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Comparison of stress dobutamine echocardiography and stress dobutamine gated myocardial SPECT for the detection of viable myocardium

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Abstract

BACKGROUND: We prospectively studied a group of patients with myocardial infarction (MI), who were candidates for surgical revascularization, to compare the efficacy of dobutamine gated myocardial SPECT with dobutamine stress echocardiography (DSE) for the detection of myocardial viability.
MATERIALS AND METHODS: We investigated 224 segments from 14 patients with MI using resting echocardiography and low dose dobutamine stress echocardiography as well as resting, low and high dose dobutamine stress 99mTc-Sestamibi gated SPECT.
RESULTS: In total, 13 men and 1 women with a mean age 54.57 years (range, 43 to 71 years) entered the study. Of the 125 dysfunctional segments, as assessed by ECG-gated examination, 53 (23.66% of total) were hypokinetic at rest, 64 (28.57% of total) were akinetic, and 8 (3.57% of total) were dyskinetic. The number of segments with resting wall motion abnormality (considered viable by low dose dobutamine ECG-gated examination) was significantly greater than those showing a contractile improvement in response to dobutamine in echocardiography (39.2% versus 32.8%, respectively, $p < 0.05$). In addition, in high dose ECG-gated examination, 42 of the 125 dysfunctional segments (33.6%) were viable. In general, the methods were well correlated.
CONCLUSION: We found a good agreement between low dose dobutamine gated SPECT and stress dobutamine echocardiography for the detection of inotropic reserve in infarcted areas.

KEY words: myocardial viability, dobutamine stress echocardiography, gated SPECT, myocardial perfusion imaging

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Background

Differentiation of dysfunctional but viable myocardium from irreversibly damaged scar tissue has important clinical implications for patients with chronic myocardial infarction and impaired left ventricular function [1]. Therefore, several imaging techniques with different approaches are used to identify viable regions with severely depressed function [1, 2].

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Dobutamine stress echocardiography (DSE), nuclear imaging by single photon emission computed tomography (SPECT), magnetic resonance imaging (MRI), positron emission tomography (PET) with F-18 fluorodeoxyglucose (18F-FDG), and tissue Doppler imaging (TDI) have been proposed as effective techniques for the evaluation of myocardial viability. Among these, DSE and MPI SPECT have been widely available in routine practice [3].

Gated myocardial SPECT is recommended for simultaneous assessment of perfusion and function, and permits objective assessment of regional function [1, 4]. Although, there are some studies showing that dobutamine gated myocardial SPECT agreed well with DSE for the identification of viability in infarcted areas, the efficacy of the application of myocardial gated SPECT in this issue has not yet been fully investigated [1, 5–7].

The main purpose of this study was to compare the accuracy of low dose dobutamine stress gated myocardial SPECT with low-dose dobutamine stress echocardiography (DSE) for the identification of viable myocardium in patients with previous myocardial infarction.

Materials and methods

Participants

Twenty-two candidates for coronary artery bypass graft surgery because of stable left ventricular dysfunction were enrolled in this study. The inclusion criteria were as following: one or more myocardial wall motion abnormality on preoperative resting echocardiography (16-segment left ventricular model), absence of recent episodes of unstable angina, absence of significant valvular disease and the presence of a normal sinus rhythm. Of these, 3 patients were found to be subsequently ineligible; 5 patients agreed to join in the study, but did not attend their appointment for five examinations; 14 subjects fulfilled the eligibility criteria and participated in the study.

All patients had undergone resting echocardiography and low dose dobutamine stress echocardiography as well as resting, low and also high dose dobutamine stress 99mTc-Sestamibi gated SPECT in short intervals within 2 weeks.

The study complies with the declaration of Helsinki and was approved by the institutional ethics committee. All patients signed a written informed consent.

Imaging protocols

Dobutamine stress echocardiography

Beta-blockers, calcium channel blockers and nitrates were discontinued at least 2 days before DSE.

Echocardiography was performed with a 3.5 MHz transducer under resting conditions and during each dobutamine infusion step. After baseline echocardiography, dobutamine was delivered intravenously beginning at 5 mg/kg/min for three minutes, followed by 2.5 mg/kg/min increments every three minutes to a maximum of 10 mg/kg/min. Blood pressure was measured periodically, and the 12-lead ECG was continuously monitored throughout the study and during the recovery phase. The test was aborted if the patient experienced a severe hypotensive or hypertensive response, prolonged angina, significant electrocardiographic changes and arrhythmias, appearance of new wall motion abnormalities in at least two segments, achievement of 85% of the maximum age-predicted heart rate, or when the protocol was completed. Echocardiographic images were analyzed off-line and a 16-segment model was used [8, 9].

