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Quantitative Analysis of Dipyridamole–Thallium Images for the Detection of Coronary Artery Disease

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To determine if the detection of coronary artery disease by dipyridamole–thallium imaging is improved by 1) quantitative versus qualitative analysis, and 2) combining quantitative variables, 80 patients with chest pain (53 with and 27 without coronary artery disease) who underwent cardiac catheterization were studied. Segmental thallium initial uptake, linear clearance, monoexponential clearance and redistribution were measured from early, intermediate and delayed images acquired in three projections. Normal values were determined from 13 other clinically normal subjects.

When five segments per view were used for quantitative analysis, sensitivity and specificity were 87 and 63%, respectively, for uptake, 77 and 67% for linear clearance, 60 and 60% for monoexponential clearance and 62 and 56% for redistribution. Of the four variables, uptake and linear clearance were the most sensitive ($p < 0.01$) and specificity did not differ significantly. Using three segments per view, the specificity of uptake increased ($p < 0.05$) to 78% without a significant change in sensitivity (85%). With this approach, sensitivity and specificity did not differ from those of qualitative analysis (85 and 78%, respectively).

Stepwise logistic regression analysis demonstrated that the best quantitative thallium correlate of the presence of coronary artery disease was a combination variable of "either abnormal uptake or abnormal linear clearance, or both." Using five segments per view, the model's specificity (85%) was greater than that of uptake alone ($p < 0.02$), with similar sensitivity (92%). Using three segments per view, the model's specificity (93%) was greater than that of uptake alone ($p < 0.05$) and of qualitative analysis ($p < 0.05$), with similar sensitivity (85%). Compared with qualitative analysis, the diagnostic accuracy of the model was greater using either five segments (90 versus 82%, $p < 0.01$) or three segments (88 versus 82%, $p < 0.05$) per view.

Quantitative analysis of dipyridamole–thallium images using single individual variables provides results comparable with those of qualitative analysis and this can be further optimized when a combination of quantitative variables is used.

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Thallium imaging after dipyridamole infusion is an alternative to exercise thallium imaging for the evaluation of coronary artery disease (1–5). Quantitative analysis of exercise thallium images improves diagnostic accuracy when compared with visual analysis alone (6–8). In addition, the observer variability with objective computer techniques is less than has been reported with subjective visual analysis of thallium images (8–10). However, the application of quantitative analysis to dipyridamole–thallium images has not been widely reported and its diagnostic value is uncertain compared with that of qualitative analysis.

Quantitative analysis of exercise thallium images has employed abnormal thallium uptake, clearance and redistribution as criteria for detection of coronary artery disease (6–8,11). Previous studies with exercise thallium imaging have indicated that some of the quantitative variables correlate better with the angiographic presence of coronary artery disease than do others and that a combination of variables is superior when compared with each alone (8) and with visual assessment (12). Because thallium kinetics

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after dipyridamole are different from those after exercise, (13), one should not assume that the relative diagnostic value of these criteria after dipyridamole is similar to that after exercise. Accordingly, we measured segmental thallium uptake, clearance and redistribution in 80 catheterized patients with chest pain who underwent dipyridamole–thallium imaging. The segmental thallium values of these 80 patients were compared with criteria derived from a second, separate group of 13 clinically normal subjects with a low probability of coronary artery disease. The sensitivity, specificity and diagnostic accuracy of these quantitative thallium variables were determined and compared with the results of qualitative analysis. Using stepwise logistic regression analysis to compare variables, the combination of quantitative variables that best differentiated patients with and without coronary artery disease was defined. Our study demonstrates the feasibility of quantitative analysis of dipyridamole–thallium images in comparison with qualitative analysis.

Methods

Study patients. There were two study groups. One group comprised 80 patients with a chest pain syndrome who were referred for coronary arteriography. The second group comprised 13 clinically normal subjects who did not undergo cardiac catheterization and who were studied with dipyridamole–thallium imaging to define a normal range of quantitative dipyridamole–thallium variables.

