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Adenosine Technetium-99m Sestamibi Myocardial Perfusion SPECT in Women: Diagnostic Efficacy in Detection of Coronary Artery Disease

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Objectives. **This study sought to assess the diagnostic efficacy of adenosine technetium-99m (Tc-99m) sestamibi myocardial perfusion single-photon emission computed tomography (SPECT) in a consecutive series of female patients.**

Background. **The utility of adenosine myocardial perfusion SPECT for the detection of coronary artery disease is not well defined in women because most studies have described a predominantly male population with a high prevalence of coronary artery disease.**

Methods. **Of the 201 consecutive female patients in the study group who had undergone adenosine Tc-99m sestamibi myocardial perfusion SPECT, 130 had coronary angiography within 2 months of the nuclear test, and the other 71 had a low likelihood (<10%, mean [±SD] 5 ± 3%) of coronary artery disease. The SPECT protocol used separate acquisition of rest thallium-201 and adenosine Tc-99m sestamibi and was visually analyzed in 20 segments with a semiquantitative five-point scoring system (0 = normal; 4 = absent uptake).**

Results. **The normalcy rate in patients with a low likelihood of coronary artery disease was 93% (66 of 71). Among the catheterized group, the overall sensitivity, specificity and predictive accuracy of adenosine sestamibi SPECT for detecting coronary artery disease (≥50% diameter stenosis) were 93% (87 of 94), 78% (28 of 36) and 88% (115 of 130), respectively. In the 103 patients without a prior myocardial infarction, the sensitivity, specificity and predictive accuracy were 91% (61 of 67), 78% (28 of 36) and 86% (89 of 103), respectively, for detecting ≥50% diameter stenosis. Of particular interest, the sensitivity and specificity were as high in patients with nonanginal symptoms (93% and 69%, respectively) as in patients with angina (92% and 83%, respectively, p = NS). The sensitivity and specificity among patients with a relatively low (<25%), intermediate (between 25% and 75%) or high prescan likelihood of coronary artery disease (>75%) were similar: 82% and 82%, 93% and 73%, and 95% and 100%, respectively. The sensitivity and specificity for detecting individual diseased vessels (≥50% diameter stenosis) were, respectively, 76% and 81% for the left anterior descending coronary artery, 44% and 90% for the left circumflex coronary artery and 75% and 77% for the right coronary artery.**

Conclusions. **Adenosine Tc-99m sestamibi SPECT is an efficient protocol with high sensitivity and specificity for the detection of coronary artery disease in women irrespective of presenting symptoms or pretest likelihood of coronary artery disease and a high normalcy rate. These findings are of particular clinical relevance because chest pain, anginal or otherwise, has been shown to be a frequent but a less specific marker for coronary artery disease among female patients.**

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Although the prevalence of coronary artery disease matched for age is lower in young and middle-aged women than men, it increases markedly after the age of 45 years and is as high as that in men by the age ≥75 years (1). Detection of coronary artery disease by noninvasive testing poses greater difficulty in women than in men. Exercise electrocardiography has been shown to be less accurate in women than men, principally because of a higher incidence of false positive results, and anginal symptoms are also less specific in women than men (2–4). Although numerous studies have demonstrated that myocardial perfusion single-photon emission computed tomography (SPECT) is an accurate method for the detection of coronary artery disease (5), few have addressed the sensitivity and specificity of SPECT in women. What little has been written has dealt with exercise stress. Pharmacologic stress testing with adenosine or dipyridamole in conjunction with myocardial perfusion SPECT is commonly used to detect coronary artery disease in patients who cannot perform adequate exercise and in a cohort of mixed genders has been shown (6,7) to have virtually identical sensitivity and specificity to exercise stress. In women, however, the diagnostic accuracy of adenosine myocardial SPECT is not well defined because most studies have included predominantly male patients (7).

