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Incremental Value of Simultaneous Assessment of Myocardial Function and Perfusion With Technetium-99m Sestamibi for Prediction of Extent of Coronary Artery Disease

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Objectives. **This study assessed the incremental value of technetium-99m myocardial single-photon emission computed tomography (SPECT) and simultaneous first-pass radionuclide angiography, when added to treadmill exercise, for prediction of the extent of coronary artery disease.**

Background. **Technetium-99m count statistics permit the simultaneous assessment of myocardial perfusion and function. However, whether this characteristic improves prediction of the extent of coronary artery disease remains unknown.**

Methods. **We studied 70 consecutive patients who had coronary angiography within 6 months of the scintigraphic study. All patients underwent a symptom-limited treadmill exercise test. Treadmill data were summarized using a previously validated score. Left ventricular ejection fraction and regional wall motion were evaluated from a first-pass radionuclide angiogram acquired at peak treadmill exercise in the anterior view. Perfusion was assessed visually. Extent of angiographic disease was expressed as the presence or absence of multivessel disease (more than two coronary artery territories with >50% stenosis) and as a score that reflects the location of severe (>75%) stenosis.**

Results. **Stepwise addition of scintigraphic data (perfusion first, followed by function) to the treadmill score showed significant incremental value for prediction of the angiographic score at each step; exercise ejection fraction alone was the strongest independent predictor. Discriminant accuracy for detection of multivessel disease was also improved by the addition of perfusion information to the treadmill score and addition of regional wall motion analysis to both of them. In this case, ejection fraction failed to show independent value.**

Conclusions. **The addition of simultaneously performed sestamibi perfusion SPECT and first-pass radionuclide angiography to the treadmill exercise test significantly improved prediction of the extent of coronary artery disease.**

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Exercise myocardial perfusion scintigraphy is an important method for the noninvasive evaluation of coronary artery disease (1–3). Data reflecting exercise ventricular function, such as left ventricular wall motion and ejection fraction, have also been shown to contain significant diagnostic and prognostic information (4–6). However, little has been published about the incremental value of both myocardial perfusion and function considered together (7).

Technetium-99m (Tc-99m) sestamibi is a perfusion tracer with high diagnostic accuracy for detection of coronary artery disease (8–10). Because of high count statistics, this agent enables the functional evaluation of the heart through first-pass radionuclide angiography (11,12) and by gated acquisition of the perfusion images (13). This characteristic of sestamibi permits assessment of both left ventricular function and perfusion within the same test (11–14).

The objective of this study was to determine whether the addition of left ventricular functional assessment from simultaneous treadmill exercise first-pass radionuclide angiography improved the determination of extent of coronary artery disease in patients undergoing exercise stress sestamibi single-photon emission computed tomography (SPECT).

Methods

Patients. We studied 70 patients (mean [±SD] age 60 ± 12 years, range 30 to 80; 57 men, 13 women), 21 of whom had a Q wave myocardial infarction on the rest electrocardiogram (ECG). Patients with previous coronary artery bypass surgery, congenital heart disease, valvular heart disease or cardiomyopathy were excluded. Symptom class before exercise was categorized as asymptomatic, nonanginal chest pain or atypical or typical angina (15).

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Simultaneous treadmill exercise perfusion/function scintigraphy. All patients performed symptom-limited treadmill exercise using the standard Bruce protocol, with 12-lead ECG recording for each minute of exercise and continuous monitoring of leads V_1, V_5 and aVF. Exercise end points were physical exhaustion, development of severe angina, sustained ventricular arrhythmia or exertional hypotension. Whenever possible, beta-adrenergic blocking agents and calcium antagonists were withheld for 48 h and long-acting nitrates for 6 h, before the stress test. Angina during exercise was classified as 0 = absent, 1 = nonlimiting, or 2 = exercise limiting. Maximal degree of ST segment depression at 80 ms of the J point was assessed, with the slope of the ST segment categorized as upsloping, horizontal or downsloping.

A treadmill score was calculated as follows (16): Duration of exercise (min) − (5 × Maximal ST segment deviation during or after exercise [mm]) − (4 × Treadmill angina index). This score was originally developed for the prognostic assessment of coronary artery disease (16) and was later shown to be of value for prediction of the angiographic extent of coronary artery disease (17). We used this score as a cluster variable to reduce the number of predictors considered for inclusion in our multiple logistic regression analysis, thereby enhancing its reproducibility (18,19).

