both techniques were performed at only rest. Our study's most important limitation was the small number of patients. Therefore, large studies are needed.

## Conclusion

Gated single-photon emission computed tomography and S-EC allow for the quantitative grading of the severity of regional and global myocardial dysfunction in patients with MI. We showed that GSPECT and S-EC were in agreement with each other. Although, cardiac MRI, computed tomographic angiography, new hybrid imaging methods with SPECT/computed tomographic (CT) or positron emission tomography/CT capabilities, or the use of fusion software will provide comprehensive evaluation of the anatomical and functional characterization of the disease, we think that new algorithms for coronary artery disease evaluation will continue to involve GSPECT in clinical practice.

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