The ST segment/heart rate slope as a predictor of coronary artery disease: Comparison with quantitative thallium imaging and conventional ST segment criteria

The ST segment shift relative to exercise-induced increments in heart rate, the ST/heart rate slope (ST/HR slope), has been proposed as a more accurate ECG criterion for diagnosing significant coronary artery disease (CAD). Its clinical utility, with the use of a standard treadmill protocol, was compared with quantitative stress thallium (Tl) and standard treadmill criteria in 64 unselected patients who underwent coronary angiography. The overall diagnostic accuracy of the ST/HR slope was an improvement over Tl and conventional ST criteria (81%, 67%, and 69%). For patients failing to reach 85% of their age-predicted maximal heart rate, its diagnostic accuracy was comparable with Tl (77% and 74%). Its sensitivity in patients without prior myocardial infarctions was equivalent to that of thallium (91% and 95%). The ST/HR slope was directly related to the angiographic severity (Gensini score) of CAD in patients without a prior infarction ($r = 0.61$, $p < 0.001$). The ST/HR slope was an improved ECG criterion for diagnosing CAD and compared favorably with Tl imaging. (Am Heart J 112:296, 1986.)

Robert S. Finkelhor, M.D., Kenneth E. Newhouse, B.A., Thomas R. Vrobel, M.D., Stefan D. Miron, M.D., and Robert C. Bahler, M.D. *Cleveland, Ohio*

An accurate noninvasive method of diagnosing coronary artery disease (CAD) has yet to be found. Standard ECG stress testing criteria suffer from many false positive and false negative results.[1-3] Although the addition of thallium (Tl) imaging to the exercise test is generally believed to improve sensitivity and specificity, the enhanced accuracy is modest and the increases in time and expense are considerable. Recently, a new approach to the analysis of ST segment depression has been proposed as an excellent predictor of both the presence and severity of CAD.[4,5] The shift in the ST segment relative to increments in heart rate with exercise was shown to be a linear response, so that the slope of this line (ST/HR slope) could be used in characterizing CAD. This ST/HR slope increased as the severity of obstructive CAD increased. These observations were based on exercise protocols that were custom made for each patient. However, if the concept of a linear relation between ST segment shift and increases in heart rate is valid, it should be applicable to other exercise protocols as well. The current study was undertaken to evaluate the clinical utility of this new criterion for diagnosing significant CAD when conventional treadmill stress testing is used and to compare the ST/HR slope with conventional ST segment criteria and quantitative Tl perfusion scanning in an unselected patient group undergoing coronary angiography.

From the Division of Cardiology, Department of Medicine, Cleveland Metropolitan General Hospital, Case Western Reserve University School of Medicine.

Supported in part by a fellowship training grant from the Northeastern Ohio Affiliate of the American Heart Association and the Edward M. Chester Scholarship Fund of the Cuyahoga County Hospital Foundation.

Received for publication Feb. 19, 1985; revision received Nov. 5, 1985; accepted Dec. 12, 1985.

Reprint requests: Robert S. Finkelhor, M.D., Division of Cardiology, Cleveland Metropolitan General Hospital, 3395 Scranton Rd., Cleveland, OH 44109.

METHODS

Patients. All patients who had both stress Tl treadmill testing and cardiac catheterization between May, 1982, and March, 1984, were considered for study. These patients, for the most part, represented difficult diagnostic problems for their physicians, who resorted to stress Tl testing and cardiac catheterization for clarification. Patients were excluded if the tests were separated by more than 6 months or they had a major cardiac event (i.e., myocardial infarction, coronary artery bypass surgery, or percutaneous transluminal coronary artery angioplasty) occurring between these two tests. Sixty-seven patients met these criteria. Three patients were subsequently excluded because of technically suboptimal coronary angiograms (one patient with an anomalous origin of the right coronary artery which could not be selectively catheterized, one patient with an inadequately visualized proximal left anterior descending coronary artery lesion, and one patient with suboptimal film penetration). The remaining 64 patients formed the study group.

All patients with technically adequate angiograms were included regardless of the presence of any noncoronary cardiac problem either known at the time of noninvasive testing or discovered at the time of angiography. Patients with cardiac problems known to be associated with false positive stress test or Tl results were not excluded, since it was not known if these cardiac problems would also cause false positive results with the use of the ST/HR slope. We chose this approach since an ideal noninvasive test for significant CAD should be able to distinguish this disease from other forms of cardiac disease. Since all patients were evaluated by each of these three methods, their relative diagnostic utilities could be compared in a heterogeneous population.

