

Comparison of exercise stress testing with simultaneous dobutamine stress echocardiography and technetium-99m isonitrile single-photon emission computerized tomography for diagnosis of coronary artery disease

H. L. Kisacik*, K. Özdemir*, E. Altinyay†, A. Oğuzhan*, T. Kural, M. Kırç, E. Kütük and S. Göksel*

*Ankara Yüksek İhtisas Hospital, Department of Cardiology, Ankara, Turkey; †Ankara University Hospital, Department of Nuclear Medicine, Ankara, Turkey

The object of our study was to compare the value of exercise stress testing with simultaneous dobutamine stress echocardiography and technetium-99m isonitrile single-photon emission computed tomography for the diagnosis of coronary artery disease. Sixty-nine patients with either suspected or proven coronary artery disease underwent simultaneous dobutamine technetium-99m isonitrile single-photon emission computed tomography and stress echocardiography, and treadmill exercise electrocardiography. Dobutamine echocardiography and technetium-99m isonitrile single-photon emission computed tomography revealed a higher overall sensitivity than exercise testing (94 vs 60%, $P<0.001$), but dobutamine stress echocardiography showed a higher specificity than both technetium-99m isonitrile single-photon emission computed tomography and exercise testing (86 vs 64%, $P<0.05$, for both tests). In addition, the diagnostic accuracy of dobutamine stress

echocardiography and technetium-99m isonitrile single-photon emission computed tomography was higher than that of exercise testing (91 vs 61%, $P<0.001$; 86 vs 61%, $P<0.001$, respectively).

Dobutamine stress echocardiography and technetium-99m isonitrile single-photon emission computed tomography are superior to exercise testing in the diagnosis of coronary artery disease, and dobutamine stress echocardiography can act as an alternative to technetium-99m isonitrile single-photon emission computed tomography. (*Eur Heart J* 1996; 17: 113–119)

Key Words: Stress echocardiography, technetium-99m isonitrile single-photon emission computed tomography, dobutamine, exercise

Introduction

Coronary artery disease is common in civilized communities^[1], and the non-invasive detection of myocardial ischaemia remains an important clinical problem. Ischaemia, which can be induced by various non-invasive stress modalities such as exercise^[2–6], pharmacological agents^[7–10], atrial pacing^[11], and hand grip^[12], can be detected by electrocardiography (ECG)^[13], single-photon emission computed tomography (SPECT)^[14–17] or echocardiography^[18–21]. Exercise ECG has gained wide acceptance and application in identifying coronary artery disease. However, it is known that exercise ECG

has only a limited sensitivity, especially in patients with one-vessel disease^[10], and nuclear perfusion studies give accurate results but are expensive^[14–17]. Stress echocardiography, when compared with these, is a more common and relatively cheap method, and exercise and pharmacological stress echocardiography have recently played an increasing role in the non-invasive diagnosis of coronary artery disease^[2–10]. Compared with exercise echocardiography, pharmacological stress echocardiography has the advantage of a better quality image and can be applied in patients unable to exercise^[6]. Pharmacological stress imaging with dobutamine has recently been used in conjunction with both thallium scintigraphy and echocardiography^[7,14–21]. With both, dobutamine provided good diagnostic accuracy for the presence of coronary artery disease. However, no study had been performed comparing the diagnostic merit of

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Correspondence: Dr Halil L. Kisacik I.cadde 41/5, 06500 Bahçelievler Ankara, Turkey.

the two methods, whereas there are studies comparing dobutamine stress echocardiography with SPECT, performed by using technetium-99m isonitrile (mibi)^[22,23]. In these studies, the sensitivity of dobutamine stress echocardiography was reported to be close to that of mibi SPECT.

The aim of this study was to compare the diagnostic value of exercise ECG, dobutamine stress echocardiography and mibi SPECT, and to evaluate the correlation between dobutamine stress echocardiography and mibi SPECT for the diagnosis and detection of coronary artery disease.