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Table 1. Clinical Characteristics of Study Patients

	Catheterized Group (n = 130)	Group With Low Likelihood of CAD (n = 71)
Age (yr)	72 ± 10	56 ± 10
Race		
White	105 (81%)	41 (58%)
Black	23 (18%)	11 (15%)
Hispanic	1 (1%)	12 (17%)
Asian	1 (1%)	7 (10%)
Relative breast size		
A or B	50 (38%)	30 (42%)
C or D	80 (62%)	41 (58%)
BSA (m^2)	1.7 ± 0.2	1.8 ± 0.2
Presenting symptoms		
Typical angina	23 (18%)	0 (0%)
Atypical angina	51 (39%)	0 (0%)
Nonanginal chest pain	22 (17%)	11 (15%)
Asymptomatic	21 (16%)	55 (77%)
Shortness of breath	13 (10%)	5 (7%)
Diabetes mellitus	41 (32%)	16 (23%)
Systemic hypertension	86 (66%)	24 (34%)
Prior MI	27 (21%)	0 (0%)
MI location		
Anterior	3 (11%)	—
Inferior	6 (22%)	—
Lateral	1 (4%)	—
Nonspecific	17 (63%)	—
Prescan likelihood of CAD (%)	59 ± 30	5 ± 3

Data presented are mean value (±SD) or number (%) of patients. BSA = body surface area; CAD = coronary artery disease; MI = myocardial infarction.

Recently, technetium-99m (Tc-99m) sestamibi has become widely used for detection of coronary artery disease and is considered particularly suited for female patients because of its higher energy and reported reduced susceptibility to breast attenuation artifacts than that of thallium (8). Currently, it is estimated that nearly 40% of myocardial perfusion SPECT in women is performed with Tc-99m sestamibi, and a large proportion of these studies are done using adenosine pharmacologic stress. Thus, the present study was undertaken to assess the diagnostic efficacy of adenosine Tc-99m sestamibi SPECT in a large consecutive series of female patients.

Methods

Study patients. The study included two groups: a catheterized group (130 patients) and a group with a low prescan likelihood of coronary artery disease (71 patients) (Table 1). The catheterized group included 130 consecutive women who underwent adenosine Tc-99m sestamibi myocardial perfusion SPECT at Cedars-Sinai Medical Center, Los Angeles, California between January 1991 and August 1994 and had diagnostic coronary angiography within 2 months of the nuclear test (30 patients before and 100 patients after the nuclear test). Patients with recent acute myocardial infarction (<72 h), unstable angina (<24 h), a history of revascularization before the nuclear test or coronary angiography and known valvular heart disease of hemodynamic significance were excluded from the study. Prior myocardial infarction, defined by history or electrocardiographic (ECG) Q waves, was present in 27 patients (21%). The angiographic characteristics of the catheterized group are shown in Table 2. Of the 130 patients studied, 94 had angiographic evidence of significant coronary artery disease when the criterion of ≥50% narrowing was considered significant. With the criterion of ≥70% coronary artery narrowing as significant, the number of patients with significant coronary artery disease was 83.

Table 2. Angiographic Characteristics of Catheterized Group Patients

	≥50% Diameter Stenosis (no. of pts)	≥70% Diameter Stenosis (no. of pts)
Normal/minor CAD (<50% diameter stenosis)	36	47
One-vessel CAD	32	35
Two-vessel CAD	30	28
Three-vessel CAD	32	20
Total with significant CAD	94	83

CAD = coronary artery disease; pts = patients.

To determine the normalcy rate (9–11), we studied a separate consecutive group of 71 women (mean [±SD] age 56 ± 10 years) who had a low prescan likelihood of angiographically significant coronary artery disease (<10%, mean 5 ± 3%) on the basis of age, gender, risk factors and symptom classification as calculated by CADENZA (12,13) and underwent clinically ordered adenosine Tc-99m sestamibi myocardial perfusion SPECT.

To analyze the sensitivity and specificity as a function of the prescan likelihood of coronary artery disease, the catheterized group were further categorized into those with a relatively low (<25%, mean 15 ± 6%, 22 patients), intermediate (25% to 75%, mean 50 ± 11%, 68 patients) and high (>75%, mean 97 ± 5%, 40 patients) prescan likelihood of coronary artery disease. The likelihood of coronary artery disease was defaulted to 100% in the 27 patients with a prior myocardial infarction. For the purpose of determining test sensitivity, the catheterized group were also categorized into those with angina pectoris (typical or atypical angina [74 patients]) and with nonanginal symptoms (nonanginal chest pain, shortness of breath, or asymptomatic [56 patients]). The prescan likelihood of coronary artery disease among patients with angina and with nonanginal symptoms was 72 ± 22% and 42 ± 31%, respectively ($p < 0.001$). Specific exclusion criteria for both groups relating to the use of adenosine were a history of asthma or other bronchospastic condition, hypotension (systolic blood pressure <85 mm Hg), decompensated congestive heart failure, presence of sick sinus syndrome, second- or third-degree atrioventricular (AV) block or concomitant oral dipyridamole treatment.