Pretest risk assessment. The likelihood of CAD before any diagnostic testing was calculated by means of the nomogram of Pryor et al.[6] To calculate the risk of CAD, this nomogram incorporates the relative importance of sex, age, type of chest pain, history of a prior myocardial infarction (MI), resting ECG, smoking history, and serum cholesterol to express the probability of disease. Fifty-two patients had their pretest risk assessed. Twelve patients had undergone prior cardiac catheterizations and were excluded from this assessment, since all had known CAD and this information could have affected the clinical assessment of their chest pain. Risks were assigned by the stratification of Prior et al.,[6] where low risk was a probability <0.33, intermediate risk was between 0.33 and 0.83, and high risk was >0.83.

Data acquisition

Exercise thallium testing. All testing was conducted after an overnight fast. Medications were continued as prescribed. Exercise testing was performed by means of either the Bruce[7] (24 patients) or modified Bruce (Sheffield) protocol[8] (40 patients). Continuous ECG monitoring of leads II, V_1, and V_5 was performed, and simultaneous, three-channel, analogue tracings of these leads were recorded at the end of each minute. Just prior to maximal symptom-limited exertion, 2 mCi Tl-201 chloride was injected into a previously inserted, peripheral intravenous line. Exercise was then continued for an additional 60 seconds.

Tl perfusion scanning began within 5 to 10 minutes of exercise termination. Images were acquired in anterior, 45-degree left anterior oblique, and 70-degree left anterior oblique projections both after maximal exertion and 3 hours later using an Anger camera fitted with a general-purpose, parallel-hole collimator. Each image was acquired for a total of 10 minutes in a 128 × 128 pixel matrix. The data were stored and processed by means of the quantitative technique developed by Watson et al.[9]

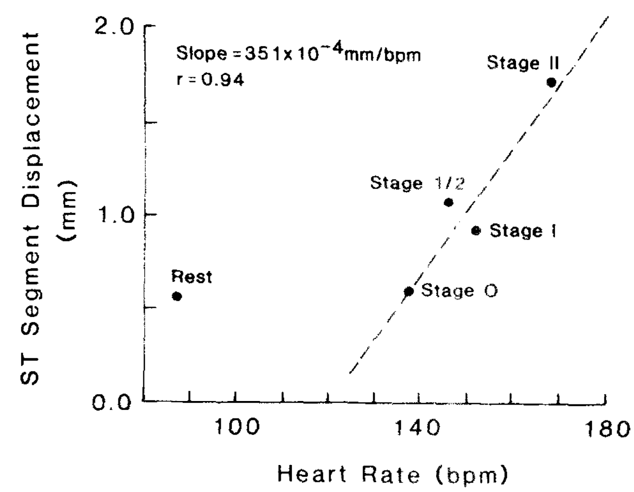

Fig. 1. Calculating the ST/HR slope. This patient was tested by means of the modified Bruce protocol. The "best fit" line for this patient did not include the resting data. Since ST segment deviation did not begin until the third data point *(stage 1/2)*, the last normal stage *(stage 0)* was included and not the resting data, as inclusion of this point decreased the correlation coefficient.

and incorporated in a commercial computer program currently in wide use (Medical Data Systems A^2 computer and software). Briefly, this method determines the centroid for each image, applies a weighted background subtraction to the analogue image, and smooths each image once. The myocardial count density is then displayed in four horizontal profiles for each view.

Cardiac catheterization. Selective coronary angiography was performed by means of either the Sones or Amplatz technique. Multiple views were taken of each coronary artery with hemiaxial angulations taken to clarify the severity of any lesion.

Data analysis

ST/HR slope. The analogue ECG tracings at rest, at the end of each stage, and at the point of maximal exertion were enlarged 3× by means of a commercial artist's enlarger (Artograph DB 3000) and then measured by means of a digitizing computer (Numonics Graphic Analyzer). With the use of the PR segment as the baseline, the ST segment depression or elevation 0.08 seconds after the J point was measured and averaged for 5 to 10 beats. The R-R intervals for these same complexes were measured and averaged. The line best fitting the ST segment depression vs heart rate was determined by means of linear regression analysis with the ST segment depression entered as a positive number for the ordinate and the heart rate entered for the abscissa. The slope of this line was noted for each of the three ECG leads, and the steepest slope was used to represent that patient (Fig. 1). If ST segment elevation was present it was entered as a negative number. If, during exercise, the ST segment progressively elevated, yielding a negative slope, the absolute value of this slope was used for analysis. This occurred in only one patient. A slope $\geq 220 \times 10^{-4}$mm/bpm was arbitrarily chosen to represent

Table I. Patient population (n = 64)

Clinical profile	*No. of patients*
Pretest likelihood of CAD	
High	16
Intermediate	28
Low	8
Severity of CAD	
Number of disease vessels*	
0	27
1	20
2	11
3†	6
Prior MI (clinical criteria)	19
Number of diseased vessels*	
0	4
1	6
2	7
3	2
Prior MI (Tl)	21
Medications	
Beta-blocking drugs	28
Ca^{++}-blocking drugs	14
Digitalis preparations	0

*Defined as ≥75% reduction in luminal diameter.
†Only two subjects had ≥50% narrowing of the left main, but both also had three-vessel disease.

an abnormal response, as this provided the optimal separation between insignificant and significant CAD. All ECG measurements and calculations were made without any knowledge of the angiographic or Tl results.