The 80 patients who had cardiac catheterization were classified into two subgroups: 53 patients with coronary artery disease (43 men and 10 women, mean age 54 ± 10 years) and 27 patients with no coronary artery disease (12 men and 15 women, mean age 51 ± 9 years). Of the 53 patients with coronary artery disease, 21 had one vessel, 14 had two vessel, 18 had three vessel and none had left main disease; 28 had had a previous myocardial infarction.

The 13 normal subjects (9 men and 4 women, mean age 24 ± 4 years) were volunteers with no history of cardiovascular disease, systemic hypertension or other significant illnesses. All were nonsmokers and took no medication. All subjects had normal findings on cardiovascular examination and had a normal electrocardiogram (ECG) at rest and during exercise.

Subjects signed a consent form approved by the Massachusetts General Hospital Subcommittee on Human Studies on December 20, 1983. The anticipated whole body and renal dosimetry for the thallium-201 tests was 0.52 and 2.2 rem, respectively, per 2.0 mCi of thallium-201.

Coronary arteriography. Coronary artery disease was defined as a ≥50% luminal narrowing of one or more major coronary arteries or their major branches on the basis of the average score of two independent experienced observers who were unaware of the thallium scan findings. The major branches included 1) the first diagonal branch of the left anterior descending artery, 2) obtuse marginal branch of the left circumflex artery, and 3) posterior descending branch of the right coronary artery in a right dominant system, or left circumflex artery in a left dominant system (three patients). A ramus intermedius artery was considered equivalent to the diagonal branch of the left anterior descending artery.

Acquisition of dipyridamole–thallium images. The dipyridamole infusion protocol has been described previously (2,14). At the beginning of the test, a peripheral intravenous infusion line was established in an antecubital vein. Heart rate, blood pressure and a 12 lead ECG were monitored throughout the procedure. The subject lay supine on a tilt table. Dipyridamole for intravenous injection was obtained from Boehringer-Ingelheim, under an investigational exemption for a new drug (no. 19,728). Dipyridamole was infused intravenously at a rate of 0.14 mg/kg per min for 4 minutes. Intravenous aminophylline was available for the reversal of severe side effects such as nausea or dizziness. At the end of the 4 minute dipyridamole infusion, the table was tilted upright. Three minutes later 2.0 mCi thallium-201 was injected intravenously and flushed with a bolus through the indwelling intravenous catheter. The table was tilted back flat 1 minute later and imaging was begun. Three sets of 8 minute planar images were obtained in the anterior, 50° and 70° left anterior oblique projections, as described previously (2,13). Early images were obtained starting at 2 to 9 minutes (mean 6 ± 1 minutes) after injection of thallium-201, intermediate images at 24 to 46 minutes (mean 36 ± 4 minutes) and delayed images at 90 to 259 minutes (mean 164 ± 34 minutes). All patients and normal subjects were in the fasting state until after the delayed images were acquired.

Qualitative analysis of dipyridamole–thallium images. The thallium images were viewed on a computer display, as described previously (10,15). Each image was interpreted by three independent observers who were unaware of the patient's cardiac catheterization findings or clinical history, and the results were averaged. The left ventricle was divided into three segments per view. Activity of thallium in each segment was subjectively graded using a five point scale in which 2 was normal and 0 indicated no activity, with half-grades permitted. In all segments except for the apical segment, a score of 2 was considered normal. In the apical segment, a score of ≥1.5 was considered normal. Redistribution (the "filling in" of an initial perfusion defect on the delayed image) was defined as an increase between initial and delayed image of ≥0.5 on the five point scale.