Methods

Study patients

We performed treadmill exercise ECG, simultaneous dobutamine stress echocardiography and mibi SPECT in 69 patients (58 male, 11 female, mean age 51 ± 10 years, range from 29 to 70) who were referred to our clinic with chest pain and admitted for coronary angiography. Of these, 31 complained of chest pain on effort, 12 at rest and 26 both on effort and at rest. Twenty-one patients had a previous myocardial infarction, of which the locations were as follows: 7 anteroseptal, 6 anterior, 6 inferior and 2 lateral. Patients with unstable angina, recent (<2 months) myocardial infarction, cardiomyopathy, congestive heart failure, significant valvular heart disease, uncontrolled systemic hypertension, major ventricular arrhythmias or permanent pacemaker were excluded from the study. Patients with a poor basal echocardiographic window or with a medical condition that precluded adequate exercise testing were also excluded. In patients receiving treatment, beta-blockers were discontinued for ≥ 48 h and long-acting nitrates and calcium antagonists for ≥ 24 h before the tests. The study protocol was approved by the hospital ethical committee on human research and all patients gave their informed consent to the study.

Exercise test

Exercise testing was performed using the Bruce protocol with continuous electrocardiographic monitoring^[24]. Blood pressure and a 12-lead ECG were recorded at the end of each stage and at peak exercise. End points included limiting symptoms, ST segment shift >2 mm, target heart rate, severe hypertension, decrease in systolic blood pressure >20 mmHg, or significant arrhythmias. A test result was considered positive when there was ≥ 1 mm horizontal or downsloping ST segment depression 80 ms after the J point in any lead except AVR, or when ≥ 1 mm ST segment elevation in leads with no pathological Q waves.

Dobutamine stress echocardiography

Dobutamine was administered intravenously using an infusion pump at an initial dose of $5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$

followed by $5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ every 3 min until the maximum dose was $40 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. Intravenous metoprolol was administered to interrupt dobutamine-induced ischaemia. In patients not achieving 85% of age-predicted maximal heart rate, atropine (up to 1 mg) was given intravenously if necessary with the continuation of dobutamine.

Two-dimensional echocardiography was performed with a Toshiba SSA 270-A ultrasound system with a 3.75 Mhz transducer using parasternal long- and short-axis views and apical two- and four-chamber views acquired in the 30° left lateral decubitus position. Images were obtained in the four views during each stage (before dobutamine infusion—base, when $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ of dobutamine infusion had been administered—low dose, when the end point had been reached—peak dose and 12 min after stopping dobutamine infusion—recovery). A Freeland Cineview was used to display digitized images for simultaneous comparison of rest and peak studies. Eight frames/cardiac cycle, triggered from the R wave at intervals of 50 ms, were displayed.

The ECG was continuously monitored throughout the dobutamine infusion, the 12-lead ECG was recorded each minute and cuff blood pressure taken every 3 min. End points for the test included: detection of a new or worsening wall motion abnormality, systolic blood pressure >220 mmHg or diastolic pressure >120 mmHg, decrease in systolic blood pressure of >20 mmHg, major ventricular arrhythmias, achievement of the target heart rate (85% of the age-predicted maximal heart rate), ST segment shift >2 mm, and symptoms intolerable for the patient.

Echocardiographic analysis

The assessment of echocardiographic images was performed after acquisition by two experienced investigators who were blind to the patients' clinical data or coronary angiograms. When there was disagreement between the two off-line assessors, a third investigator viewed the images without knowledge of the previous assessments and a majority decision was achieved. For this semi-quantitative assessment, the left ventricular wall was divided into 16 segments, as described by The American Society of Echocardiography^[25] and scored using a four point scale: 1= normal, 2=hypokinetic, 3=akinetic, 4=dyskinetic. Both systolic wall thickening and inward wall motion were visually evaluated. An increase in score between rest and stress in one or more segments, that is, a new or worsened wall motion abnormality, constituted a positive test.

Technetium-99m mibi SPECT

Approximately 60 s before termination of the stress test, an injection of $0.2 \text{ mCi} \cdot \text{kg}^{-1}$ $^{99\text{m}}\text{Tc}$ mibi was administered. The stress mibi SPECT images were acquired, on

average, 1.5 h after the end of the dobutamine infusion. Sixty-four projections (180° scanning) were obtained with an acquisition time of 20 s/projection. For each patient, eight oblique (short axis) slices from the apex to the base, eight vertical long axis slices from the septum to the lateral wall, and eight horizontal long axis slices from the inferior to the anterior wall were defined. For resting studies, the same protocol was applied at least 24 h after the first study. Two experienced observers visually assessed the uptake of radiotracer in studies both at rest and during exercise, giving a semi-quantitative score based on a scale of 4 gradings (1=normal, 2=decreased uptake, 3=severely decreased uptake, 4=absence of uptake). A persistent perfusion defect was defined when a score ≥ 2 in one or more segments was present both during exercise and at rest. A perfusion defect was considered reversible when the score at rest improved by at least one grade with respect to the exercise scan in two or more contiguous segments. A significant but incomplete improvement of perfusion from the exercise to the rest scan (persistence of at least one segment with a score ≥ 2 in the scan at rest) was regarded as an ischaemic response and, for the purpose of data analysis, was classified as reversible.