Adenosine Tc-99m sestamibi myocardial perfusion SPECT protocol (Fig. 1). Adenosine myocardial perfusion SPECT was performed using a rest thallium-201/stress Tc-99m sesta-

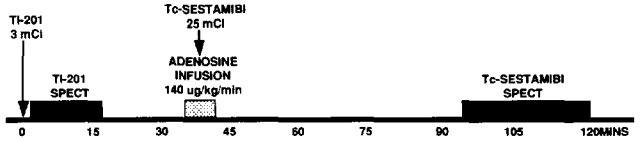

Figure 1. Injection and acquisition protocol for adenosine dual-isotope study. Tc-SESTAMIBI = technetium-99m sestamibi; Tl-201 = thallium-201.

mibi separate acquisition protocol recently described by our group (14) and validated with exercise (10) and pharmacologic stress (11) in mixed gender populations. Patients were instructed not to consume coffee or caffeine-containing products for 24 h before the test. Thallium-201 (2.5 to 3.5 mCi) was injected at rest, and SPECT was performed 10 min later. After baseline ECG, heart rate and blood pressure measurements, adenosine was infused at a rate of 140 μg/kg body weight per min through an antecubital vein with an infusion pump for 6 min. At the end of the third minute of infusion, a 20- to 30-mCi dose of Tc-99m sestamibi was injected intravenously through an antecubital vein in the opposite arm. Leads V_1, V_5 and aVF were continuously monitored, and a 12-lead ECG and blood pressure were monitored at each minute of adenosine infusion. Significant ST segment depression during adenosine stress test was defined as ≥1 mm of horizontal or downsloping or ≥1.5 mm of upsloping ST segment depression occurring 80 ms after the J point. Technetium-99m sestamibi SPECT imaging was begun ~60 min after the radiopharmaceutical injection.

SPECT acquisition protocol. In all SPECT acquisitions, a large field of view gamma camera and a high resolution collimator were used to obtain 64 projections at 20 s/projection over a semicircular 180° arc extending from the 45° right anterior oblique to the 45° left anterior oblique position. For thallium-201 imaging, two energy windows were utilized, a 30% window centered on the 68- to 80-keV peak and a 10% window centered on the 167-keV peak. For Tc-99m sestamibi SPECT, a 15% window centered on the 140-keV peak was used. All projection images were stored on a magnetic disk with the use of a 64 × 64 16-bit matrix. All images were subject to quality control measures, including cinematic display for assessment of patient motion and corrections for field nonuniformity and center of rotation (10). Preprocessing was performed using a Butterworth filter, order 10, with a cutoff frequency of 50% Nyquist for thallium-201 and a Butterworth filter, order 5, with a cutoff frequency of 66% Nyquist for Tc-99m sestamibi images. Short-axis as well as vertical and horizontal long-axis tomograms of the left ventricle were extracted from the filtered transaxial tomograms by performing coordinate transformation with appropriate interpolation. No attenuation or scatter correction was used.

Image interpretation. Visual interpretation was performed using short-, vertical long- and horizontal long-axis tomograms and a 20-segment model as previously described (10). These segments were assigned on six evenly spaced regions in the apical, midventricular and basal slices of the short-axis views and two apical segments on the midventricular vertical long-axis slice. Each segment was scored by consensus of two expert observers using a five-point scoring system (0 = normal; 1 = equivocal; 2 = moderate; 3 = severe reduction of isotope; and 4 = absence of detectable tracer uptake in a segment). The SPECT study results were judged abnormal if there were two or more segments with a stress score ≥2 or at least one segment with a stress score ≥3. A reversible perfusion defect was defined as a stress defect (score 2 to 4) associated with a rest score ≤1 or a stress defect with a score of 4 and an associated rest score of 2. Defects considered secondary to breast attenuation were assigned scores of 1. Similarly, fixed stress defects considered secondary to attenuation were scored 1.

Assignment of tomographic myocardial segments to coronary artery territories. The method of assignment of tomographic myocardial segments to vascular territories was performed as previously described (10,11). An abnormal coronary territory was defined as having at least one segment with stress perfusion defect score ≥2.