At near-maximal exercise, a 20- to 30-mCi dose of Tc-99m sestamibi was injected, with dose variation based on patient weight. Immediately after the bolus injection of sestamibi, and while patients continued to exercise at the same work load for 1 min, a first-pass radionuclide angiogram was obtained using a Scinticor SIM-400 camera equipped with a high resolution collimator (20). Patients were positioned against the camera during acquisition, which was performed in the anterior position using 40 frames/s for 25 s. A point source of americium (14 mCi) was placed between ECG leads V_2 and V_3 as a reference for motion correction. One minute after the sestamibi injection, the work load was decreased by one stage, and the patient exercised for an additional 2 min when tolerated (9).

First-pass radionuclide angiographic processing and interpretation. We used commercially available algorithms for processing (20). Regional wall motion was visually analyzed in a dynamic continuous display by consensus of two observers who had no knowledge of any other patient data. The anterior view of the left ventricle was subdivided into five segments (Fig. 1), which were assigned to one of three regions for wall motion analysis (Fig. 1). Wall motion abnormalities in the anterolateral and inferior segments were attributed to the left anterior descending and right coronary artery, respectively. Abnormalities in the apex were considered nonspecific for any coronary territory.

A five-point score was used: 3 = normal; 2 = mild hypokinesia; 1 = severe hypokinesia; 0 = akinesia; −1 = dyskinesia. A segment with a score <3 was considered abnormal. A summed wall motion score was calculated adding the scores from all analyzed segments.

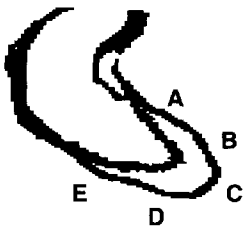


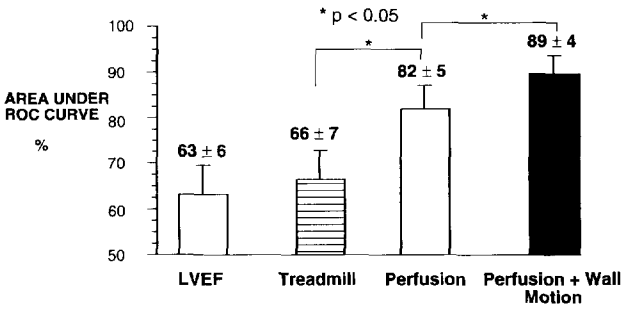
Figure 1. Schematic representation of segments in first-pass radionuclide angiogram. End-systolic and end-diastolic frames are superimposed. **Segments A and B** (anterolateral wall) were assigned to the left anterior descending coronary artery territory; **segments D and E** (inferior wall) were assigned to the right coronary artery territory; **segment C** (apex) was considered nonspecific.

Single-photon emission computed tomographic acquisition protocol. Single-photon emission computed tomographic scanning was performed and interpreted as previously described (9,10). Visual interpretation of SPECT perfusion images used short-axis and vertical long-axis tomograms divided into 20 segments/patient (9). Segments were scored by an experienced observer using a five-point scoring system (0 = normal; 1 = equivocal; 2 = moderate; 3 = severe reduction of radioisotope uptake; 4 = absence of detectable radiotracer in the segment). The observer was unaware of clinical history and stress test and coronary angiographic results.

A segment was considered abnormal in the presence of a stress score ≥2. Assignment of SPECT defects to vascular territories was as previously described (9). A summed stress perfusion score was obtained by adding the scores of all 20 myocardial segments.

Integration of perfusion and wall motion regional assessment. The first-pass radionuclide angiogram was obtained only in the anterior view, which permits assessment of territories corresponding to the left descending and right coronary arteries but not the left circumflex coronary artery. Because of this limitation of the radionuclide angiogram, the contribution of regional wall motion analysis to determination of the extent of coronary artery disease was always assessed considering perfusion SPECT data as given information. A region was considered "abnormal" if either perfusion or wall motion was

Figure 2. Receiver operating characteristic (ROC) curve areas for prediction of multivessel disease by treadmill and scintigraphic methods. LVEF = left ventricular ejection fraction.



abnormal; a region was considered "normal" if perfusion and wall motion were preserved.

