

Assessing Coronary Artery Disease with Thallium-201 Rest and Technetium-99m-Sestamibi Stress Testing at Two Centers

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Objective: In this study we assessed the specific location(s) of cardiac wall abnormalities in a population of patients referred for coronary artery disease and compared gender differences in the interpretation of nuclear medicine rest/stress results.

Methods: The study group consisted of 846 patients referred to 2 nuclear medicine outpatient cardiology centers for assessment between November 1998 and April 1999. All patients received dual-isotope perfusion ^{201}Tl rest/ $^{99\text{m}}\text{Tc}$ -sestamibi stress tests. A retrospective analysis of patient results was performed.

Results: In both facilities the largest percentage of defects was identified in the inferior wall (35.5%), followed by the anterior wall (26.5%). Cardiac defects identified in 3 other walls were much lower: lateral wall (14.2%), septal (13.8%), and apical (9.5%). In both outpatient clinics the normalcy rate was much higher for women than men. The normalcy rate in men was 40%, whereas women demonstrated a normalcy rate of 60%. An analysis of treadmill stress versus pharmacologic stress did not illuminate the cause of this difference.

Conclusion: The most common site of myocardial wall abnormalities occurred in the inferior wall followed by the anterior wall. A large disparity was identified between the results for men compared with those for women. Men had nearly twice the number of defects as women in this study.

Key Words: technetium-99m-sestamibi stress test; thallium-201 rest test; coronary artery disease; gender differences

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Over the past 25 y there has been a marked reduction in the morbidity and mortality rates in the United States from coronary artery disease (CAD). This reduction may be attributed, in part, to increased public awareness and prevention that is due to earlier detection and improved intervention techniques. For several years, nuclear cardiology has been the most rapidly growing specialty within nuclear medicine. Several studies have demonstrated that separate acquisition, dual-

isotope myocardial perfusion SPECT using $^{99\text{m}}\text{Tc}$ -sestamibi stress and ^{201}Tl rest can accurately assess CAD and that the results correlate well with rest/stress $^{99\text{m}}\text{Tc}$ -sestamibi studies for assessing defect reversibility and image quality is good to excellent (1,2). In this retrospective study, cardiology patients at 2 outpatient clinics were referred to nuclear medicine for CAD assessment. All the outpatients involved in this study had dual-isotope perfusion (^{201}Tl rest/ $^{99\text{m}}\text{Tc}$ -sestamibi stress) tests. This study identified and categorized the specific location(s) of cardiac wall abnormalities on the basis of cardiologists' interpretations of the diagnostic images. Differences between men's and women's results then were assessed.

MATERIALS AND METHODS

The study group consisted of 846 patients referred to 1 of 2 outpatient nuclear medicine laboratories for assessment of myocardial viability and regional wall abnormalities between November 1998 and April 1999. All patients signed consent forms before testing began. All patients had dual-isotope perfusion (^{201}Tl rest/ $^{99\text{m}}\text{Tc}$ -sestamibi stress) testing. Data for this study consisted of a retrospective analysis of the results of all patients' rest and stress myocardial studies.

Evaluation of each patient included a rest perfusion ^{201}Tl test followed by stress using a treadmill or administration of persantine (dipyridamole) and gated acquisition using $^{99\text{m}}\text{Tc}$ -sestamibi. There were 4 patients who used adenosine or dobutamine either because of physician preference or the presence of a contraindication to persantine. The resting patient protocol began with an injection of 3.5 mCi (130 mBq) ^{201}Tl . Imaging was performed at 1 site using a low-energy, high-resolution collimator on a gamma camera (SPX4; Elscint, Haifa, Israel) and at the other site using a low-energy, high-resolution collimator on a gamma camera system (FX830; Picker, Cleveland, OH). At both facilities, patients were imaged in a supine position with their arms extended overhead. Image acquisition required approximately 20 min. The cameras and computers at each site were set for a thallium window. This was 70 keV (20%) and 167 keV (10%) at site 1, and 75 keV (40%) and 167 keV (20%) at site 2. Images were acquired over 180° starting at 45° RAO and ending at 45° LPO. The computers

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TABLE 1
Location of Identified Myocardial Abnormalities

Sex and no. of patients	Myocardial wall				
	Anterior	Inferior	Apical	Septal	Lateral
Men					
165 (site 1)	40	73	20	16	16
230 (site 2)	53	65	22	44	46
Women					
56 (site 1)	18	26	4	3	5
111 (site 2)	38	36	9	15	13
Totals patients					
562	149	200	55	78	80
Percent	26.5%	35.5%	9.7%	13.8%	14.2%

acquired data in a 64 × 64-byte mode using an angle step of 3° in a clockwise direction and a frame time of 20 s at site 1, and 15 s at site 2.