Wall motion, including wall thickening, of every segment was scored with a 4-point scoring system, from normal wall motion to dyskinesia.

Normal, hypokinetic, akinetic, and dyskinetic segments were scored from 1 to 4, respectively. We defined a segment as hypokinetic (HK) in the existence of minimal wall thickening with an inadequate inward motion of < 2 mm, as akinetic in the lack of systolic wall motion, and as dyskinetic in the existence of systolic outward wall motion with thinning.

Viability was mentioned to be present in a dysfunctional segment when wall motion showed an improvement of at least one point of the scoring system during the infusion of low dose dobutamine.

All studies were read by an experienced investigator who was unaware of the clinical information and the radionuclide information.

In each patient, the wall motion score index, which is the sum of the segment scores divided by 9, was acquired for baseline and dobutamine echocardiograms [10]. The difference between baseline and the dobutamine wall motion score was defined as the contractile reserve [10].

Low and high dose dobutamine protocol SPECT

A low dose, incremental infusion of dobutamine was injected intravenously at a starting dose of 5 mg/kg/min incremented by 2.5 mg/kg/min at 3-min intervals. ECG-gated SPECT was then carried out during the dobutamine infusion (10 mg/kg/min). In addition, TNG was administered in another hand via a serum micro-set accompanied with low dose dobutamine infusion. Moreover, for high dose dobutamine protocol graded infusion of dobutamine was injected intravenously at a starting dose of 10 mg/kg/min and incremented by 5 mg/kg/min at 3-min intervals and then increased to 20 mg/kg/min. The test was aborted in the case of hypotension, angina, and significant ventricular arrhythmia.

The patients underwent incessant ECG monitoring, and blood pressure was recorded at 1 min intervals using an automated cuff.

SPECT acquisition and processing

Patients were instructed to fast for at least 4 h before the study. Beta-blockers and calcium channel blockers were discontinued 48 h, and the patients were advised not to take caffeine or aminophylline 24 h before the test.

A commercial sestamibi kit (AEOI, Tehran, Iran) was used and the labeling and quality control procedures were performed according to the manufacturer's instructions.

The first gated myocardial SPECT was done after the injection of 740–925 MBq 99mTc-sestamibi at rest. The second and third gated SPECT were conducted after low or high dose dobutamine infusion, respectively. In all three protocols, radiotracer was administered intravenously; 30 min after injection of 99mTc-sestamibi, the patients were requested to eat a fatty snack to accelerate hepatobiliary excretion of the radiotracer. After 60 minutes of radiotracer administration to patients, image acquisition was performed using a rotating, dual head gamma camera (Siemens, Germany) equipped with a low-energy high resolution (LEHR) parallel hole collimator in supine position. A 20% window around the 140 keV energy peak of 99mTc-sestamibi was applied.

Thirty-two azimuth images, 60 s/projection, were acquired in a 180° circular orbit, beginning from 45° right anterior oblique to 135° left posterior oblique with step and shoot acquisition on a $64 \times 64 \times 16$ matrix and 38.5 cm detector mask (1.22 zoom) using a gated mode with prefixed R–R interval at a rate of eight frames per cardiac cycle and beat acceptance window of 40%. The raw data from stress acquisition were prefiltered by ramp and then by Butterworth filters Filtered back-projected data was rebuilt into short-axis, vertical long-axis and horizontal long-axis slices. An expert nuclear physician used the cine display of the rotating planar projections to evaluate sub-diaphragmatic activities, attenuations and patient motion to make the best of the technical quality of the images.

SPECT Image Interpretation

The interpretation of the images was based on short-axis slices, longitudinal slices, and transverse long-axis slices [9]. The analysis was performed visually with the help of quantitative measurement. For SPECT evaluation, the polar map displays were divided into 16 segments, matching with the echocardiographic ones. Endocardial wall motion was assessed visually and scored from 1 to 4 as normal, hypokinetic, akinetic, and dyskinetic respectively. Hypokinetic areas with a ≥ 1 point improvement in the score were considered as viable myocardium. Moreover, we used the wall motion score indexes (WMSIs) in three ECG-gated examinations.