Coronary angiography. All coronary angiograms were acquired using the Judkins method and were analyzed by two observers who were unaware of the clinical or scintigraphic data. No patient had any cardiac event in the interval between dual-isotope SPECT and coronary angiography. For the definition of significant coronary artery disease, two arbitrary cutoff points were used: ≥50% and ≥70% diameter narrowing of a major coronary artery or one of its major branches. Left main coronary artery stenosis in the absence of other diseases in the left anterior descending or left circumflex artery was regarded as two-vessel disease, and ≥50% to ≥70% left main stenosis were lumped to ≥70% stenosis criteria.

Statistical analysis. Results are expressed as mean value ± SD. Comparisons between groups of continuous variables were made using paired and unpaired Student *t* tests. Comparisons of proportions were computed by using a chi-square statistic or when appropriate by using the Fisher exact test. A p value <0.05 was considered statistically significant. Normalcy rate was defined as the proportion of patients with a low likelihood of coronary artery disease who had normal scintigraphic study results (9). Sensitivity, specificity and predictive accuracy were calculated as follows: Sensitivity (%) = 100 × (True positive results)/(True positive results + False negative results); specificity (%) = 100 × (True negative results)/(True negative results + False positive results); and predictive accuracy (%) = 100 × (True positive results + True negative results)/(Total number of patients).

Results

Sensitivity and specificity for detection of coronary artery disease and normalcy rate. The overall sensitivity, specificity and predictive accuracy of adenosine Tc-99m sestamibi SPECT for detecting coronary artery disease defined by ≥50% stenosis were 93% (87 of 94), 78% (28 of 36) and 88% (115 of 130),

Table 3. Sensitivity, Specificity, Predictive Accuracy and Normalcy Rate of Adenosine Technetium-99m Sestamibi SPECT

Patient category	≥50% Diameter Stenosis			≥70% Diameter Stenosis			Normalcy Rate
	Sensitivity	Specificity	Predictive Accuracy	Sensitivity	Specificity	Predictive Accuracy	
Low likelihood of CAD (<10%, n = 71)							93% (66/71)
Catheterized group							
All (n = 130)	93% (87/94)	78% (28/36)	88% (115/130)	95% (79/83)	66% (31/47)	85% (110/130)	
No prior MI (n = 103)	91% (61/67)	78% (28/36)	86% (89/103)	95% (54/57)	67% (31/46)	83% (85/103)	
Anginal (n = 74)	92% (47/51)	83% (19/23)	89% (66/74)	96% (44/46)	75% (21/28)	88% (65/74)	
Nonanginal (n = 56)	93% (40/43)	69% (9/13)	88% (49/56)	95% (35/37)	53% (10/19)	80% (45/56)	
Relatively low likelihood of CAD (<25%, n = 22)	82% (9/11)	82% (9/11)	82% (18/22)	88% (7/8)	71% (10/14)	77% (17/22)	
Intermediate likelihood of CAD (25% to 75%, n = 68)	93% (43/46)	73% (16/22)	87% (59/68)	97% (38/39)	62% (18/29)	82% (56/68)	
High likelihood of CAD (>75%, n = 40)	95% (35/37)	100% (3/3)	95% (38/40)	94% (34/36)	75% (3/4)	93% (37/40)	

Data presented are percent (number) of patients. CAD = coronary artery disease; MI = myocardial infarction.

respectively, whereas the corresponding results were 95% (79 of 83), 66% (31 of 47) and 85% (110 of 130), respectively, for detecting coronary artery disease with the ≥70% stenosis criterion (Table 3). Among 71 patients with a low prescan likelihood of coronary artery disease, the normalcy rate was 93%. In 103 patients without a prior myocardial infarction, the sensitivity, specificity and predictive accuracy were 91% (61 of 67), 78% (28 of 36) and 86% (89 of 103), respectively, for detecting ≥50% stenosis and 95% (54 of 57), 67% (31 of 46) and 83% (85 of 103), respectively, for detecting ≥70% stenosis.

Sensitivity for detection of patients with coronary artery disease as a function of number of stenotic vessels. In patients with single-vessel disease, 84% (27 of 32) with ≥50 diameter stenosis and 91% (32 of 35) with ≥70% diameter stenosis were correctly detected as having an abnormal response by adenosine Tc-99m sestamibi SPECT. The corresponding sensitivities were, respectively, 93% (28 of 30) and 96% (27 of 28) for double-vessel disease and 100% (32 of 32) and 100% (20 of 20) for triple-vessel disease.