Interobserver and intraobserver variability in measuring the ST/HR slope was assessed by repeated measurements of 10 tracings, which were selected by an unbiased party to represent the spectrum of the slopes encountered.

Conventional ST segment criteria. The ST segment at rest and at the point of maximal exertion was measured in the same manner as that described for the ST/HR slope analysis. An ischemic response was considered to be present if the ST segment at test termination exhibited horizontal depression of ≥1.0 mm or upsloping depression of ≥1.5 mm. If ST segment elevation occurred with exercise, an elevation ≥1.0 mm at test termination was considered to represent ischemia.

Patients who failed to reach 85% of their age-predicted maximal heart rate and who did not meet the conventional ECG criteria for test positivity were initially assigned a negative test result rather than an inconclusive one. This was done since analogous heart rate levels at which the Tl and ST/HR slope results should be considered inconclusive are not established. Thus strict criteria for positive and negative results were uniformly applied. Patients who did not reach 85% of their age-predicted maximal heart rate were later analyzed as a separate group.

Tl perfusion. The criteria for abnormal myocardial perfusion were those reported for quantitative Tl testing.[9-11] Perfusion was considered abnormal if, on the initial image, the count density was reduced by more than 25% when compared with the contralateral or adjacent myocardial wall. This criterion was applied to all areas except for the inferior or apical regions where, to be considered abnormal, the count density had to be reduced by more than 35%. If the ratio of the abnormal to normal count densities remained unchanged on the reperfusion image, it was considered to be a scar. If the count density in the abnormal region partially or totally approached that of the normal region during the reperfusion image, it was considered to be a zone of ischemia. If no focal defects were found on the initial image and there was little or no reduction of myocardial counts on the reperfusion image, despite adequate exercise, multivessel disease was considered to be present.

Coronary angiograms. Two observers experienced in interpreting coronary angiograms, who had no prior knowledge of the clinical or stress testing data, independently evaluated the angiograms and then reached a consensus for each patient. Significant CAD was considered to be present if there was a 75% or greater luminal diameter narrowing in at least one major coronary artery or a 50% or greater reduction in the luminal diameter of the left main coronary artery.

To provide a semiquantitative assessment of the angiographic severity of the CAD the Gensini scoring system was used.[12] Thereby, the extent of CAD and amount of myocardium potentially subject to ischemia could be described as a continuum, allowing for the use of linear regression analysis to examine the relation between the extent of disease and the ST/HR slope. The Gensini score allocates a number for the degree of luminal diameter narrowing (1% to 25% = 1, 26% to 50% = 2, 51% to 75% = 4, 76% to 90% = 8, 91% to 99% = 16, and total occlusion = 32). This number is then multiplied by a factor accounting for the importance of the lesion's position in the coronary arterial tree (left main ×5, proximal left anterior descending ×2.5, proximal right coronary artery ×1, etc.). The total severity of a patient's CAD is then expressed as the sum of the scores for the individual lesions. The Gensini system assumes a right dominant system. To account for the variable right coronary anatomy, the Gensini score was modified as follows: with a left dominant system, a multiplier of 2× was applied to the score for the left coronary artery system and the score for the right coronary artery reduced to 0.5 of its original value; with a balanced circulation, the left system was increased by 1.5× and the right coronary artery score reduced to 0.75× its original value. Patients who were being evaluated after coronary artery bypass surgery had their grafts scored as if they were the native vessels they replaced.

Statistics. To compare the various diagnostic methods the sensitivity, specificity, and diagnostic accuracy were expressed as a percentage and calculated as follows: sensitivity = true positive results /(true positive results + false negative results), specificity = true negative results /(true negative results + false positive results), and the diagnostic accuracy = (true positive results + true negative results)/ the total sample population.

Since the numerical values of these test descriptors are

Table II. Concomitant cardiac problems (19 patients)

Problems	*No. of patients*
Postcoronary artery bypass surgery	5
Postpercutaneous coronary angioplasty	1
Clinically suspected coronary artery spasm	2
Mitral valve prolapse in the absence of CAD	3
Idiopathic cardiomyopathy	2
Left ventricular hypertrophy	2
Incomplete aortic coarctation repair (2 decades after surgery)	1
Aortic valve disease	2
Coronary artery arteriovenous malformation	1
Left bundle branch block	1
Right bundle branch block	2

dependent upon the cut point chosen for test positivity, a method that is independent of cut point was used to further compare the relative utility of the ST/HR slope and the conventional measurement of ST segment depression. This method plots the sensitivity (true positive ratio) against one minus the specificity (false positive ratio) at various cut points to generate curves for each diagnostic method. These curves are called receiver-operating characteristic curves, and the areas under these resultant curves can then be compared by statistical means to identify which diagnostic method has the greater utility.[13-15]

The influence of the noninvasive testing on the pretest risk of CAD was assessed by Bayes' theorem.[16] This analysis was restricted to subjects with an intermediate likelihood of disease prior to the exercise test. Linear regression analysis by means of the least-squares method was used to describe the intra/interobserver variability and to test relationships between the Gensini score and the ST/HR slope. One-way analysis of variance was used to test for differences between the means of the ST/HR slopes for one; two; and three-vessel disease. The Bonferroni multiple-comparison procedure (*t* test) was applied to test for pairwise differences between the means.