Quantitative analysis of dipyridamole–thallium images. A previosuly describmed computer method was used to determine myocardial thallium activity on a segmental basis (8,12,16,17). In brief, an elliptical region of interest was placed around the left ventricle and the region corre-

sponding to the valve planes was excluded. The steps of serial image registration, background subtraction and determination of thallium-201 activity in five equal-sized segments per view in the early, intermediate and delayed images were automatically carried out. These segments were numbered 1 to 5 clockwise around the left ventricle with segment 3 always representing the apex. The count activities within the myocardium in the three images of each projection were normalized to the 3 × 3 pixel region, with the greatest thallium activity in the ellipse of the early image, and represent relative thallium uptake expressed as a percent of the maximum. Segmental thallium activity of the intermediate and delayed images was also normalized a second time, to the 3 × 3 pixel region, with the greatest thallium activity within the ellipse of the image being analyzed. Once segmental thallium activity was measured, segmental clearance and redistribution were calculated. The normal limits of segmental quantitative thallium values were defined as 2.5 SD from the mean observed in the normal group, and are detailed in Table 1. The interobserver and intraobserver variability of this computer method of determining segmental thallium activity has been determined to be very small (8).

Four aspects of myocardial thallium kinetics were compared in the patient group: uptake, linear clearance, monoexponential clearance and redistribution. These variables were analyzed using both the early image and the intermediate image as the initial image.

1) Uptake. A segment of a specific image was considered abnormal if the measured value was less than the lower normal limit for that specific segment and image. The normal lower limits for uptake in the early and intermediate images are shown in the second and third columns of Table 1.

2) Linear clearance. This was calculated as the percent decrease in the thallium activity between the initial and delayed image and expressed as percent per hour. This method assumes a linear model for thallium clearance. A segment was considered abnormal if the measured linear clearance value was less than the lower normal limit for that specific segment and image pair. The normal lower limits for linear clearance are shown in the fourth and fifth columns of Table 1.

3) Monoexponential clearance. This was calculated by fitting a monoexponential curve to the unnormalized thallium activity in the initial and delayed images, knowing the time interval between these images and assuming that activity at infinite time was zero. A monoexponential fit was chosen because of experimental evidence, obtained in anesthetized dogs monitored continuously with cadmium telluride probes, indicating that myocardial thallium clearance after dipyridamole infusion is monoexponential (18). Monoexponential clearance was expressed as a half-life of thallium in each segment in hours. A segment of a specific image was considered abnormal if the measured monoexponential clearance half-life value was negative (indicating

Table 1. Normal Limits for Thallium Uptake, Clearance and Redistribution

	Uptake (%)		Clearance: Linear (%/h)		Clearance: Monoexponential (h)		Redistribution (%)	
Segment	E	I	E-D	I-D	E-D	I-D	E-D	I-D
Anterior								
1	40	51	−9	0	27	25	22	18
2	71	75	−5	3	26	30	16	12
3	65	66	−5	5	22	30	16	11
4	74	79	−3	4	22	27	11	8
5	22	38	−14	3	18	23	25	18
50° Left anterior oblique								
1	55	56	−7	−5	27	23	11	9
2	82	79	−7	−9	24	18	10	8
3	54	53	−7	−10	24	17	12	8
4	45	51	−7	−8	25	18	9	8
5	27	33	−9	−5	25	20	10	7
70° Left anterior oblique								
1	65	64	2	0	38	30	16	12
2	83	79	−5	1	26	29	13	8
3	59	72	−6	−1	21	24	13	11
4	41	50	−1	−2	27	29	8	8
5	28	29	−2	0	27	35	15	11

D = delayed image; E = early image; I = intermediate image.

Table 2. Thallium Uptake, Clearance and Redistribution Data in 80 Patients

Thallium Variable	No CAD (n = 27)	CAD (n = 53)	p Value
Uptake (%)			
Early image	78.4 ± 13.7	72.2 ± 17.6	0.001
Intermediate image	85.8 ± 15.1	78.5 ± 19.7	0.0005
Linear clearance (%/h)			
Early to delayed image	4.1 ± 11.3	−2.8 ± 17.1	0.01
Intermediate to delayed image	7.8 ± 11.2	3.2 ± 13.9	0.05
Monoexponential clearance (1/h)			
Early to delayed image	0.09 ± 0.17	−0.01 ± 0.01	0.005
Intermediate to delayed image	0.15 ± 0.18	0.07 ± 0.01	0.05
Redistribution (%)			
Early to delayed image	9.0 ± 14.0	8.8 ± 13.5	NS
Intermediate to delayed image	1.6 ± 13.2	2.5 ± 13.4	NS

CAD = coronary artery disease on angiography. NS = $p > 0.05$.

redistribution) or positive and greater than the upper normal limit for that segment. The normal upper limits for monoexponential clearance half-lives are shown in the sixth and seventh columns of Table 1.