Detection of individual diseased vessels. By the ≥50% diameter stenosis criterion, the sensitivities and specificities for detecting individual diseased coronary arteries were, respectively, 76% and 81% for the left anterior descending coronary artery, 44% and 90% for the left circumflex coronary artery and 75% and 77% for the right coronary artery, whereas the corresponding results by the ≥70% diameter stenosis criteria were, respectively, 83% and 77% for the left anterior descending artery, 54% and 89% for the left circumflex artery and 77% and 71% for the right coronary artery. For both ≥50% and ≥70% diameter stenosis criteria, the sensitivities for the detecting a diseased left circumflex artery were lower than those for the other vessels ($p < 0.05$ for both the left anterior descending and right coronary arteries).

Sensitivity and specificity by symptom classification. Among patients with symptoms of angina, the sensitivity and specificity of adenosine Tc-99m sestamibi SPECT for detecting coronary artery disease with ≥50% diameter stenosis were 92% (47 of 51) and 83% (19 of 23), respectively, and the corresponding values for the group of patients with nonanginal symptoms were 93% (40 of 43) and 69% (9 of 13), respectively (p = NS) (Table 3). For the ≥70% diameter stenosis criterion, the sensitivity and specificity were, respectively, 96% (44 of 46) and 75% (21 of 28) in patients with angina and 95% (35 of 37) and 53% (10 of 19) in patients with nonanginal symptoms (p = NS).

Sensitivity and specificity as a function of pretest likelihood of coronary artery disease. Among the catheterized group with a relatively low prescan likelihood of coronary artery disease, the sensitivity and specificity of adenosine Tc-99m sestamibi SPECT for detecting coronary artery disease with ≥50% stenosis were 82% (9 of 11) and 82% (9 of 11), respectively, whereas the corresponding values were 93% (43 of 46) and 73% (16 of 22), respectively, for patients with an intermediate prescan likelihood of coronary artery disease. For patients with a high prescan likelihood of coronary artery disease, the test sensitivity and specificity were 95% (35 of 37) and 100% (3 of 3), respectively. Comparisons between sensitivity and specificity among the three subgroups yielded no statistical significance (Table 3). With the ≥70% diameter stenosis criterion, the sensitivity and specificity were, respectively, 88% (7 of 8) and 71% (10 of 14) for patients with a low prescan likelihood, 97% (38 of 39) and 62% (18 of 29) for patients with an intermediate prescan likelihood and 94% (34 of 36) and 75% (3 of 4) for a high prescan likelihood of coronary artery disease (p = NS).

Sensitivity and specificity in patients with hypertension and left ventricular hypertrophy. Among patients with a history of systemic hypertension (n = 86), the sensitivity and specificity of adenosine Tc-99m sestamibi SPECT for detecting coronary artery disease with ≥50% diameter stenosis were 94% (63 of 67) and 74% (14 of 19), respectively, whereas for the ≥70% diameter stenosis criterion, the corresponding results were 97% (57 of 59) and 59% (16 of 27), respectively. Electrocardiographic evidence of left ventricular hypertrophy (15) was present in 24 of these patients (28%). In this small

Table 4. Frequency of Adverse Effects During Adenosine Infusion

Symptom	Catheterized Group (n = 130)	Group With Low Likelihood of CAD (n = 71)
Chest or throat pain	46 (35%)	12 (17%)
Flushing	21 (16%)	14 (20%)
Dyspnea	17 (13%)	10 (14%)
Headache	20 (15%)	9 (13%)
Nausea	6 (5%)	12 (17%)
AV block II	4 (3%)	0 (0%)
GI discomfort	10 (8%)	6 (8%)
Light-headedness	5 (4%)	2 (3%)

Data presented are number (%) of patients. AV = atrioventricular; CAD = coronary artery disease; GI = gastrointestinal.

subset, the sensitivity and specificity were 94% (17 of 18) and 67% (4 of 6), respectively, for detecting ≥50% diameter stenosis and 94% (16 of 17) and 57% (4 of 7), respectively, for detecting ≥70% diameter stenosis.