Coronary angiography. Coronary angiography was performed by conventional Sones or Judkins technique within 6 months of the scintigraphic study. No patient had a coronary event or a significant increase in cardiac symptoms in the interval between the scintigraphic study and coronary angiographic evaluations. Angiographic studies were analyzed visually to determine the degree of lumen diameter narrowing, expressed as percent stenosis. A cutoff point of 50% lumen diameter narrowing was applied to define the presence of significant coronary artery disease. Multivessel disease was defined as the presence of significant stenosis in more than two major coronary arteries. A significant stenosis in the left main coronary artery was considered double-vessel disease because it compromised the circulation to both the left anterior descending and left circumflex coronary arteries.

The Califf score (21), a comprehensive variable of known prognostic value that considers the location and severity of the stenoses, was calculated for each patient.

Statistical analysis. Comparisons between patient groups were performed using the unpaired *t* test for continuous variables and the chi-square or Fisher exact test for categoric variables.

All continuous variables are summarized as mean value ± SD. The kappa statistic and its standard error were used to assess agreement between the number of vessels with significant angiographic disease and the corresponding predictions from perfusion and wall motion analyses. A value of 1 denotes perfect agreement; 0 indicates no agreement beyond chance. In general, kappa values >0.75 denote excellent reproducibility, values between 0.4 and 0.75 denote good reproducibility, and values <0.4 denote marginal reproducibility (22). Correlation between continuous variables was assessed by the Pearson correlation coefficient.

Stepwise multiple logistic regression was used to determine the incremental value of scintigraphic variables for the diagnosis of multivessel disease when added to the treadmill exercise score. The model was built by adding to the treadmill score perfusion information first, followed by function information. Multivariate prediction of the angiographic score was evaluated by multiple linear regression in a similar stepwise fashion.

Because sensitivity and specificity of alternative testing strategies are often interdependent (increases in sensitivity occur in association with decreases in specificity), receiver operating characteristic curves were used as the basis for comparison, using methods described by Hanley and McNeil (23–25).

The receiver operating characteristic curve represents the relation between the true positive and false positive rates of a test as the threshold for abnormality is changed (23,25). Each of the logistic models was first used to compute a probability of multivessel disease for each patient. Receiver operating characteristic curves were then generated for each of the models on the basis of these probabilities. For each logistic model, a continuous curve was constructed from the true and false positive rates for all possible thresholds of the event probability. The discriminant accuracy of each logistic model was thereby quantified in terms of the areas under these curves. An area of 0.5 represented no discrimination; an area of 1 represented perfect discrimination. The difference in area between different models represents the increment in discrimination. Statistical comparisons of receiver operating characteristic areas were performed using the method of Hanley and McNeil (24).

All analyses were performed using True Epistat software (22).

Table 1. Univariate Comparison of Clinical Characteristics of Angiographic Groups

	Multivessel Disease (n = 36)	Control Group (n = 34)	p Value
Age (yr)	62.6 ± 9.4	57.6 ± 12.2	0.058
Male gender	30 (88)	27 (79)	0.488
Symptom			0.064
Asymptomatic	5 (14)	12 (35)	
Nonanginal chest pain	5 (14)	8 (23)	
Atypical angina	13 (42)	6 (18)	
Typical angina	11 (31)	8 (24)	
Previous myocardial infarction	11 (30)	10 (29)	0.843
Diabetes mellitus	6 (17)	2 (6)	0.294
Hypercholesterolemia	15 (42)	16 (47)	0.806
Hypertension	19 (53)	18 (53)	0.811
Smoker	5 (14)	10 (29)	0.298
Family history	13 (36)	9 (26)	0.519

Data presented are mean value ± SD or number (%) of patients.

Results

Four patients had normal coronary arteries, and 30 had single-, 17 had double-, and 19 had triple-vessel disease. Patients with normal coronary arteries included those with minor, nonsignificant stenoses and those with completely normal arteries. Seven patients had left main coronary artery stenosis, and all had concomitant disease in the right coronary artery territory. Seventeen patients did not achieve 85% of maximal predicted heart rate during the exercise test, nine of whom had multivessel disease.