For each technique, three different responses to stress were defined: normal (absence of rest and stress abnormalities), ischaemic (reversible scintigraphic perfusion defects and transient wall motion abnormalities during stress echocardiography) and fixed abnormalities—infarction (fixed scintigraphic perfusion defects, echocardiographic wall motion abnormalities at rest without worsening at peak stress). When both reversible and fixed defects were present, the response was classified as ischaemic. To allow a valid comparison of each technique in localizing ischaemia, the 47 segments of the left ventricle on SPECT and the 16 echocardiographic segments were grouped into the following six major regions: anterior, posterior, lateral, interventricular septum (subdivided in anterior and posterior septum) and apex. Furthermore for analysis of regional agreement the six major regions were further grouped into three myocardial areas: 1, anterior and septal; 2, posterior and lateral; and 3, apical.

All the tests and coronary angiography were performed in random order on different days within a 4-day period.

Coronary angiography

Coronary angiography and left ventriculography were performed in all patients after the tests. Angiograms were evaluated by two independent observers unaware of the patient's clinical data. A coronary stenosis was considered significant if the vessel diameter was narrowed by $>50\%$.

Statistical analysis

All data are expressed as mean \pm SD. Sensitivity, specificity, predictive value and accuracy of the tests were

Table 1 Adverse effects during dobutamine echocardiography and exercise electrocardiography (ECG)

	Dobutamine	Exercise
Symptomatic hypotension	1 (1.5%)	1 (1.5%)
Systemic hypertension	0	5 (7%)
Palpitations	19 (28%)	2 (3%)
Headache	8 (12%)	0
Tremor	3 (4.5%)	0
Nausea	8 (12%)	0
Ventricular arrhythmia	24 (35%)	8 (12%)
VPC	18 (26%)	6 (9%)
Bigeminy or couplets	5 (7%)	2 (3%)
Non-sustained VT	1 (1.5%)	0
Supraventricular arrhythmia	9 (13%)	4 (5.6%)

VPC=ventricular premature complex; VT=ventricular tachycardia.

calculated with standard formulae. Statistical significance was determined by comparing two proportions for independent groups, by using the Hypothesis tests on the Microsta Computer Programme. A *P* value <0.05 was considered statistically significant. The agreement between mibi SPECT and stress echocardiography was defined as the percentage of concordant diagnosis and was also assessed by calculating the kappa value; kappa values between 0.75 and 1 were considered indicative of good agreement, those between 0.40 and 0.75 indicative of moderate agreement and those between 0 and 0.40 indicative of poor agreement.

Results

The dobutamine and exercise stress tests were completed without serious complications in any patient (Table 1), and end points were reached in all patients. Target heart rate was reached by administering atropine in 23 (33%) patients in whom maximum heart rate was not reached during the dobutamine stress test. Changes in heart rate, systolic blood pressure and double product during dobutamine and exercise stress testing are given in Table 2. Double product at the ischaemic threshold was significantly higher during exercise than dobutamine testing.

Coronary angiography showed coronary artery disease to be evident in 47 patients and insignificant in the remaining 22. Exercise stress testing showed a sensitivity of 60% and specificity of 64%, leading to a diagnostic accuracy of 61% (Table 3). Dobutamine stress echocardiography had a 94% sensitivity for diagnosis of coronary artery disease, and 86% specificity and a 91% diagnostic accuracy. Sensitivity and specificity of dobutamine mibi SPECT were 96 and 64%, respectively, with a diagnostic accuracy of 86%. The sensitivity of dobutamine stress echocardiography and mibi SPECT in the detection of coronary artery disease was significantly higher than that of exercise stress testing (94 vs 60%, $P<0.001$; 96 vs 60%, $P<0.001$, respectively); however, stress echocardiography showed higher specificity