Hemodynamic effects. Adenosine caused a significant increase in heart rate (72 ± 15 vs. 84 ± 17 beats/min, $p < 0.001$) and a significant decrease in systolic and diastolic blood pressure (157 ± 32 vs. 138 ± 36 mm Hg, $p < 0.001$; 77 ± 13 vs. 66 ± 16 mm Hg, $p < 0.001$, respectively). There was a slight but significant increase in rate–blood pressure product during adenosine infusion ($p = 0.015$).

Frequency of adverse side effects. Adverse side effects are summarized in Table 4. Adverse effects were seen in 73% (95 patients) of the catheterized group and 58% (41 patients) of the group with a low likelihood of coronary artery disease. Most of the side effects were mild, and virtually all were transient in nature. No patient developed third-degree AV block during adenosine infusion. Transient second-degree AV block was observed in four patients; none required early termination of infusion. No serious event (acute myocardial infarction, death or sustained arrhythmias) occurred as a result of adenosine infusion.

Electrocardiographic changes during adenosine infusion. Ischemic ST segment depression occurred in only 13 patients, all in the catheterized group. Angiographic evidence of significant coronary artery disease was present in all these patients. The sensitivity of adenosine-induced ST segment depression in detecting significant coronary artery disease with ≥50% diameter stenosis was low at 14% (13 of 94), whereas the specificity was 100% (36 of 36). For ≥70% diameter stenosis, the corresponding results were 16% (13 of 83) and 100% (47 of 47), respectively.

Discussion

Sensitivity, specificity and predictive accuracy for detection of coronary artery disease. The present study demonstrates that adenosine Tc-99m sestamibi myocardial perfusion SPECT is highly accurate for the detection of coronary artery disease in women irrespective of the presenting symptoms or the pretest likelihood of coronary artery disease. The overall sensitivity, specificity and predictive accuracy of adenosine sestamibi SPECT for detecting coronary artery disease (≥50% diameter stenosis) were 93%, 78% and 88%, respectively. Because contamination with patients who had previous myocardial infarction could partly inflate the test sensitivity, subanalysis was performed in the subgroup of patients without a prior myocardial infarction, and it demonstrated similarly high sensitivity (91%), specificity (78%) and predictive accuracy (86%). In the present series of 130 women, the high sensitivities and specificities were similar to previous reports of adenosine myocardial perfusion imaging using thallium-201 or Tc-99m sestamibi in a predominantly male cohort (7).

Comparisons of previous studies. To our knowledge, no studies to date have assessed the sensitivity and specificity of adenosine myocardial perfusion SPECT specifically in women. What little has been reported in women has been in exercise studies and has used predominantly the planar imaging technique with thallium-201 (16–18). Hung et al. (17) demonstrated in 92 symptomatic women that exercise planar thallium-201 perfusion variables provided incremental value in the diagnosis of coronary artery disease over exercise and electrocardiographic variables. Previous studies (16–18) that analyzed the diagnostic accuracy of exercise planar myocardial perfusion scintigraphy demonstrated sensitivities between 70% and 75%, and the specificities exceeded 90%. With exercise myocardial perfusion SPECT, Chae et al. (19) demonstrated in women a sensitivity of 71% and a specificity of 65%, whereas Van Train et al. (9,20), by separate analysis of female patients, demonstrated a sensitivity and specificity of 95% and 62% using exercise thallium-201 and 94% and 31% using exercise Tc-99m sestamibi. The apparent decline in test specificity in the latter studies (9,19,20) is probably related to the increasing prevalence of posttest referral bias, whereby positive nuclear test responders were preferentially referred for coronary angiography (21). Exercise echocardiography for detection of coronary artery disease in women has also been reported (22,23) and has demonstrated sensitivities and specificities ranging from 80% to 88% and 46% to 86%, respectively. However, only one published study (24) of dipyridamole pharmacologic stress echocardiography has been reported. That study (24) showed a sensitivity of 79% and a specificity of 93% in 83 women. Therefore, although two-dimensional echocardiography may potentially offer comparable results to adenosine myocardial perfusion SPECT, the number of patients studied for pharmacologic stress echocardiography is still too small for comparative evaluation.