The gated image sets were read independently by 2 expert observers who were unaware of patient identity or the results of DSE. Furthermore, segment tracer activity was scored by 2 using a 5-point scoring scheme: 0 — normal, 1 — mildly reduced, 2 — moderately reduced, 3 — severely reduced, and 4 — absent uptake [11]. Discrepancies were resolved by consensus.

The extent of infarct (expressed as the total number of segments with abnormal uptake), and the severity index of the infarct (calculated as the number of segments with severely decreased 99mTc-sestamibi uptake divided by the total number of segments with abnormal uptake) were determined for each infarct zone [10].

Statistical analysis

Continuous variables are expressed as mean ± SD, and categorical variables as the absolute values and percentages. The correlation between modalities for the assessment of myocardial segment viability was expressed as value of Kappa (κ). A chi-squared test was used to compare the statistical parameters of this technique. A p-value < 0.05 was considered statistically significant. Statistical analysis was performed using an IBM computer and PASW software, version 18.0 (SPSS, Inc., Chicago, IL).

Results

In total, 14 patients constituted the final study population (mean age: 54.57 years ranging from 43 to 71). Thirteen patients were men and one was woman. Median angiographic left ventricular ejection fraction was 22.5% (interquartile range, 18.75–28.75%). Six patients had two-vessel disease, defined as diameter stenosis of a major coronary artery of > 50%; and eight patients had three-vessel disease.

Mean left ventricular ejection fraction was 24.00% (19.25–31.50%) as measured by quantitative gated SPECT images was considerably increased following low and high dose dobutamine infusion (Table 1).

For analysis, a total of 224 myocardial segments from the 14 patients were evaluated. Regional contractile function, as assessed by resting ECG-gated examination, demonstrated normal contraction in 99 (44.19%) segments and abnormal contraction in 125 (55.80%) segments. We excluded the 99 normal segments. The remaining 125 dysfunctional regions were subjected to further analysis. Of the 125 dysfunctional segments, 53 (23.66% of total) were hypokinetic at rest, 64 (28.57% of total) were akinetic, and 8 (3.57% of total) were dyskinetic.

In stress echocardiography findings, 41 of the 125 dysfunctional segments (32.8%) were viable. Viability was found in 28/49 (57.14%) hypokinetic and 13/70 (18.57%) akinetic regions. All 6 dyskinetic segments were nonviable.

In low dose ECG-gated examination findings, 49 of the 125 dysfunctional segments (39.2%) were viable. Viability was found in 43/53 (81.13%) hypokinetic and 6/64 (9.37%) akinetic regions. All 8 dyskinetic segments were nonviable (Figure 1).

In high dose ECG-gated examination findings, 42 of the 125 dysfunctional segments (33.6%) were viable. Viability was found in 33/53 (62.26%) hypokinetic and 3/64 (4.68%) akinetic regions. All 8 dyskinetic segments were nonviable (Figure 1).

The mean baseline wall motion score index (WMSI) in echocardiography was [median 0.35, interquartile range (0.32–0.46)]. The dobutamine infusion protocol was concluded in all patients without complications and mean WMSI in low dobutamine echocardiography was 0.34, 0.30–0.37. According to the comparison between baseline and dobutamine WMSI, 3 patients showed no change in contractile reserve, and the remaining 11 had a decrease in WMSI (0.00, 01–0.10). All 11 patients with a significant difference in the dobutamine-induced change in WMSI showed significant LVEF improvement (> 5%).

The mean baseline WMSI in gated myocardial SPECT was [median 0.37, interquartile range (0.34–0.41)]. The low dobutamine infusion protocol was conducted in all patients without complications and mean WMSI was 0.37, 0.32–0.37. According to the comparison between baseline and dobutamine WMSI, 3 patients showed no change in contractile reserve, and the remaining 11 had a decrease in WMSI (0.00, 0.01–0.08). All 11 patients with a significant difference in the dobutamine-induced change in WMSI showed significant LVEF improvement (> 5%).