4) Redistribution. Redistribution for each segment was determined by normalizing the 3 × 3 pixel myocardial segment with the greatest thallium activity of the delayed image to 100% and by calculating the difference in relative thallium uptake between the delayed and initial images. A segment of a specific image was considered abnormal if the measured redistribution value was greater than the upper normal limit for that segment. The normal upper limits for redistribution for normal subjects are shown in the eighth and ninth columns of Table 1.

Quantitative variables for detection of coronary artery disease. The criteria of uptake, linear and monoexponential clearance and redistribution were used to define eight separate diagnostic variables (four using the early image as the initial image and four using the intermediate image as the initial image). These single criterion variables were considered abnormal for a patient if a single segment was determined to be abnormal. In addition, double criteria variables were created by combining two single criteria on a segmental basis to create variables with greater specificity or sensitivity. Only certain combinations of variables were used.

Uptake was combined with clearance in two ways: 1) "uptake and clearance" was abnormal for a segment if both uptake and clearance were abnormal, and 2) uptake or clearance was abnormal for a segment if either uptake or clearance, or both, was abnormal. In this way, uptake was combined separately with linear clearance and monoexponential clearance. Uptake was also combined with redistribution as "uptake and redistribution," which was abnormal for a segment if both uptake and redistribution were abnormal. Double criteria variables were derived using the early image

Table 3. Sensitivity, Specificity and Diagnostic Accuracy (%) of Each Quantitative Thallium Variable Based on Single Criteria

Variable	Five Segments/View			Three Segments/View		
	Sens (%)	Spec (%)	Acc (%)	Sens (%)	Spec (%)	Acc (%)
Uptake						
Early	87	63	79	85	78*	82
Intermediate	70§	67	69‡	68§	67	68§
Linear clearance						
Early to delayed	77	48	67	68*	59	65
Intermediate to delayed	77	48	68	70*	52	64
Monoexponential clearance						
Early to delayed	60	59	60	45†	70	54
Intermediate to delayed	75§	52	68	66§	52	61*
Redistribution						
Early to delayed	62	44	56	58	44	54
Intermediate to delayed	53	48	51	42*,†	55	46

*$p < 0.05$; †$p < 0.01$ (five versus three segments per view); ‡$p < 0.05$; §$p < 0.01$ (early versus intermediate image as the initial image). Acc = diagnostic accuracy; Sens = sensitivity; Spec = specificity.

Table 4. Effect on the Sensitivity and Specificity of Uptake by Adding a Second Criterion to Derive a Double Criteria Variable

Variable	Five Segments		Three Segments	
	Sens (%)	Spec (%)	Sens (%)	Spec (%)
Uptake	87	63	85	78
Uptake and linear clearance	64†	78*	57†	85
Uptake and monoexponential clearance	43†	82*	36†	89
Uptake and redistribution	38†	89†	34†	89
Uptake or linear clearance	94*	37†	89	67
Uptake or monoexponential clearance	92	48*	89	67

*$p < 0.05$; †$p < 0.01$ (uptake alone versus uptake with a second criterion). Abbreviations as in Table 3.

as the initial image and also using the intermediate image as the initial image, resulting in 10 double criteria variables.

Statistical analysis. All values were expressed as mean ± 1 SD. To determine the significance of differences in mean values of uptake, clearance and redistribution between patients with and without coronary artery disease, a multivariate analysis of variance was used (BMDP:P4V, Department of Biomathematics, University of California at Los Angeles, revised 1983). Sensitivity, specificity and diagnostic accuracy were compared using the McNemar test (BMDP:P4F) for correlated proportions.