Normalcy rate. Because of the inherent posttest referral bias (21), our group has advocated the use of the normalcy rate as a proxy for specificity in myocardial perfusion studies (9). In the present study, the normalcy rate of adenosine Tc-99m sestamibi SPECT in a group of 71 women with a low likelihood of coronary artery disease was high at 93%. Similarly, high normalcy rates have been reported in mixed-gender groups by our group with exercise (95%) (10) and pharmacologic stress dual-isotope SPECT (96%) (11). These results are higher than

the previously reported normalcy rates with thallium-201 SPECT, which ranged from 82% to 89% (25–27). The apparent improvement in the normalcy rate by the sestamibi studies is most likely related to the generally improved image quality afforded with Tc-99m sestamibi and the ability to repeat studies with this agent when artifact is suspected on the initial acquisition. Unlike thallium-201, Tc-99m sestamibi demonstrates minimal redistribution over time (8,28). Therefore, repeat acquisition may be performed without concerns of underestimating stress perfusion defect size or severity.

Patients with nonanginal or atypical chest pain syndrome or with low to intermediate pretest likelihood of coronary artery disease. In women with atypical chest pain or with low to intermediate pretest likelihood of coronary artery disease, the noninvasive detection of coronary artery disease is particularly challenging. There is a smaller prevalence of coronary artery disease in this patient group (29), which may affect test sensitivity and specificity (30). Nonetheless, it has been shown that serial noninvasive testing, including exercise thallium-201, may be effective in arriving at the proper diagnosis in these patients (18). In the present series, among patients who presented with nonanginal symptoms, the diagnostic accuracy of adenosine Tc-99m sestamibi was high and was not different from that among the patients presenting with anginal symptoms and thus a higher prescan likelihood of coronary artery disease (Table 3). Further analysis along these lines showed that patients with low to intermediate prescan likelihood of coronary artery disease had a high test accuracy similar to those patients with a high prescan likelihood of coronary artery disease. These findings have direct clinical relevance because the utility of nuclear studies to provide accurate diagnosis in these patients subgroups will have an impact on the management process of these patients with suspected coronary artery disease.

ST segment depression and frequency of side effects during adenosine infusion. The frequency of ST segment depression during adenosine infusion was low (10%). The sensitivity of adenosine stress electrocardiography for detecting significant coronary artery disease was also low (14% to 16%), whereas the specificity was very high (100%). These results were in agreement with the previous studies using pharmacologic coronary vasodilators in the predominantly male cohort (31–35). Similar to the findings from the adenosine multicenter trial registry (36) and other studies with a predominantly male cohort (31–35), the majority of patients in our series of 201 women experienced side effects (Table 4), most of which, however, were mild and transient in nature.

Use of rest thallium-201/adenosine Tc-99m sestamibi separate-acquisition dual-isotope myocardial perfusion SPECT. The imaging protocol used in this study, rest thallium-201/stress Tc-99m sestamibi separate-acquisition dual-isotope myocardial perfusion SPECT, has been validated as an accurate method for the diagnosis of coronary artery disease (10,11,14). The use of Tc-99m sestamibi provides several advantages over thallium-201 in the performance of stress myocardial perfusion SPECT in women (8,28). The studies are somewhat less susceptible to breast attenuation artifact because of the higher energy of Tc-99m than thallium-201. When breast attenuation is suspected because of the lack of redistribution of Tc-99m sestamibi, image acquisition can be repeated with the breast in a different position. Alternatively, although it was not used in this study, gated SPECT (37) can easily be performed with this agent and facilitates the identification of breast artifact as a region with fixed defect that moves and thickens normally (38). When another artifact is suspected (e.g., motion, diaphragm or breast), imaging with this agent can be repeated in the prone position (39). The use of Tc-99m sestamibi also allows performance of a first-pass study of ventricular function (40). The use of rest thallium-201 in this protocol optimizes assessment of myocardial viability because it permits redistribution imaging if a rest defect is present (10,41). However, because detection of coronary artery disease in this protocol is predominantly determined by the stress portion of the study, the results regarding sensitivity and specificity for detection of coronary artery disease would most likely be the same for any of the validated high dose stress technetium sestamibi protocols (42).

Conclusions. In the present study of a large consecutive series of women, adenosine Tc-99m sestamibi myocardial perfusion SPECT demonstrated high sensitivity and specificity for the detection of coronary artery disease in women irrespective of presenting symptoms or pretest likelihood of coronary artery disease and a high normalcy rate. These results are comparable with previously reported studies using adenosine thallium-201 or adenosine Tc-99m sestamibi in a predominantly male cohort. These findings are of particular clinical relevance because chest pain syndromes, anginal or otherwise, have been shown to be more frequent and yet less specific markers for coronary artery disease among patients of female than male gender.

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