In addition, high dobutamine infusion protocol was conducted in all patients which angina occurred in 7 patients during the test. The median WMSI was 0.37, 0.33–0.40. Five patients showed new or worsening of preexisting wall motion abnormalities and higher WMSI in high-dose dobutamine infusion protocol compared with

Table 1. Patients' hemodynamics during five different modalities

	RE	LDDSE	RGMSPECT	LDDMGSPECT	HDDMGSPECT
SBP [mm Hg]	105.71 ± 17.18	110.00 ± 17.32	102.27 ± 13.66	107.72 ± 18.62	119.09 ± 23.75
DBP [mm Hg]	68.57 ± 10.69	72.85 ± 12.53	76.36 ± 14.15	74.54 ± 14.39	79.54 ± 12.73
HR	76.14 ± 12.83	80.28 ± 15.85	79.27 ± 18.18	94.36 ± 18.09	121.81 ± 23.90

RE — rest echocardiography; LDDSE — low dose dobutamine stress echocardiography; RGMSPECT — rest gated myocardial SPECT; LDDMGSPECT — low dose dobutamine myocardial gated SPECT; HDDMGSPECT — high dose dobutamine myocardial gated SPECT

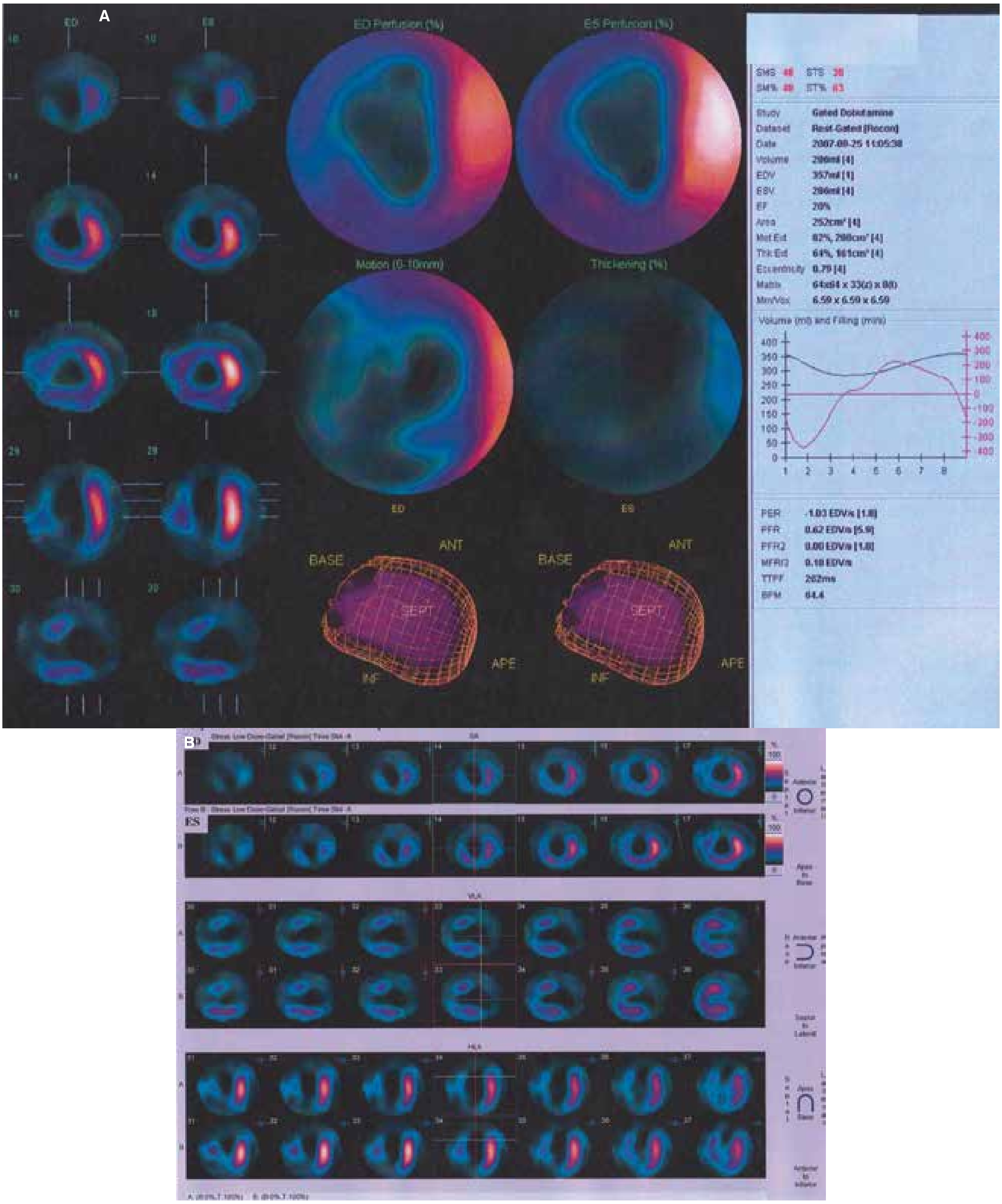
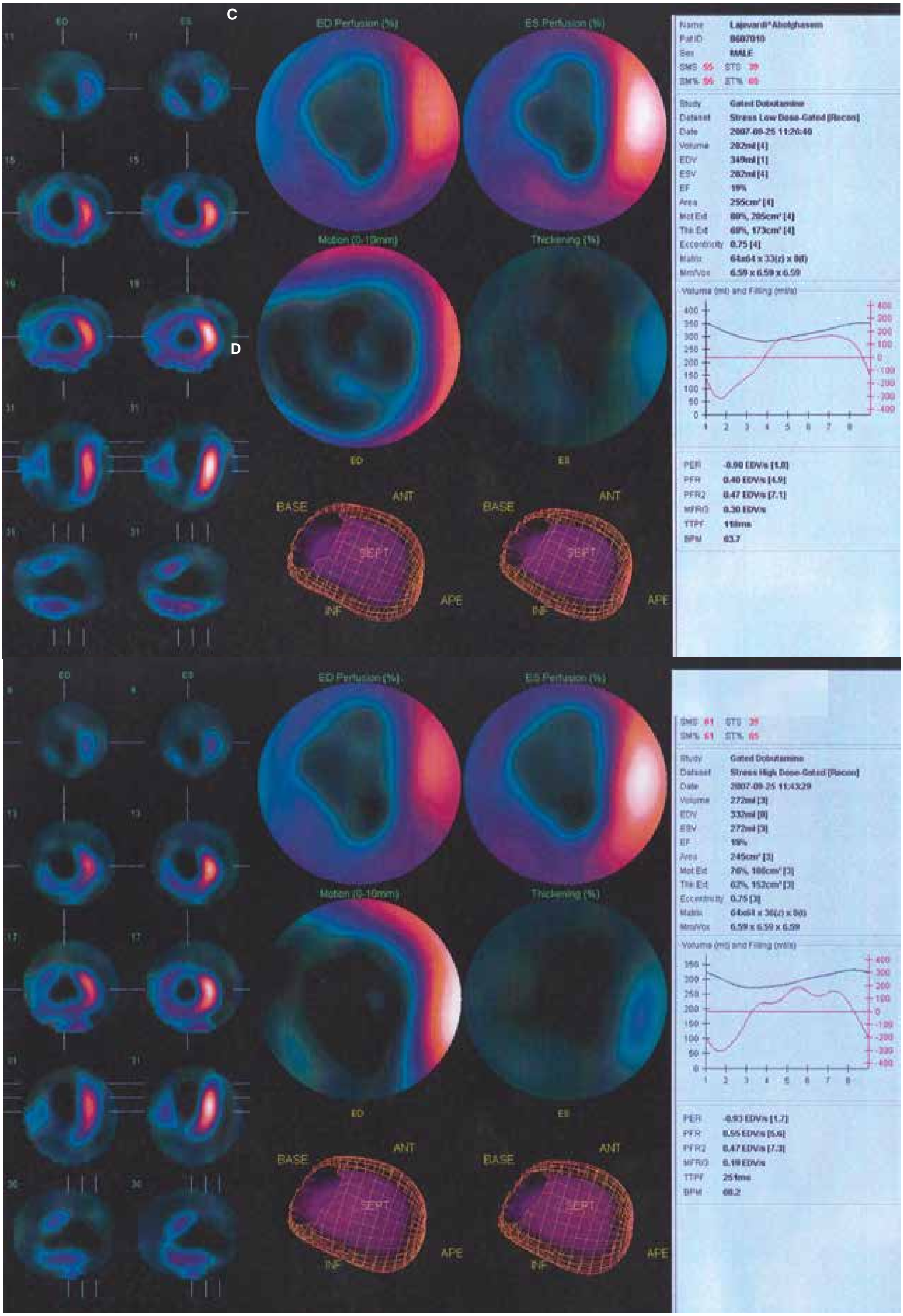


Figure 1. Five echocardiography and myocardial perfusion imaging examinations of a 64-year-old patient with two-vessel disease. Angiographic left ventricular ejection fraction was 15%. There are severe perfusion defects of mid-anterior and apex segments with extension to anteroseptal and inferior walls on the resting ECG-gated myocardial perfusion SPECT imaging (**A**). After low (**B**, **C**) and high (**D**, **E**) dose dobutamine infusion during ECG-gated myocardial perfusion imaging acquisition, there is no clear evidence of improvement of the wall motion and thickening in the aforementioned regions.