RESULTS

Patient population. The mean age of the patients was 51.4 years (range 29 to 78 years). Nineteen were women and 45 were men. All but two of the 64 patients were assessed for either typical (34 patients) or atypical (28 patients) anginal symptoms. Of the two who were without chest pain, one was electively evaluated 6 months after successful coronary angioplasty and the other after an uncomplicated inferior MI. The clinical profile of the patient population is listed in Table I. The population exhibited a broad range of pretest likelihoods for CAD, slightly biased toward high risk.

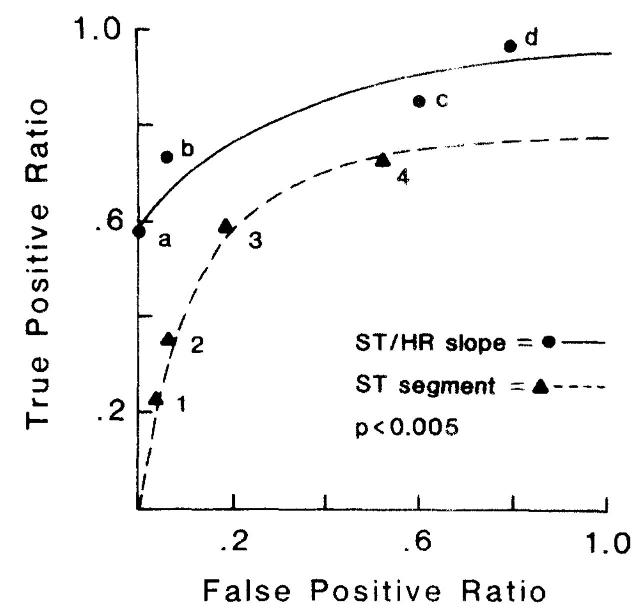

Fig. 2. The receiver-operating characteristic curves for the ST/HR slope and the ST segment. Curves for the true positive ratio (sensitivity) vs the false positive ratio (1 − specificity) are generated by using different cut points for test positivity (i.e., *a* = 300, *b* = 225, *c* = 150, *d* = 75 × 10^{-4} mm/bpm; *1* = 2.5, *2* = 2.0, *3* = 1.5, and *4* = 1.0 mm). The areas under the resultant curves are independent of cut point and can be compared by statistical means. This shows that the ST/HR slope was a significantly improved diagnostic modality compared with the ST segment.

Nineteen subjects had at least two out of three clinical indicators of a prior MI (a history of prolonged anginal chest pain, pathologic Q waves on the resting ECG, or enzyme changes consistent with a MI). Twenty-one patients had evidence of a scar on Tl perfusion scanning, 11 of whom also had clinical evidence of a prior MI.

The heterogeneity of the population was further evidenced by the following: (1) 30 patients had resting ECGs exhibiting either nonspecific ST-T wave changes or early repolarization; (2) 35 of the patients failed to reach 85% of their age-predicted maximal heart rate, 28 of whom were taking a beta-blocking drug; (3) 9 of the 27 patients classified as having insignificant CAD by the criterion of 75% reduction in luminal diameter did have lesions with a 50% to 75% reduction in luminal diameter, four of whom had evidence of a prior MI; and (4) 19 patients were found to have one or more cardiac problems which could have further complicated the interpretation of their exercise test (Table II).

Measurement of the ST/HR slope and its reproducibility. The Bruce and modified Bruce protocols provided a mean of 4.3 points with a range of 2 (two patients) to 7 points with which to identify the "best fit" line describing the slope of the ST segment vs

Table III. Test comparisons

Group	*Test*	*Sensitivity*	*Specificity*	*Diagnostic accuracy*
Total (n = 64)	ST/HR slope	76	89	81
	ST	62	78	69
	Tl	95	30	67
Without prior infarction	ST/HR slope	91	87	89
(n = 45)	ST	77	83	80
	Tl	95	26	60
Intermediate pretest	ST/HR slope	87	93	90
risk (n = 28)	ST	60	86	73
	Tl	93	38	68
<85% predicted	ST/HR slope	75	82	77
maximal heart rate	ST	54	91	66
(n = 35)	Tl	100	18	74
≥85% predicted	ST/HR slope	77	94	86
maximal heart rate	ST	77	75	76
(n = 29)	Tl	85	38	59

Tl = thallium.

heart rate. The mean r value for these lines, excluding the two patients with only 2 points, was 0.94 ($p < 0.01$). The reproducibility of the intraobserver and interobserver measurements was very high ($r = 0.99$, SEE = 10×10^{-4} mm/bpm and $r = 0.98$, SEE = 10×10^{-4} mm/bpm, respectively).