Using stepwise logistic regression, a mathematical model of the probability of coronary artery disease was derived from the quantitative thallium variables (8,12,15). For each myocardial segment of each patient, 18 variables (8 single and 10 double criteria) were evaluated for abnormality. The number of abnormal segments was summed for each variable. Stepwise logistic regression analysis (BMDP:PLR) chose variables to include in the model according to their ability to correlate with the presence of coronary artery disease. Potential variables were ranked in the order of their individual relation to the presence of disease using their chi-square values. Variables were included first in the model on the basis of their chi-square values. The model describes the correlation between the selected variables and the presence of coronary artery disease as a probability or likelihood function with the coefficients of each variable in the model being adjusted to maximize the likelihood in the observed sample of 80 patients. As each variable is entered into the model, the probability or likelihood of disease increases and the log-determined likelihood of disease becomes less negative. Thus, the increases in log likelihood observed as each variable is entered into the model indicate a better correlation of the model with the presence of disease.

The probability of coronary artery disease (from 0 to 1.0) for each patient was determined using the derived probability function of the model using the quantitative thallium data. After choosing a "threshold probability" above which the diagnosis of disease was acceptable, the sensitivity, specificity and diagnostic accuracy of the model were determined.

In a previous study (8) of quantitative analysis of exercise thallium images, specificity was improved without loss of sensitivity by excluding the two basal segments (segments 1 and 5) in each view from the analysis. Accordingly, the sensitivity, specificity and diagnostic accuracy of the same quantitative variables were derived using three segments per view (excluding the basal two segments in each view) and were compared with those obtained using five segments per view.

Results

Comparison of uptake, clearance and redistribution (Table 2). Mean segmental thallium uptake was significantly less in the patients with coronary artery disease. Mean linear and monoexponential clearance was significantly slower in patients with coronary artery disease. However, mean redistribution was not significantly different between the two groups.

Sensitivity, specificity and diagnostic accuracy of quantitative variables. The sensitivities, specificities and diagnostic accuracies of the single criteria variables are de-

Table 5. Univariate Ranking of the Top Five Quantitative Thallium Variables in Order of Their Individual Ability to Predict the Presence of Coronary Artery Disease

Variable	Chi-Square		Log Likelihood
	Value	p Value	
Uptake or linear clearance	62.4	0.0001	−20.0
Uptake and redistribution	49.6	0.0001	−26.3
Uptake	45.8	0.0001	−28.2
Uptake or monoexponential clearance	40.1	0.0001	−30.1
Uptake and linear clearance	38.0	0.0001	−32.2

Table 6. Effect of Stepwise Entry of Variables on the Logistic Regression Model

Step	Variable Entered	Log Likelihood	Improvement	
			Chi-square	p Value
0		−51.2		
1	Uptake or linear clearance (early to delayed image)	−20.0	62.4	0.0001
2	Uptake and linear clearance (early to delayed image)	−17.1	4.5	0.03

tailed in Table 3. Of the variables based on single criteria, uptake in the early image had the greatest diagnostic accuracy ($p < 0.01$).

The effect of using the intermediate image as the initial image, rather than the early image, on sensitivity, specificity and diagnostic accuracy is also shown in Table 3. Sensitivity and diagnostic accuracy decreased significantly for uptake, whereas sensitivity increased for monoexponential clearance.

The effect of using three rather than five segments per view (excluding the basal segments) on sensitivity, specificity and diagnostic accuracy is also shown in Table 3. Specificity of uptake in the early image significantly increased, whereas sensitivity significantly decreased for linear clearance, monoexponential clearance and redistribution.

The sensitivities and specificities of the double criteria variables are shown in Table 4. Variables based on the combined criteria of "uptake in the early image *and* a second criterion (linear or monoexponential clearance or redistribution)" had significantly greater specificity using five segments per view, but had lower sensitivity using either five or three segments per view compared with uptake alone. Variables based on the combined criteria of "uptake *or* a second criterion (linear or monoexponential clearance)" using five segments per view had significantly greater sensitivity but lower specificity compared with uptake alone.