There is also moderate hypoactivity of lateral and anterolateral walls which is normalized on the delayed views. The rest of left ventricle myocardium shows partial response to dobutamine infusion. The examination demonstratedated non-viable tissues in apex, apical parts of the inferior and anteroseptal walls and mid-anterior segment. In addition, viable but ischemic myocardium (hibernated tissue) was observed in the remaining parts of the anteroseptal and inferior walls (except for its apical parts) and anterobasal segment.

Dobutamine stress echocardiography was done without any complication. It showed non-viable myocardium in anteroseptal, mid anterior, septum, anterior and apex.


C
D
ED Perfusion (%)
ES Perfusion (%)
Motion (0-10mm)
Thickening (%)
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BASE
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Figure 1. C, **D**

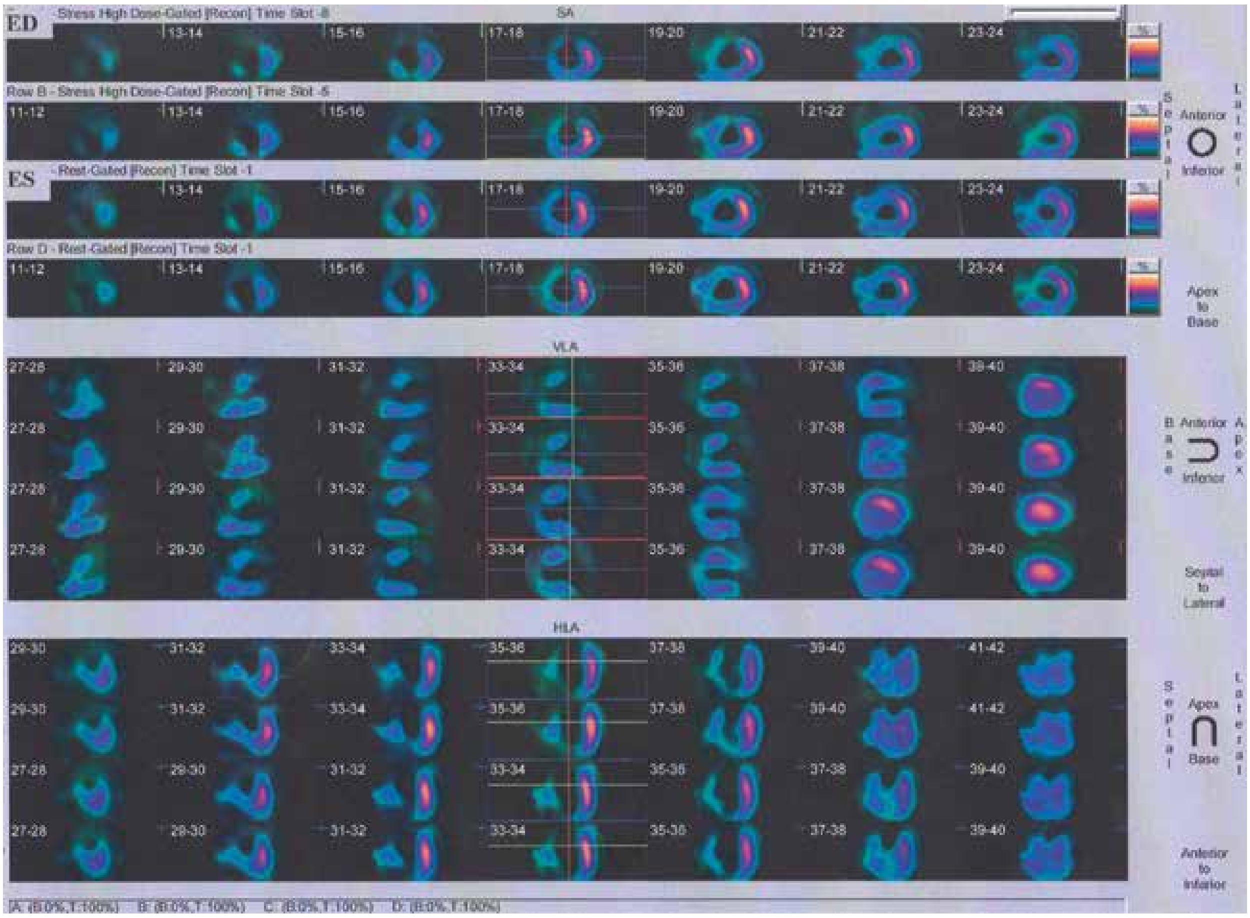

Figure 1. E

Table 2. Association between the number of abnormal perfusion segments and the severity index of the infarct variables with wall motion index score in five different examinations