Table 2 Changes in heart rate, blood pressure and double product during dobutamine and exercise stress testing

	Heart rate (beats · min ⁻¹)		Systolic blood pressure (mmHg)		Double product mmHg × (beats · min ⁻¹) × 10 ⁻²	
	Basal	Peak	Basal	Peak	Basal	Peak
Dobutamine	74 ± 13	139 ± 18*	136 ± 21	156 ± 23*	101 ± 26	215 ± 40*
Exercise	79 ± 12	162 ± 20*†	138 ± 19	180 ± 33*†	110 ± 24	289 ± 66*†

* $P < 0.05$ vs basal values; † $P < 0.05$ vs peak values of dobutamine test.

Table 3 Comparative sensitivity, specificity and diagnostic accuracy of exercise electrocardiography (ECG), dobutamine technetium-99 isonitrite single-photon emission computed tomography (mibi SPECT) and dobutamine echocardiography

	Sensitivity (%)	Specificity (%)	Diagnostic accuracy (%)
Exercise ECG	28/47 (60)	14/22 (64)	42/69 (61)
Dobutamine mibi SPECT	45/47 (96)*	14/22 (64)	59/60 (84)****
Dobutamine echocardiography	44/47 (94)**	19/22 (86)***	63/69 (91)†

* $P < 0.001$ vs exercise; ** $P < 0.001$ vs exercise; *** $P < 0.05$ vs exercise and mibi SPECT, **** $P < 0.001$ vs exercise; † $P < 0.001$ vs exercise.

than both mibi SPECT and exercise stress testing (86 vs 64%, $P < 0.05$, for both). Dobutamine stress echocardiography reached the highest diagnostic accuracy, but the difference between this test and dobutamine mibi SPECT was not statistically significant ($P > 0.05$). However, the diagnostic accuracy of both dobutamine stress echocardiography and dobutamine mibi SPECT was significantly higher than that of exercise stress testing (91 vs 61%, $P < 0.001$; 86 vs 61%, $P < 0.001$, respectively). Sensitivity and specificity of ischaemic electrocardiographic changes for coronary artery disease diagnosis were 40 and 91% for dobutamine and 60 and 64% for exercise stress testing, respectively; chest pain had a sensitivity and specificity for coronary artery disease diagnosis of 45 and 86% for dobutamine, 53 and 77% for exercise testing, respectively.

Angiographic correlations

The results of tests in patients with one-, two- and three-vessel coronary artery disease are summarized in Table 4. The sensitivity of dobutamine, echocardiography and mibi SPECT in identifying one-vessel coronary artery disease was significantly higher than that of exercise stress testing (94 vs 37%, $P < 0.001$; 88 vs 37%, $P < 0.01$, respectively). In the same way, the sensitivity of dobutamine stress echocardiography and mibi SPECT was significantly higher than that of exercise testing for diagnosis of two-vessel coronary artery disease (89 vs 61%, $P < 0.05$; 100 vs 61, $P < 0.001$, respectively). The three tests showed a similar high sensitivity for detecting

three-vessel coronary artery disease (100 and 100 and 85%, $P > 0.05$, respectively). The location of stress-induced wall motion abnormalities and perfusion defects correlated with the distribution of a critically stenotic coronary artery in all patients with positive results on dobutamine stress echocardiography and mibi SPECT.

Correlation with baseline wall motion

In basal conditions, 47 patients (68%) had a normal wall motion in all segments, whereas 22 (32%) had localized wall motion abnormalities. Of the 47 patients with normal wall motion, 26 (55%) had significant coronary artery disease and 21 (45%) no critical lesion, whereas of the 22 patients with abnormal wall motion, 21 (95%) had significant coronary artery disease, and in the remaining one (5%) who had undergone percutaneous transluminal coronary angioplasty (PTCA) before, control angiography revealed no lesion. The sensitivity of dobutamine stress echocardiography for coronary artery disease was 88% in patients with normal wall motion, and 100% in those with asynergy at rest. The specificity was 90% in patients with normal wall motion. In 11 of the 22 patients with baseline wall motion abnormalities, either there was no coronary artery disease (one patient), or abnormal segment wall motion was limited to the area with coronary artery lesion; 11 showed significant lesions in at least one coronary vessel supplying regions with normal wall motion at rest. No remote wall motion abnormality developed in eight of 11 patients without remote coronary artery disease during dobutamine