In five patients the "best fit" line was not statistically significant for the number of data points. Three of these patients had no clear directional change of the ST segment during exercise, so that their ST/HR slope was approximately horizontal and they did not have significant CAD. The remaining two patients had lines with correlation coefficients of 0.76 for 3 points and 0.75 for 4 points. For both of them, the calculated slopes correctly predicted CAD. One patient completed only stage 1 of the Bruce protocol so that the CAD slope was based on 2 points. As expected by such a short exercise time and as confirmed by the slope of the ST/HR response and by conventional stress testing criteria, this patient had significant CAD. A second patient was only able to complete the first stage of the modified Bruce protocol. He was elderly, hypertensive, and had mild aortic valvular disease but was not found to have any CAD. The slope of the line from the two points available gave a false positive result.

Comparison of the ST/HR slope with other diagnostic criteria. The sensitivity, specificity, and diagnostic accuracy of the ST/HR slope, conventional ST criteria, and Tl test for the diagnosis of CAD are given in Table III. The ST/HR slope consistently had the highest diagnostic accuracy when compared with conventional ST segment criteria and quantitative Tl imaging for the entire study population as well as for each group.

However, sensitivity, specificity, and diagnostic accuracy are all dependent on the cut point for test positivity chosen. With the use of a statistical method which is independent of cut point, the receiver-operating characteristic curve, the ST/HR slope was still a significant improvement over the conventional ST segment deviation (Fig. 2).

The ST/HR slope was helpful in altering an intermediate probability of CAD. Twenty-seven out of the 28 intermediate-risk patients had their post-test risk changed to either a high or a low probability of CAD by the ST/HR slope and 25 of these 27 changes were correct. Conventional ST segment criteria and quantitative Tl fared worse in altering the probability and in doing so correctly. The ST segment shifted 14 of 28 probabilities and 10 were shifted correctly. Quantitative Tl imaging changed 23 of 28 with 14 correctly predicting CAD.

Relation of the ST/HR slope to severity of CAD. The correlation between the ST/HR slope and the Gensini score was highly significant for all patient groups except for those with evidence of a MI by either clinical criteria or Tl testing (Table IV). It is important to note that the correlations remained significant for the group that did not reach 85% of their predicted maximal heart rate and for those patients with concomitant cardiac problems which could have interfered with testing. Eleven out of 14 of the patients using calcium channel–blocking drugs also had prior MIs, so the effect of these drugs on the ST/HR slope could not be independently assessed. The use of the ST/double-product slope

Table IV. Correlations of Gensini score and parameters of the exercise stress test

	n	r *Value*
ST/HR slope		
All patients	64	0.53*
No MI	45	0.61*
MI	19	0.36
No scar on Tl imaging	43	0.65*
Heart rate < 85% age-predicted maximum	35	0.55*
Patients using beta blockers	28	0.59*
Concomitant cardiac problems	19	0.82*
ST segment change from baseline		
All patients	64	0.23
No prior MI	45	0.25
Exercise duration†		
All patients	64	−0.12
No prior MI	45	−0.24

*$p < 0.001$; all others not significant.
†Measured from the beginning of stage 1 of the Bruce protocol.

decreased the correlation of slope with the severity of coronary disease ($r = 0.37$, $p < 0.01$). In our population, neither the absolute degree of ST segment change nor the duration of exercise correlated significantly with the Gensini score.

Although the slopes for insignificant and significant disease were very different ($p < 0.001$), the slopes did not clearly discern the groups with single; double; and triple-vessel disease in this relatively small population (Table V).

The ST/HR slope criterion resulted in very few false positive tests (Table VI) and nine false negative tests. Seven of these had clinical evidence of a prior MI, and the other two failed to reach 85% of the age-predicted maximal heart rate and were also taking calcium channel blockers. Conventional ST criteria yielded more false positive tests (Table VI) and 14 false negative tests. Nine of these had a prior MI and the remaining five failed to reach 85% of their age-predicted miximal heart rate. Three of them were taking both a calcium channel blocker and a beta-blocker. Tl imaging resulted in many false positive tests (Table VI). Even if the cut point for significant CAD were to be lowered to ≥50% reduction in luminal diameter, 13 false positive tests would remain. However, there were only two false negative tests with the use of Tl. None of the patients with bundle branch blocks (two right and one left) had false results by an testing modality.

DISCUSSION

The ST/HR slope, as determined from a conventional treadmill protocol, improved the ability to detect or exclude CAD when compared with conventional ST segment criteria and quantitative Tl testing. It was most useful in patients without a prior MI and it appeared to be less adversely affected by the inability of a patient to reach 85% of predicted maximal heart rate or by beta-blocking drugs.