	RE	P value	LDDSE	P value	RGM-SPECT	P value	LDDMG-SPECT	P value	HDDMG-SPECT	P value
Number of abnormal segments	0.733	0.002*	0.123	0.66	0.895	0.000*	0.106	0.70	0.178	0.52
Severity index	0.118	0.67	0.654	0.008	0.043*	0.87	0.82	0.000*	0.387	0.15

*Spearman's linear correlation coefficient

**The values were significant ($p < 0.05$)

RE — rest echocardiography; LDDSE — low dose dobutamine stress echocardiography; RGMSPECT — rest gated myocardial SPECT; LDDMGSPECT — low dose dobutamine myocardial gated SPECT; HDDMGSPECT — high dose dobutamine myocardial gated SPECT

low-dose dobutamine infusion protocol, whereas 3 patients did not show any change in these two protocols. On the other hand, 6 cases showed less WMSI in high dobutamine infusion protocol and showed significant LVEF improvement (> 5%).

The median number of abnormal segment was 6.50 (6.00––11.25) and the severity index of the infarct ranged from 0 to 1.00, with a median of 0.66 (0.36–1.00). The number of abnormal segments was associated with WMSI in echocardiography and gated examinations at rest whilst severity index of the infarct was associated with low-dose dobutamine echocardiography and gated examinations. In addition, the number of abnormal segments and the severity index of the infarct did not show any association with WMSI in high dose dobutamine gated examination ($p > 0.05$) (Table 2).

In general, the methods were well correlated (Table 3). The number of segments with resting wall motion abnormality considered viable by low dose dobutamine gated was significantly greater than those showing a contractile improvement in response to dobutamine in echocardiography(39.2% versus 32.8%, respectively, $p < 0.05$).

Discussion

The assessment of residual viability in regions with chronic contractile dysfunction is important for the prediction of improvement after revascularization [1, 12]. Gated SPECT has been applied for the objective assessment of left ventricular function [13, 14]. We

Nuclear Medicine Review 2014, Vol. 17, No. 1

Table 3. Agreement rate among rest and low dose dobutamine stress echocardiography as well as rest, low dose and high dose dobutamine stress ECG-gated myocardial perfusion imaging in detection of viability of different functioning segments

	RE	LDDSE	RGMSPECT	LDDMGSPECT	HDDMGSPECT
RE	—	0.59 (0.51–0.68)	0.82 (0.76–0.89)	0.63 (0.55–0.71)	0.57 (0.49–0.65)
LDDSE	0.59 (0.51–0.68)	—	0.52 (0.44–0.61)	0.77 (0.70–0.84)	0.55 (0.47–0.64)
RGMSPECT	0.82 (0.76–0.89)	0.52 (0.44–0.61)	—	0.65 (0.57–0.72)	0.68 (0.61–0.76)
LDDMGSPECT	0.63 (0.55–0.71)	0.52 (0.44–0.61)	0.65 (0.57–0.72)	—	0.75 (0.67–0.83)
HDDMGSPECT	0.57 (0.49–0.65)	0.55 (0.47–0.64)	0.68 (0.61–0.76)	0.75 (0.67–0.83)	—

*Spearman's linear correlation coefficient

**All the values were significant ($p < 0.05$)

RE — rest echocardiography; LDDSE — low dose dobutamine stress echocardiography; RGMSPECT — rest gated myocardial SPECT; LDDMGSPECT — low dose dobutamine myocardial gated SPECT; HDDMGSPECT, high dose dobutamine myocardial gated SPECT

have applied gated SPECT for the assessment of regional function under low-dose dobutamine infusion. In this study, a head-to-head comparison of the individual segments showed a 77% agreement between low-dose dobutamine stress echocardiography and ECC-gated myocardial SPECT. This finding is consistent with the previous report showing good agreement between DS SPECT and DSE in the recognition of inotropic reserve in infarcted areas [13]. Panza et al. [4] mentioned 68% agreement between DSE and thallium scan and Bax et al. [1] found 72% agreement between DSE and technetium scan. However, the prior studies did not analyze these results with other methods of viability, such as PET measurements of viability or functional recovery.