Tables 1 and 2 show the univariate comparisons between patients with multivessel disease and those with normal coronary arteries and single-vessel disease (control group). Patients with multivessel disease exercised for a significantly shorter time (6.7 ± 2.5 min vs. 8.0 + 2.7 min, $p = 0.04$) and had a lower peak exercise left ventricular ejection fraction (53.3 ± 13.4% vs. 59.6 ± 11.9%, $p = 0.042$) than those in the control group. They also had perfusion defects and wall motion abnormalities in more coronary artery territories ($p < 0.001$).

Exact agreement between perfusion sestamibi and angiography regarding the number of diseased vessels was marginal (54%, kappa 0.28, $p < 0.001$) (Table 3).

Table 2. Univariate Comparison of Exercise and Scintigraphic Characteristics of Angiographic Groups

	Multivessel Disease (n = 36)	Control Group (n = 34)	p Value
Peak exercise HR (beats/mm)	140.3 ± 18.2	147.4 ± 18.9	0.118
≥85% maximal predicted	27 (75)	26 (76)	0.892
Peak exercise SBP (mm Hg)	165.9 ± 26.2	171.8 ± 21.7	0.302
Exercise duration (min)	6.7 ± 2.5	8.0 ± 2.7	0.040
ST segment depression (mm)	1.9 ± 1.4	1.5 ± 1.6	0.269
ST segment slope (depression present)			0.0561
Upsloping	11 (38)	11 (55)	
Horizontal	6 (21)	7 (35)	
Downsloping	12 (41)	2 (10)	
ST segment depression onset (min)	1.12 ± 2.4	2.14 ± 2.9	0.113
HR at ST segment depression onset (beats/min)	51.6 ± 63.4	48.4 ± 57.4	0.782
Exercise angina			0.146
0 = none	21 (58)	27 (79)	
1 = nonlimiting	9 (25)	5 (15)	
2 = exercise limiting	6 (17)	2 (6)	
No. of diseased vessels by perfusion			< 0.001
0	1 (3)	8 (24)	
1	12 (34)	24 (71)	
2	20 (55)	2 (6)	
3	3 (8)		
No. of diseased vessels by perfusion + wall motion			
0	—	4 (12)	< 0.001
1	6 (17)	28 (82)	
2	21 (58)	1 (3)	
3	9 (25)	1 (3)	
Peak exercise LVEF	53 ± 13	60 ± 12	0.042
Medical therapy*	14 (38)	9 (26)	0.413

*Patients who underwent stress testing with anti-ischemic medication. Data presented are mean value ± SD or number (%) of patients. HR = heart rate; LVEF = left ventricular ejection fraction; SBP = systolic blood pressure.

When a coronary territory was considered abnormal because of abnormal perfusion or wall motion, exact agreement with angiography improved (63%, kappa 0.43, $p < 0.001$) (Table 4).

Discriminant accuracy for detection of multivessel disease (Fig. 2). The treadmill score alone provided significant information for discrimination between patients with and without multivessel disease (receiver operating characteristic area 66 ± 7%, $p < 0.001$). However, perfusion SPECT provided significantly better accuracy (receiver operating characteristic area 0.82 ± 0.05, $p = 0.035$ vs. treadmill score). Perfusion SPECT accuracy was further improved when first-pass segmental wall motion information was added: Sensitivity for multivessel disease detection increased from 64% to 83%, whereas specificity remained at 94% (receiver operating characteristic area increased to 89 ± 4%, $p = 0.01$ vs. perfusion alone). Peak exercise ejection fraction had the poorest discrimination of all variables analyzed for presence of multivessel disease (receiver operating characteristic area 63 ± 6%).