The thallium rest test was followed either by stressing the patient on a treadmill if the patient was capable of exercising or pharmacologically inducing stress if the patient was not capable of exercise. Patients capable of treadmill exercise followed a Bruce or modified Bruce (3) protocol, which involved steps of increasing treadmill speed and elevation until the patient reached 85% of maximal heart rate or as close to 85% maximal heart rate as the patient was capable. At peak exercise each patient was injected with 25 mCi (925 mBq) ^{99m}Tc-sestamibi and then continued on the treadmill for 1 min postinjection.

All of the patients who were pharmacologically stressed (n = 300) used persantine (dipyridamole) except for 4 who received adenosine. Persantine dose calculation was based on patient weight in kilograms × 0.57 mg/kg persantine. The maximum persantine dose was 60 mg. The persantine dose was diluted in 45–50 mL saline and was administered over 4 min through a continuous pump. Blood pressure was monitored continuously during infusion. If a 10-point drop in the diastolic pressure was noted, patients were immediately injected with 25 mCi (925 mBq) ^{99m}Tc-sestamibi. If no such drop in blood pressure was noted, patients were injected with the radiopharmaceutical 8 min after the start of infusion. Imaging at both sites began 30 min after ^{99m}Tc-sestamibi injection.

The procedure for imaging after stress, either by treadmill or pharmacologically, included a 3-lead ECG and camera parameters based on a step-and-shoot gated acquisition. Data were gated to the R wave of the patient's ECG. A good signal was mandatory and efforts were made to obtain an optimal trigger before imaging started. Acquisition parameters were a 15% window setting at 140 keV at both sites, 8 frames/cycle, in a 64 × 64 matrix, angle step of 3° and step time of 20 s (site 1) and 15 s (site 2). Stress images were obtained starting at 45° RAO and ending at 45° LPO. Standard processing of data included normalization of raw data, background subtraction, alignment of the heart in the center of image, and outlining of the left ventricle. Rest/stress horizontal long-axis, vertical long-axis, and short-axis images and a cine of the gated myocardium motion were generated. A three-dimensional bull's-eye image

of the left ventricle also was generated, including a composite of the slices of the heart in 3 planes at site 1.

A cardiologist at each site evaluated each patient's history, patterns of blood perfusion to each portion of the heart, and viewed the dynamic cine for quality of wall motion. The cardiologist graded each patient as normal myocardial perfusion, ischemic (CAD) perfusion, or infarction. A hard copy of the final report was placed in each patient's file. The results were categorized on the basis of the specific locations identified as abnormal: apical, lateral, septal, anterior, or inferior. Abnormalities identified by the cardiologist as multiple walls were categorized as multiple defects in different walls.

RESULTS

The inferior wall demonstrated the largest percentage of defects recorded (35.5%), followed by the anterior wall (26.5%) at both outpatient facilities. The lateral wall (14.2%), septal wall (13.8%), and the apical wall (9.7%) demonstrated lower defect rates (Table 1).

Of the 846 patients tested, 424 were diagnosed as having abnormal results. There were 338 ischemic areas identified and 224 infarcted areas (Table 2). Some patients had multiple myocardial wall abnormalities identified. The normalcy rate in men was approximately 40%, whereas women demonstrated a normalcy rate of 63% (Table 3).

The data were categorized by stress method (exercise versus pharmacologic) and evaluated (Table 4). Of the 354 men who

TABLE 2
Type of Myocardial Abnormalities Identified

Sex	Ischemic areas identified	Infarcted areas identified
Men (site 1)	112	53
Men (site 2)	133	97
Women (site 1)	33	23
Women (site 2)	60	51
Total	338	224

In 846 patients, 562 myocardial defects were identified.

TABLE 3
Results of Dual-Isotope Rest/Stress Testing

Site and sex	Number of patients	Results	
		Normal	Abnormal
Site 1			
Men	181	71	110 (60.8%)
Women	124	81	43 (34.6%)
Site 2			
Men	298	120	178 (59.7%)
Women	243	150	93 (38.2%)
Total men	479	191 (39.9%)	288 (60.1%)
Total women	367	231 (62.9%)	136 (37.1%)
Total patients	846	422	424

had treadmill stress testing, 145 (41%) were identified as normal. Of 125 men who had pharmacologic stress, 46 (37%) were identified as normal. Of the 192 women who had treadmill stress, 143 (75%) were identified as normal. Of 175 women who were pharmacologically stressed, 88 (50%) were considered normal.