Table V. The relation between the ST/HR slope and the number of diseased vessels

No. of diseased vessels	*ST/HR slope**	
	Total patients	*Without clinical MI*
0	145 ± 75* (n = 27)	156 ± 74† (n = 23)
1	329 ± 111 (n = 20)	357 ± 100 (n = 14)
2	355 ± 234 (n = 11)	526 ± 233 (n = 4)
3	411 ± 321 (n = 6)	541 ± 318 (n = 4)

*Values are mean ± SD; slopes are $\times 10^{-4}$ mm/bpm.
†$p < 0.001$ for 0- vs 1-vessel disease only (Bonferroni's t test)

Table VI. Analysis of false positive results

Associated cardiovascular problems	*ST/HR slope*	*ST*	*Thallium*
Intermediate CAD* (n = 9)	0	1	4
Coronary bypass surgery (n = 5)	1	1	2
Presumed coronary artery spasm (ergonovine testing not done) (n = 2)	0	0	2
Idiopathic cardiomyopathy (n = 2)	0	0	2
Aortic valve disease (n = 2)	2	1	1
Postcoarctation repair (n = 1)	0	0	1
Coronary artery AVM (n = 1)	0	0	1
MVP without other disease (n = 3)	0	1	2
No cardiovascular disease found (n = 4)	0	2	4
Total false positive results in the entire population	3	6	19

AVM = arteriovenous malformation; MVP = mitral valve prolapse.
*Reduction in luminal diameter of ≥50% but <75%.

Relation of CAD severity and the ST/HR slope. The ST/HR slope also correlated with the severity of CAD, as expressed by the Gensini score, in patients without a prior MI. This is not unexpected since it is accepted that a markedly positive ECG stress test at low levels of exertion suggests more severe disease, in particular triple-vessel or left main pathology.[17,18] With a fixed coronary stenosis, myocardial ischemia will be directly proportional to increases in heart rate, since myocardial oxygen demand is proportional to heart rate.[19,20] The degree of myocardial ischemia and the resulting ST segment depression will also be influenced by the number and severity of the stenoses. Thus, in severe CAD relatively small increments in heart rate would lead to ST segment depression and a steep ST/HR slope. These factors may account for both the linear relation between heart rate and the ST segment deviation that we and others have observed as well as the steeper ST/HR slopes with increasing severity of disease.[4, 5, 21, 22]

The concept that the ST/HR slope may reflect the extent of ischemia is also supported by the data of Kligfield et al.,[23] who showed that the ST/HR slope is inversely related to the change in left ventricular ejection fraction with exercise. Recent reports have already suggested that the ST/HR slope may reflect the degree of revascularization following coronary artery bypass surgery[24] and after percutaneous transluminal coronary angioplasty.[25] If these observations are confirmed by other investigators, the ST/HR slope may prove to be a useful indicator of the functional severity of CAD.

The absence of a correlation between the ST/HR slope and the Gensini score in subjects with a prior MI is not surprising. Many of these patients may have relatively little myocardium remaining at risk of stress-induced ischemia, even though they have a high Gensini score. This can occur because this scoring system assigns a proportionately higher value for totally occluded vessels. These vessels are most likely to be associated with an infarction, and there may or may not be additional myocardial areas that are at risk of developing ischemia. Thus there may be no correlation between a potential method for detecting stress-induced ischemia and a scoring system that does not reflect whether there is viable muscle beyond the occlusion.

Effect of beta-blockade on the ST/HR slope. Beta-blockade reduces heart rate at any level of work and thereby reduces myocardial oxygen demand and presumably ischemia at each workload.[26, 27] At maximal effort, the heart rate is lower and the maximal amount of ST segment depression is less. It is important to note that a reduction in maximal heart rate need not mean that the extent to which ST depression occurs relative to increases in heart rate should substantially differ from that which occurs without beta-blockade. Recent work from other groups supports this concept that the ST/HR slope need not be altered by beta-adrenergic blockade[22, 28] and the data from the present study suggest that the diagnostic accuracy of the ST/HR slope is less adversely affected by beta-blockade than are conventional ECG stress testing criteria.

Clinical utility of the ST/HR slope. None of the prior studies of the ST/HR slope assessed the pretest risk of CAD or determined how this diagnostic criterion altered a subject's risk. Pretest risk assessment is important, since in patients with a very low probability of CAD before exercise testing, angiography may not be warranted even with a positive exercise test. Those most likely to have disease by risk assessment gain little from exercise testing. Diagnostic testing is most useful in those patients where the test outcome is likely to alter the diagnostic evaluation, that is, those with an intermediate pretest risk.[29, 30] In our population with an intermediate pretest risk, the ST/HR slope correctly polarized the risk of CAD in 88% of the patients, which further attests to its clinical diagnostic potential.