Incremental value for detection of multivessel disease. Stepwise multiple logistic regression was performed in three steps. First, the predictive value of the treadmill score was determined. Subsequently, the number of diseased vessels predicted by perfusion SPECT was added. Finally, first-pass radionuclide angiogram data were incorporated. After each

Table 3. Agreement for Number of Diseased Vessels

No. of Diseased Vessels by Angiography	No. of Diseased Vessels by Perfusion			
	0	1	2	3
0	3	1		
1	5	23	2	
2	1	5	10	1
3		7	10	2

Table 4. Agreement for Number of Diseased Vessels

No. of Diseased Vessels by Angiography	No. of Diseased Vessels by Perfusion + Wall Motion			
	0	1	2	3
0	3	1		
1	1	27	1	1
2		4	9	4
3		2	12	5

Table 5. Stepwise Multiple Logistic Regression for Prediction of Multivessel Disease

	Coefficient	SE	p Value
Step 1			
Treadmill	−0.056	0.039	0.044
Intercept	−0.109		
Step 2A			
Treadmill	−0.0270	0.034	0.420
Perfusion	2.4816	0.650	0.000
Intercept	−3.0928		
Step 2B			
Treadmill	0.002	0.039	0.966
Perfusion + wall motion*	3.286	0.739	0.000
Step 3			
Treadmill	0.003	0.039	0.945
Perfusion + wall motion	3.538	0.798	0.000
LVEF	0.039	0.036	0.272
Intercept	−7.301		

*Because single-view radionuclide angiography permitted evaluation of only two coronary artery territories, wall motion analysis was included together with perfusion data. When perfusion was considered alone, it also showed independent value (step 2A). LVEF = left ventricular ejection fraction.

Table 7. Stepwise Multiple Linear Regression for Prediction of Angiographic Score

	Coefficient	SE	p Value
Step 1			
Treadmill score	−0.104	0.041	0.015
Intercept	3.546		
Step 2			
Treadmill score	−0.082	0.037	0.033
Summed perfusion score	0.15	0.035	< 0.001
Intercept	1.799		
Step 3			
Treadmill score	−0.068	0.035	0.045
Summed perfusion score	0.107	0.041	0.010
Summed wall motion score	−0.248	0.123	0.048
Intercept	5.245		
Step 4			
Treadmill	−0.0681	0.036	0.059
Summed perfusion score	0.081	0.041	0.053
Summed wall motion score	−0.050	0.144	0.729
LVEF	−0.089	0.037	0.018
Intercept	11.008		

LVEF = left ventricular ejection fraction.

addition, chi-square analysis for improvement of the model was used to test for incremental information. Also, differences in discriminant accuracy for prediction of multivessel disease by each multivariate model were assessed by receiver operating characteristic curve analysis.

Single-photon emission computed tomographic perfusion assessment of extent of multivessel disease showed independent value by stepwise multiple logistic regression when added to the treadmill data ($p < 0.001$) (Table 5). Furthermore, when regional wall motion and left ventricular ejection fraction from the first-pass radionuclide angiogram were added to the model, wall motion assessment provided additional information to the multivariate model ($p = 0.001$), but left ventricular ejection fraction failed to do so.

When the discriminant accuracy of these multivariate models was evaluated by receiver operating characteristic curve analysis (Fig. 3), there was a statistically significant improvement in area under the receiver operating characteristic curve when SPECT perfusion was added to the treadmill model (from 66 ± 7% at step 1 to 86 ± 4% at step 2, $p = 0.035$) and when regional wall motion analysis of the first-pass radionuclide angiogram was incorporated with both of them (from 86 ± 4% at step 2 to 91 ± 4% at step 3, $p = 0.048$).

Table 6. Univariate Correlations With Angiographic Score

	Correlation Coefficient	p Value
Treadmill score	−0.29	0.015
Summed stress perfusion score	0.478	< 0.001
Summed wall motion score	−0.548	< 0.001
LVEF	−0.618	< 0.001

LVEF = left ventricular ejection fraction.

Correlation with angiographic score. Correlation with angiographic score was analyzed for the following variables: treadmill, summed stress perfusion and summed wall motion scores and left ventricular ejection fraction (Table 6). Left ventricular ejection fraction had the best univariate correlation with angiographic score. Stepwise multiple linear regression showed that addition of the summed stress perfusion score improved prediction of angiographic score by treadmill data (Table 7).

When the summed wall motion score was incorporated, it also provided a significant improvement, making the other variables nonsignificant. When left ventricular ejection fraction was added, it produced a similar effect and remained the only independent predictor of angiographic score.