Table 4 Sensitivity of exercise electrocardiography (ECG), dobutamine technetium-99m isonitrile single-photon emission computed tomography (mibi SPECT) and dobutamine echocardiography for detection of one-, two- and three-vessel coronary artery disease

	Sensitivity (%)		
	1-Vessel	2-Vessel	3-Vessel
Exercise ECG	6/16 (37)	11/18 (61)	11/13 (85)
Dobutamine mibi SPECT	14/16 (88)*	18/18 (100)****	13/13 (100)
Dobutamine echocardiography	15/16 (94)**	16/18 (89)***	13/13 (100)

* $P < 0.01$ vs exercise; ** $P < 0.001$ vs exercise; *** $P < 0.05$ vs exercise; **** $P < 0.001$ vs exercise.

		ECHO		
		Normal	Ischaemia	Infarction
SPECT	Normal	15	1	0
	Ischaemia	6	35	1
	Infarction	1	8	2

Figure 1 Results of simultaneous dobutamine echocardiography and mibi SPECT. The boxes marked 15, 35 and 2 show the number of patients classified concordantly by both methods. Infarction = a rest wall motion abnormality without further worsening during stress on echocardiography and a fixed perfusion defect on SPECT; Ischaemia = a new or worsening wall motion abnormality on echocardiography and a reversible perfusion defect on SPECT.

echocardiography (specificity for remote coronary artery disease 73%). Remote wall motion abnormalities in regions supplied by diseased vessels developed in six of 11 patients with remote coronary artery disease during dobutamine stress echocardiography (sensitivity for remote coronary artery disease 55%). The remaining five patients had worsening wall motion abnormality in the region with baseline asynergy.

Relations between wall motion and myocardial perfusion

The results of dobutamine stress echocardiography and dobutamine mibi SPECT in the 69 patients are presented in Fig. 1. Echocardiography revealed new wall motion abnormalities in 44 patients and wall motion abnormalities at rest, without further worsening at peak stress, in three patients. Test results were negative in 22 patients. On mibi SPECT, reversible perfusion defects were detected in 42 patients, and fixed perfusion defects in 11; the test results were negative in 16 patients. The

		ECHO					
		+	-		+	-	
SPECT	+	4	3		15	1	Anterior-septal
	-	10	31		1	4	
			Agreement : 78% Kappa = 0.44				
SPECT	+	10	11		6	0	Posterior-lateral
	-	0	27		1	14	
			Agreement : 82% Kappa = 0.64				
SPECT	+	8	5		9	4	Apical
	-	2	33		4	4	

Figure 2 Regional agreement for ischaemia between dobutamine echocardiography (ECHO) and ^{99m}technetium isonitrile single-photon emission computed tomography (SPECT) in 207 regions. The set of 2 × 2 tables on the left represents data of patients without previous myocardial infarction, and the column on the right represents data of those with previous myocardial infarction. The agreement was slightly higher in patients with infarction.

two methods concordantly classified 52 patients (75%, kappa=0.55). The majority of discrepancies were mainly due to pattern discordance in which both tests showed an abnormal pattern but the type of abnormality was different, that is, rest wall motion abnormality vs reversible perfusion defect (1) or new wall abnormality vs fixed perfusion defect (8). In these nine patients, both tests were definitely abnormal but, by definition, results were discordant.

The overall regional agreement was 80% (kappa=0.52). Slightly better agreement was found if the group with previous infarction was separated from that without previous infarction (82%, kappa=0.64; 78%, kappa=0.44, respectively, Fig. 2). Altogether, 42 areas were found with diverging results, 31 areas in 46 patients without previous myocardial infarction and 11 areas in 21 patients with previous infarction.

Discussion

Recognition of coronary artery disease is important for the treatment of morbidity and the prevention of mortality. Screening methods are therefore of primary importance. Exercise ECG, though widely applied, has only a limited sensitivity especially in one-vessel disease^[13]. Myocardial SPECT is a well recognized method with high sensitivity, and pooled data from exercise thallium-201 SPECT studies indicated 90% (range 82 to 98) overall sensitivity for this method of detecting coronary artery disease^[15]. The combination of dipyridamole, a pharmacological agent, with SPECT has been shown to be superior to dobutamine, because it results in flow heterogeneity and coronary artery vasodilatation leading to subendocardial ischaemia^[17]. However, this technique has the disadvantage of being expensive, exposing the patient to radiation and restricted availability.