DISCUSSION

Thallium-201 redistribution after a stress study indicates the presence of viable myocardium. Recently there have been descriptions of delayed imaging and/or reinjection studies also showing the presence of viable myocardial tissue. The positive imaging characteristics of ^{99m}Tc has given rise to a marked increased use of ^{201}Tl rest/ ^{99m}Tc -sestamibi stress testing to assess patients for CAD (4). This combination has shown a high sensitivity for detecting coronary stenosis. Patients also spend a much shorter time in the department compared with single-tracer studies using ^{201}Tl or ^{99m}Tc -sestamibi alone. Thallium-201 is an analog of potassium, which does not collect in the myocardium permanently. It is used by the myocardium during contraction. Thallium-201 is constantly being pumped in and out of the myocardial cells, and this phenomenon makes ^{201}Tl an ideal agent to assess the extent of CAD and determine the viability of affected myocardium. Unlike ^{201}Tl , ^{99m}Tc -sestamibi

TABLE 4
Results by Stress Method

Site	Treadmill stress results			
	Men (n = 354)		Women (n = 192)	
	Normal	Abnormal	Normal	Abnormal
Site 1	51 (39%)	82 (61%)	36 (69%)	16 (31%)
Site 2	94 (43%)	127 (57%)	107 (86%)	33 (24%)
Total	145 (41%)	209 (59%)	143 (74.5%)	49 (25.5%)
Site	Pharmacological stress results			
	Men (n = 125)		Women (n = 175)	
	Normal	Abnormal	Normal	Abnormal
Site 1	20 (42%)	28 (58%)	45 (62%)	27 (38%)
Site 2	26 (34%)	51 (66%)	43 (42%)	60 (58%)
Total	46 (37%)	79 (63%)	88 (50%)	87 (50%)

has little or no redistribution, which provides significant flexibility in terms of imaging (5,6). A review of the literature revealed little information regarding the identification and comparison of various sites of cardiac wall abnormalities. Studies by Zua and Potts (7) and Damm et al. (8) evaluated myocardial ischemia by regional wall motion abnormalities. They both found that the segment of the heart most commonly affected was the septal wall. A study by Hattori (9) evaluated regional abnormalities in the hearts of patients with diabetes and found the most common abnormalities to be in the inferior wall. Barendswaard et al. (10) assessed wall abnormalities in chemotherapy patients and found the highest levels of defects in the anteroseptal and apex regions. A comparison between planar and tomographic radionuclide imaging by Lee et al. (11) for detecting cardiac wall abnormalities revealed that tomographic imaging was best at detecting inferior wall abnormalities while the planar LPO projection was second best and the septal projection was the least effective in evaluating inferior wall abnormalities.

Distinct differences between CAD in men and women have been recognized. Women are on average 10 y older than men at the time of initial onset of CAD and are 20 y older at the time of first myocardial infarction (12,13). The incidence of nonfatal CAD has doubled among women in the past decade and the rate of referral of women for intervention testing and revascularization also has increased. Several studies have found that CAD in women is identified less often and at later stages than men (14). Several studies (predominately of men) have shown that the sensitivity and specificity of radionuclide myocardial perfusion imaging during treadmill exercise or after pharmaceutical vasodilation are superior to treadmill exercise ECG testing alone (4,15). Minimal data exist on the clinical value of perfusion scintigraphy for the noninvasive diagnosis of CAD in women. A 1994 study by Udelson et al. (16), using ^{201}Tl and ^{99m}Tc -sestamibi SPECT imaging, found similar sensitivity for detecting CAD in both men and women.

This study evaluated a fairly large population of patients at 2 cardiac outpatient facilities. Our data were collected over 6 mo, which may not have been adequate to consider false-negative and false-positive results. False-positive results might be caused by anterior breast attenuation artifacts or inferior diaphragm attenuation artifacts (3,17,18). Generalizations of results beyond the sample population must be made with caution.

All the cardiologists involved in this study were nuclear medicine board certified. Multiple cardiologists in the evaluation process may have affected the results.

CONCLUSION

This retrospective study evaluated the results of 846 myocardial imaging studies performed at 2 outpatient cardiology centers over a 6-mo period. The largest percentage of abnormalities, both ischemia and infarction, were found in the inferior wall followed by the anterior wall. A comparison of results in men and women recognized a large disparity in their normalcy rates, which was not based on differences in the stress methods (exercise versus pharmacologic). Men had almost twice the number of defects compared with women. These identified

differences were found to be statistically significant (Table 5). We did not identify the reason for this difference.

TABLE 5
Observed and Expected Normalcy Rates in Men and Women

Result	Men	Women	Total
Normal	O = 191 E = 238.93	O = 231 E = 183.06	422
Abnormal	O = 288 E = 240.06	O = 136 E = 183.93	424
Total	479	367	846

Chi-Square Value = 44.4, >3.84 is the Critical Value at $P = 0.05$. O = observed; E = expected.

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