Combining the quantitative thallium variables. Of the 18 potential quantitative thallium variables based on single and double criteria using five segments per view, the initial univariate ranking of the top five variables in order of their individual relation to the presence of coronary artery disease is shown in Table 5. Variables with the best correlation with the presence of coronary artery disease have the least negative log likelihood values. All of the variables chosen used the early image and not the intermediate as the initial image.

When these variables were analyzed in a stepwise logistic regression analysis, only two were chosen: 1) "uptake in the early image or linear clearance measured between the early and the delayed image" and 2) "uptake in the early image and linear clearance between the early and the delayed image" (Table 6). The first variable entered, "uptake or linear clearance," resulted in a major increase in log likelihood and had a large improvement chi-square value. The second variable entered, "uptake and linear clearance," had a smaller effect on log likelihood and a smaller but significant improvement in chi-square value. The final model described the probability of coronary artery disease [P (CAD)], using the following equation:

$$P\,(CAD) = \frac{e(-3.15+1.8a+1.7b)}{1 + e\,(-3.15+1.8a+1.7b)},$$

where −3.15 is a constant, a = number of segments with "abnormal early uptake or abnormal linear clearance or both," and b = number of segments with "abnormal early uptake and abnormal linear clearance."

The probability of coronary artery disease (from 0 to 1.0) for each patient was determined using the probability function. A range of sensitivities, specificities and diagnostic accuracies can be determined for the model depending on the threshold probability chosen as the probability above which the diagnosis of disease is made (Table 7). Increasing the threshold probability necessary for the diagnosis of disease maximizes specificity, whereas a decrease in the threshold probability increases sensitivity. For this analysis using five segments per view, we chose a threshold probability of 0.45, resulting in a sensitivity of 92% and a specificity of 85%. Compared with the variable of uptake, which was the best single criterion variable using five segments, the regression model significantly improved specificity and diagnostic accuracy while maintaining sensitivity (Table 8).

Using three segments per view, a similar logistic regression model was derived from the same double criteria variables. This model had a sensitivity of 85% and a specificity

Table 7. Sensitivity, Specificity and Diagnostic Accuracy (%) of the Regression Model Using Five Segments per View With Corresponding Threshold Probabilities of Coronary Artery Disease

Sensitivity	Specificity	Diagnostic Accuracy	Threshold Probability
100	37	79	0.12
92	85	90	0.45
85	93	89	0.59
83	96	88	0.75
81	100	88	0.89

Table 8. Comparison of the Sensitivity, Specificity and Diagnostic Accuracy of Qualitative and Quantitative Analyses (uptake and the regression model)

Analysis	Sensitivity (n = 53) (%)	Specificity (n = 27) (%)	Diagnostic Accuracy (n = 80) (%)
Qualitative			
Initial defect	85	78	82
Redistribution	66‖	78	70‖
Quantitative (five segments)			
Uptake	87	63*	79
Model	92	85‡	90†,§
Quantitative (three segments)			
Uptake	85	78	82
Model	85	93*,‡	88*,‡

*$p < 0.05$; †$p = 0.01$ (versus qualitative-initial defect); ‡$p < 0.05$; §$p < 0.01$ (uptake versus model); ‖$p < 0.01$ (initial defect versus redistribution).

of 93%, values similar to the results of the model based on data from five segments per view. Compared with the variable of uptake, which was the best single quantitative variable using three segments per view, the regression model significantly improved specificity and diagnostic accuracy without loss of sensitivity (Table 8).

Comparison of qualitative and quantitative analyses. The comparison of the sensitivities, specificities and diagnostic accuracies of qualitative and quantitative analyses is shown in Table 8. Using five segments per view, comparing qualitative and quantitative analysis, qualitative analysis had significantly greater specificity. However, the regression model based on two combined criteria variables had significantly greater diagnostic accuracy than did qualitative analysis and had similar sensitivity and specificity.