Detection of myocardial ischaemia by exercise echocardiography was first shown by Wann *et al.* in 1979^[26]. Subsequently, promising results were reported^[2-6]. Compared to exercise echocardiography, pharmacological stress echocardiography — which depends on the principle of induction of ischaemia by pharmacological agents and detection of this echocardiographically — has advantages such as fewer motion artifacts, allowing examination of patients unable to perform physical exercise, low cost, and wide availability of equipment^[6]. The combination of dobutamine^[27], which acts in a similar way to physical exercise by increasing myocardial oxygen demand on induction of ischaemia with echocardiography, is the preferred choice^[7,9-10,18-21]. In these studies the sensitivity, specificity and diagnostic accuracy of dobutamine stress echocardiography ranged from 54%^[19] to 95%^[20], 78%^[9] to 93%^[18], and 67%^[19] to 92%^[20], respectively. To our knowledge, there are only two studies in which simultaneous stress echocardiography and mibi SPECT have been compared^[22-23], but they were not compared with exercise stress testing, and in one of them^[22] coronary angiography was not considered as a standard reference in most of the patients. In the current study, ischaemia, which was induced at the same dobutamine stress levels, was detected by echocardiography and perfusion scintigraphy and, using coronary angiography as the standard reference, comparisons were made with exercise echocardiography. The results suggest that dobutamine echocardiography has comparable sensitivity to dobutamine stress perfusion scintigraphy and that the extent of perfusion and wall motion abnormalities shows a similar correlation with the anatomical extent of coronary artery disease. Dobutamine echocardiography and mibi SPECT showed a higher sensitivity than exercise electrocardiography for the diagnosis of coronary artery disease. This difference is mainly due to the significantly higher sensitivity of dobutamine echocardiography and mibi SPECT in detecting one-vessel coronary artery disease, whereas the ability of the three tests to detect multivessel coronary artery disease is comparable.

Among the studies comparing dobutamine echocardiography with exercise testing, the one performed by Hoffman *et al.*^[6] reported that the sensitivity of dobutamine echocardiography was significantly higher than that of exercise testing and this significantly higher sensitivity was due to superiority of dobutamine echocardiography in detecting one-vessel disease, whereas there was no significant difference in the sensitivities of either test in detecting multivessel disease.

Among the studies comparing dobutamine mibi SPECT with dobutamine echocardiography, in the one performed by Forster *et al.*^[22], coronary angiography was carried out in only 21 patients and the sensitivity of dobutamine mibi SPECT and echocardiography was 83 and 75%, respectively; the specificity for both tests was 89%. In the study by Marwick *et al.*^[23], coronary angiography was performed in all the patients enrolled in the study and the sensitivity for dobutamine mibi SPECT and echocardiography was 76 and 72%, respectively; the specificity was 67 and 83%, respectively, for the same tests when coronary angiography was considered as the standard reference. Compatible with the results^[22,23], in our study dobutamine mibi SPECT also reached the highest sensitivity, but as its specificity was relatively lower than that of echocardiography, its diagnostic accuracy has also remained lower.

In our study, we reached compatible results in 52 patients by both tests (agreement=75%, kappa=0.55). In the study performed by Forster *et al.*^[22], agreement was found between the two tests in 69 of the patients (agreement=68%, kappa=0.51). In patients with baseline asynergy, dobutamine echocardiography showed a specificity for detecting remote coronary artery disease comparable to that reported by Sawada *et al.*^[7], whereas the 55% sensitivity found in our study was lower than that reported (81%) in the same study^[7]. This discrepancy may be explained by the fact that in our study five of 11 patients with remote coronary artery disease had worsening asynergy in the region with baseline wall motion abnormalities before remote asynergy could develop.

Conclusion

In this study, dobutamine stress echocardiography had a similar sensitivity but a higher specificity than that of dobutamine mibi SPECT and it reached the highest diagnostic accuracy. When the disadvantages, such as inadequate diagnostic accuracy of exercise electrocardiography, high cost of perfusion scintigraphy, limited availability of equipment and exposure of the patient to radiation were considered, dobutamine stress echocardiography could be seen as a positive alternative to these tests.

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