We observed discordance between the two methods in both AK and HK segments which found to be viable by 99mTc-sestamibi imaging SPECT, but did not show contractile reserve by DSE. In other words, LDD MPI SPECT (matched for echocardiographic segments) indicated the presence of viable myocardium more frequently than did LDDE in both segments.

Similar results were reported by Panza et al. [4] who tested 201thallium imaging with dobutamine echocardiography, and demonstrated that a large number of segments with 201 thallium uptake may lack contractile reserve. The difference may arise from the mechanisms of the detection of myocardial viability by the two modalities; the cellular processes dependable for a positive inotropic response to adrenergic stimulation require a higher degree of myocyte functional integrity than those responsible for thallium uptake [4].

Schinkel et al. reported 17 direct comparative studies with dissimilar settings that applied stress echocardiography and perfusion imaging in the same patients [1]. The study depicted that both methods are helpful for the evaluation of patients with chronic coronary artery disease, although small differences between their accuracy are reported in different settings. They presented that to evaluate myocardial viability after acute infarction, the techniques seem to be equally sensitive, whereas stress echocardiography is more specific [6, 9].

A previous study was performed to compare dobutamine stress echocardiography and myocardial perfusion scan to detect viable myocardium in 46 patients with coronary artery disease and low ejection fraction. They showed that the proportion of segments showing a positive response to dobutamine is significantly lower than those with technetium uptake [7]. This finding was observed in the non-gated MPI SPECT study while this study was done by gated MPI SPECT.

Low-dose dobutamine echocardiography has been used as an effective method for evaluating myocardial viability. This method can predict the recovery of regional function after revascularization with sensitivities ranging from 74% to 92% and specificities ranging from 74% to 96% [1, 2, 14]. Previous studies comparing nuclear modalities with DSE confirmed the high sensitivity and high negative predictive value of PET and thallium SPECT imaging [6, 15, 16]. In contrast, DSE was found to be slightly less sensitive but more specific for predicting functional improvement [3]. The sensitivities was 78% for DSE% vs. 76% for dobutamine myocardial SPECT, and the specificities was 96% for DSE vs. 100% for dobutamine myocardial SPECT. Therefore, DS SPECT was relatively sensitive and highly specific in predicting functional recovery [1].

Although FDG PET is considered the most reliable method for the determination of viability, it is not widely available. In addition, using FDG PET to diabetic and glucose-intolerant patients may develop some difficulties [5].

The echocardiographic approaches are attractive from both an acquisition time and an economic point of view. However, echocardiography is not suitable for obese or elderly patients with lung disease [6]. On the other hand, DS SPECT can be performed in almost every patient regardless of body size or age. In addition, because of availability of objective assessment with SPECT, gated SPECT can be used to evaluate regional wall motion, even in areas inadequately assessed by echocardiography. Thus, LDD MPI SPECT is a practical protocol that improves the detection of viability by simultaneous myocardial perfusion and motion analysis in addition to coronary flow reserve assessment in one study. Moreover no extra imaging time or radioactivity is required compared with the routine protocol [17, 18].

Meanwhile, there are some issues which need to be addressed in further studies. Firstly, in this study and most other studies, viable myocardium was considered as myocardium that depicted dysfunction at rest which gets better in function after revascularization (contractile reserve) [19]. But, we should accept the fact that myocardial viability explains myocardial cells that are alive, whether applied to a myocyte or to a segment of the myocardium, implies nothing regarding contractile state.

Secondly, although sensitivity and specificity of all modalities have been assessed by different investigations, there is no general consensus regarding the sufficient number of viable segments to forecast a better outcome after revascularization. Thirdly, the end point of all of these investigations was functional improvement and it is questionable whether other main items such as the prevention of ventricular remodeling and also life-threatening arrhythmias are better predicted by these modalities.

Study limitations

The most important limitation of this study was that we could not follow our patients after coronary artery bypass surgery. Echocardiographic and scintigraphic tests after revascularization could determine the statistical parameters of each method. In addition, although a similar 16-segment model was applied for DSE and SPECT data, misalignment may have affected the results.

The next limitation was the limited number of dysfunctional segments included in the present study, although our analysis included 224 segments. Therefore, these findings should be validated in larger and well-designed studies.

Conclusions

This study demonstrated a good agreement between low dose dobutamine gated SPECT and low dose dobutamine stress echocardiography for the detection of inotropic reserve in infarcted areas.

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