Using three segments per view, qualitative and quantitative analysis had similar sensitivity, specificity and diagnsotic accuracy. However, the regression model based on two combined criteria variables using three segments per view had significantly greater specificity and diagnostic accuracy than did qualitative analysis, with similar sensitivity.

Discussion

Quantitative versus qualitative analysis. Quantitative analysis based on thallium kinetic data was applied to dipyridamole thallium imaging and achieved results that were comparable with or superior to those of qualitative analysis by three reviewers, depending on the quantitative approach used. Using three segments per view, the sensitivity, specificity and diagnostic accuracy of initial thallium uptake in the early image were similar to those of qualitative analysis. In a second approach, logistic regression analysis was used to select among several quantitative thallium variables to form a probability model that significantly improved specificity and diagnostic accuracy compared with those obtained with the single quantitative variable of uptake. Also, this regression model based on data using three segments per view had significantly greater specificity and diagnostic accuracy than did qualitative analysis.

Single quantitative thallium variables. The best single quantitative thallium variable for the detection of coronary artery disease using dipyridamole imaging was uptake in the early image. This criterion was also chosen as the single most important quantitative marker for coronary artery disease in a previous study of exercise thallium imaging (8). The use of linear or monoexponential clearance as an additional criterion "abnormal uptake or abnormal clearance or both") resulted in a large significant reduction in specificity with minimal improvement in sensitivity. Thus, the quantitative variable of clearance appears to be less useful with dipyridamole imaging than has been reported with exercise imaging using a similar quantitative approach (6,7,11). Furthermore, because dipyridamole and exercise are different stresses, it is likely that the myocardial clearance to be anticipated with each stress is different.

In a previous preliminary study (13), we examined the possible diagnostic role of quantitative analysis of thallium clearance after dipyridamole infusion. Clearance rates in the previous study were derived using a monoexponential model from data obtained without background subtraction from manually drawn regions of interest placed on images acquired at intermediate and delayed imaging times. Using criteria for abnormality based on canine studies, a sensitivity of 75% and a specificity of 85% were obtained in a study of 66 patients. Compared with the results of our current study using monoexponential clearance measured from the intermediate to the delayed image, sensitivity is similar but specificity differs with a lower specificity of 52% in our current study. This difference in specificity may be related to the use of different criteria for abnormality and the use of background subtraction in our study.

Effect of a delay in obtaining the initial images. With exercise thallium imaging, redistribution may occur early (19,20) and result in filling in of defects observed on the early image. Previously, we have shown (21) that a delay of 18 minutes in obtaining the initial thallium images after exercise resulted in decreased sensitivity with no change in specificity. In our study, we demonstrated decreased sensitivity and diagnostic accuracy using the variable uptake from the intermediate image compared with the early image with no difference in specificity. Thus, imaging after dipyridamole infusion should begin within minutes of thallium injection, as with exercise.

Value of combining variables. Using stepwise logistic regression, a mathematical model describing the probability of coronary artery disease was derived. Two double criteria variables were chosen over single variables: "uptake or linear clearance," a variable with high sensitivity and "uptake and linear clearance," a variable with high specificity. According to the derived probability function, the probability of disease increased as the number of abnormal segments increased. Segments that were abnormal by the more specific variable were weighted more heavily. This approach allows the degree of scan abnormality to be expressed as a probability of disease. The clinician can then interpret this test probability as being a positive or negative test result, depending on the threshold probability of disease considered acceptable for the presence of disease. The sensitivity and specificity of the test can be varied by changing the threshold probability, according to the test indication. For example, for screening purposes a low threshold probability could be used.

Clinical implications. Objective computer methods of analyzing dipyridamole–thallium images provide results comparable with those of qualitative analysis and with less observer variability. Combining quantitative variables in a logistic regression model optimizes the quantitative approach and leads to improved specificity.

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