Some of the differences in sensitivity and specificity between our study and those reported by other groups with the use of this new criterion may be explained by differences in patient population and methodology.[31] The study population of Elamin et al.[5] may have been skewed by having predominantly patients with either a very low or a high pretest risk of CAD. This is indirectly supported by the fact that none of their patients had coronary artery lesions between 50% and 75% luminal diameter narrowing. Thus, without many patients with an intermediate degree of CAD, they found a very high sensitivity and specificity. In contrast, the relatively poor results of Quyyumi et al.[32] may have been the result of their excluding patients if they did not have a statistically significant ST/HR slope or if they had either a baseline ST segment elevation or progressive ST elevation with exercise. Excluding these patients may have partly contributed to their poorer sensitivity and specificity.

Sensitivity and specificity are also greatly influenced by the cut point selected to determine a positive result. Had we selected the lower cut point proposed by Elamin et al.[5] (130×10^{-4} mm/bpm), our sensitivity would have improved (92%) but at the expense of a much poorer specificity (37%). These values are almost identical to those obtained by Quyyumi et al.[32] which used the same lower cut point. The most appropriate ST/HR slope for identifying significant and insignificant CAD must still be determined in relation to the population being tested and the goals of the physician(s) performing the test (Fig. 2).[13]

Quantitative Tl testing. This study was not intended to compare Tl testing with prior reports of this technique. Rather, our object was to compare the ST/HR slope with Tl testing and standard ST segment criteria in the same patient population. Nevertheless, we did observed a lower specificity for quantitative Tl testing than has been reported.[10, 33] This may be partly due to the low number of true negative tests (eight subjects). Because quantitative

Tl is generally perceived as being quite sensitive, a patient with a negative Tl test would be less likely to be referred for angiography and thus become part of our study population. Our specificity was also reduced by many false positive results and, as has been previously reported,[34] many of the false positive results occurred in patients with cardiac disease other than CAD. It is of interest that only 4 of the 15 subjects with false positive Tl scans were free of any detectable cardiac disease. In the remaining 11 subjects the Tl abnormalities could reflect vascular or microvascular disease that standard angiography is incapable of detecting. This highlights one of the limitations of using angiography as the "gold standard" for assessing the severity of ischemic disease, especially since the relationship of angiographically observed coronary artery narrowing to coronary blood flow and ischemia is still being debated.[35,36] Had we restricted the calculations of sensitivity and specificity to subjects whose only cardiac problem was CAD uncomplicated by a MI and subjects not found to have any cardiac disease (total n = 39) and had we defined significant CAD as 50% reduction in luminal diameter, we would have reported a sensitivity of 88% and a specificity of 70%. These values are more similar to other reports where the criteria of $\geq$50% coronary artery narrowing was applied to a restricted population.[10,33] This emphasizes the major influence of both the study population and the cut point for positivity on the apparent diagnostic accuracy of a test.[37]

Conclusions. This study showed that the ST/HR slope had a greater diagnostic accuracy for CAD than either conventional ST segment criteria or a widely used method for quantitative Tl imaging, and the ST/HR slope also correlated with the severity of the CAD as determined by the Gensini scoring system. If substantiated by further work, this new ECG criterion could easily become an on-line parameter with modern, computerized exercise testing equipment.

We thank George Williams, Ph.D., and Christine McLaren, Ph.D., for suggestions regarding the statistical approach and Louise Cretu for help in preparing this manuscript.