Discussion

Incremental value of exercise first-pass scintigraphy in identification of extensive disease. Our results show that 1) assessment of regional myocardial perfusion using Tc-99m sestamibi SPECT provides a statistically significant increment of information over that provided by the exercise ECG alone in predicting the anatomic extent of coronary artery disease, and 2) assessment of regional myocardial function using the anterior view exercise first-pass radionuclide angiogram provides an additional significant increment of information over that provided by assessment of perfusion. Although the present study was not designed to identify the reasons for this improvement in diagnostic accuracy, we conjecture that in the presence of multivessel coronary artery disease there can be a lack of definite perfusion defects in regions supplied by arteries with relatively less stenosis (26). Thus, wall motion and left ventricular ejection fraction can improve detection of abnormal areas.

In planar thallium-201 imaging, detection of slow washout

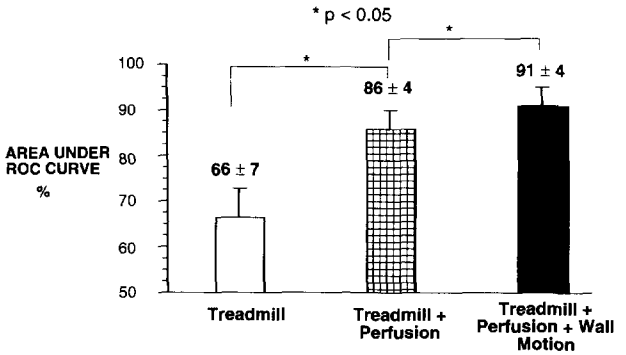


Figure 3. Improvement in receiver operating characteristic (ROC) curve area for prediction of multivessel disease by stepwise addition of scintigraphic data.

of the radiotracer has been demonstrated to improve assessment of the extent of coronary artery disease (26,27). However, in general, in thallium-201 SPECT this washout analysis has not been found to be effective. Washout analysis of Tc-99m sestamibi is also not likely to produce useful evidence of multivessel disease because the washout rates of normal and ischemic myocardium do not differ significantly (28). Additional indirect assessments from thallium-201 imaging have been shown to be useful in evaluating the extent of coronary artery disease, including lung uptake of thallium-201 (29) and transient ischemic dilation of the left ventricle (30). Although Tc-99m sestamibi imaging does not appear to provide useful information with regard to lung uptake, this approach is helpful in assessing the extent of disease through analysis of transient ischemic dilation of the left ventricle (31). The results of the present study illustrate that direct information regarding exercise left ventricular function can be derived from Tc-99m sestamibi studies through assessment of the first-pass radionuclide angiogram.

Angiographic disease extent: categoric versus continuous variable. We used the angiographic information as the reference standard for our analysis both as a categoric variable and as a continuous variable. In the categoric approach, a conventional but arbitrary threshold in visually assessed lumen diameter stenosis >50% was used as the definition of significant coronary artery disease. All patients were grouped into two categories (with and without multivessel disease) to obtain a binary variable suitable as an outcome for multiple logistic regression and receiver operating characteristic curve analysis. Our results demonstrated that treadmill data provided significant information with regard to presence of multivessel disease, SPECT perfusion assessment showed independent value when added to treadmill data, and wall motion assessment provided further significant incremental information to the multivariate model, as shown by stepwise multiple logistic regression (Table 5) and receiver operating characteristic curve analysis (Fig. 3).

However, classification of patients into those with and without multivessel disease artificially simplifies a much more complex situation. It groups together patients with a variety of anatomic findings with potentially different clinical relevance and ignores the changes in diameter reduction beyond the cutoff point and the location of the stenoses (e.g., a patient with two 50% distally located stenoses is in the same group as another patient with three proximal 90% stenoses). We therefore also used a comprehensive angiographic score (21) as the reference standard in linear regression modeling. It has been shown to purport significant prognostic information, performing better than a categoric classification by number of diseased vessels (21). We were able to confirm the incremental value for prediction of extent of coronary artery disease by addition of the scintigraphic variables to treadmill exercise data. Although left ventricular ejection fraction did not provide any increment of information for prediction of multivessel disease when added to the multiple logistic regression model, it appeared to be the only independent predictor of angiographic score in the final multiple linear regression model. These findings are consistent with those of others (32) who have previously reported good correlation of ejection fraction with angiographic score despite relatively poor discrimination of the presence of multivessel disease.

Additional clinical benefits of simultaneous exercise perfusion/function scintigraphy. There are several potential benefits that derive from the integration of regional myocardial function and perfusion in addition to increased accuracy of identification of multivessel disease. With regard to diagnosis, incorporation of functional data can improve the specificity of perfusion studies. Thus, the presence of normal wall motion in a region that appears hypoperfused might lead to identification of perfusion artifacts. In this sense, it has been reported (33) that regional wall motion assessment from gated Tc-99m sestamibi SPECT improves the differentiation between attenuation artifacts and infarcted zones. Regional wall motion analysis of the first-pass radionuclide angiogram might provide similar information (14,20).

Furthermore, addition of functional information might help diagnosis in patients with an intermediate probability of coronary artery disease after the perfusion study. A similar approach has been used for many years, with studies performed sequentially (34), where the posttest probability of each test is considered to be the pretest probability of the next test. For example, if the probability of coronary artery disease remains ~0.5 after perfusion scintigraphy, equilibrium radionuclide angiography or stress echocardiography might be recommended. A very low or very high probability of coronary artery disease at any point during patient evaluation makes further testing unnecessary. The difference between the sequential approach and the method evaluated in the present report is that now the supplementary functional information can be gathered in a single study. Whether this simultaneous assessment of function and perfusion is more cost-effective than a sequential strategy remains undetermined.

There are also implications for the prognostic assessment of coronary artery disease. We report here that the extent of coronary artery disease can be better predicted when exercise, perfusion and function are integrated. This improved predic-

tion of the extent of coronary artery disease has obvious implications in risk assessment. Furthermore, the first-pass radionuclide angiogram permits measurement of left ventricular ejection fraction, which has been shown to be a potent predictor of outcome both by itself and when added to clinical and angiographic data (35,36).

Study limitations. The present study was performed in a relatively small group of patients and used visual analysis of Tc-99m sestamibi perfusion SPECT images and coronary angiograms. Although a variety of methods exist for the semiautomated quantitation of regional myocardial perfusion (37) and degree of coronary artery stenosis, we believe that our visual assessments are relevant to the current generation of clinical laboratories, which continue to rely on subjective visual assessment of these tests. In this respect, our study defines the practical effectiveness of the integrated analysis of myocardial function and perfusion rather than its maximal potential efficacy.

The exercise first-pass radionuclide angiogram study used a specialized scintillation camera that is not available in most laboratories. The treadmill exercise first-pass study has been validated using this equipment only (20). However, bicycle exercise first-pass radionuclide angiography, can be performed with recent-vintage standard nuclear medicine systems. The exercise radionuclide angiogram studies were obtained in the anterior view only, a view in which the left circumflex coronary territory is not observed. In our study group, seven patients had double-vessel disease with the left circumflex coronary artery as one of the compromised vessels. In these patients, the wall motion data provided by the anterior radionuclide angiogram view was limited to the other vessel (left anterior descending or right coronary artery). However, this did not prevent wall motion analysis from contributing significant information in all patients. It is possible that if biplane exercise first-pass radionuclide angiography had been used, an increased ability to discriminate patients with multivessel disease might have been shown.

Although quantitative analysis of the myocardial perfusion SPECT study might improve the reproducibility of interpretation, it is unlikely that it would improve the ability to detect multivessel disease over that provided by expert visual analysis. In this regard, even with quantitative analysis, when balanced reduction of flow is present, myocardial perfusion SPECT might underestimate the true extent of hypoperfused myocardium. In this circumstance, the exercise radionuclide angiogram may still provide incremental information over even quantitatively analyzed myocardial perfusion studies.

Finally, although 17 of our patients did not to reach 85% of the maximal predicted heart rate, thereby jeopardizing the sensitivity of the exercise perfusion study, they were evenly distributed among patients with and without multivessel disease (8 and 9 patients, respectively), and the scintigraphic/angiographic correlations showed trends similar to those for the entire group.

Summary. Addition of Tc-99m sestamibi perfusion SPECT significantly improves prediction of the extent of coronary artery disease when added to treadmill exercise data. Incorporation of functional information from first-pass radionuclide angiography further enhances that predictive ability.

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