REFERENCES

1. Fortuin NJ, Weiss JL: Exercise stress testing. Circulation **56**:699, 1977.
2. Erikssen J, Enge I, Forfang K, Storstein O: False positive diagnostic tests and coronary angiographic findings in 105 presumably healthy males. Circulation **54**:371, 1976.
3. Kramer N, Susmano A, Shekelle RB: The "false negative" treadmill exercise test and left ventricular dysfunction. Circulation **57**:763, 1978.
4. Elamin MS, Mary DASG, Smith DR, Linden RJ: Prediction of severity of coronary artery disease using slope of submaximal ST segment/heart rate relationship. Cardiovasc Res **14**:681, 1980.
5. Elamin MS, Boyle R, Kardash MM, et al: Accurate detection of coronary heart disease by new exercise test. Br Heart J **48**:311, 1982.
6. Pryor DB, Harrell FE, Lee KL, Califf RM, Rosati RA: Estimating the likelihood of significant coronary artery disease. Am J Med **75**:771, 1983.
7. Bruce RA, Hornsten TR: Exercise stress testing in evaluation of patients with ischemic heart disease. Prog Cardiovasc Dis **11**:371, 1969.
8. Sheffield LT, Roitman D: Stress testing methodology. Prog Cardiovasc Dis **19**:33, 1976.
9. Watson DD, Campbell NP, Read EK, Gibson RS, Teates CD, Beller GA: Spatial and temporal quantitation of plane thallium myocardial images. J Nucl Med **22**:577, 1981.
10. Berger BC, Watson DD, Taylor GJ, et al: Quantitative thallium-201 exercise scintigraphy for detection of coronary artery disease. J Nucl Med **22**:585, 1981.
11. Bateman TM, Maddahi J, Gray RJ, et al: Diffuse slow washout of myocardial thallium-201: A new scintigraphic indicator of extensive coronary artery disease. J Am Coll Cardiol **4**:55, 1984.
12. Gensini GG: A more meaningful scoring system for determining the severity of coronary heart disease. Am J Cardiol **51**:606, 1983.
13. Hanley JA, McNeil BJ: The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology **143**:29, 1982.
14. Hanley JA, McNeil BJ: A method of comparing the areas under receiver operating characteristic curves derived from the same cases. Radiology **148**:839, 1983.
15. Lusted L: Decision-making studies in patient management. N Engl J Med **284**:416, 1971.
16. McNeil BJ, Keeler E, Adelstein SJ: Primer on certain elements of medical decision making. N Engl J Med **293**:211, 1975.
17. Weiner DA, McCabe CH, Ryan TJ: Identification of patients with left main and threee vessel coronary disease with clinical and exercise test variables. Am J Cardiol **46**:21, 1980.
18. Colby J, Hakki A, Iskandrian AS, Mattleman S: Hemodynamic, angiographic and scintigraphic correlates of positive exercise electrocoardiograms: Emphasis on strongly positive exercise electrocardiograms. J Am Coll Cardiol **2**:21, 1983.
19. Kitamura K, Jorgensen CR, Gobel FL, Taylor HL, Wang Y: Hemodynamic correlates of myocardial oxygen consumption during upright exercise. J Appl Physiol **32**:516, 1972.
20. Gobel FL, Nordstrom LA, Nelson RR, Jorgensen CR, Wang Y: The rate-pressure product as an index of myocardial oxygen consumption during exercise in patients with angina pectoris. Circulation **57**:549, 1978.
21. Okin PM, Kligfield P, Amelsen O, Goldberg HL, Borer JS: Improved accuracy of the exercise electrocardiogram: Identification of three-vessel coronary disease in stable angina pectoris by analysis of peak rate related changes in ST segments. Am J Cardiol **55**:271, 1985.
22. Gao C, Dressendorfer RH, Gordon S, Timmis GC: Adjusting for heart rate increment improves sensitivity of exercise electrocardiography in exertional chest pain (abstr). J Am Coll Cardiol **3**:520, 1984.
23. Kligfield P, Okin PM, Ameisen O, Wallis J, Borer JS: Correlation of the exercise ST/HR slope with anatomic and radionuclide cineangiographic findings in stable angina pectoris. Am J Cardiol **56**:418, 1985.
24. Kardash MM, Boyle RM, Watson DA, Stoker JB, Mary DASG, Linden RJ: Assessment of aortocoronary bypass grafting using exercise ST segment/heart rate relation. Br Heart J **51**:386, 1984.
25. Silverton NP, Elamin MS, Smith DR, et al: Use of exercise maximal ST segment/heart rate slope in assessing the results of coronary angioplasty. Br Heart J **51**:379, 1984.
26. Gianelly RE, Treister BL, Harrison DC: The effect of propa-

nolol on exercise-induced ischemic S-T segment depression. Am J Cardiol **24**:161, 1969.
27. Jorgensen CR, Wang K, Wang Y, Gobel FL, Nelson RR, Taylor H: Effect of propanolol on myocardial oxygen consumption and its hemodynamic correlates during upright exercise. Circulation **48**:1173, 1973.
28. Kardash M, Boyle R, Elamin MS, Stoker JB, Mary DASG, Linden RJ: Detection of severity of coronary artery disease by the ST segment/heart rate relationship in patients on beta-blocker therapy. Cardiovasc Res **16**:508, 1982.
29. Griner PF, Mayewski RJ, Greenland P: Selection and interpretation of diagnostic tests and procedures: Principles and applications. Ann Intern Med **94**:553, 1981.
30. Epstein SE: Implications of probability analysis on the strategy used for noninvasive detection of coronary artery disease. Am J Cardiol **46**:491, 1980.
31. Philbrick JT, Horwitz RI, Feinstein AR: Methodologic problems of exercise testing for coronary artery disease: Groups, analysis and bias. Am J Cardiol **46**:807, 1980.
32. Quyyumi AA, Raphael MJ, Wright C, Bealing L, Fox KM: Inability of the ST segment/heart rate slope to predict accurately the severity of coronary artery disease. Br Heart J **51**:395, 1984.
33. Maddahi J, Garcia EV, Berman EV, et al: Improved noninvasive assessment of coronary artery disease by quantitative analysis of regional stress myocardial distribution and washout of thallium-201. Circulation **64**:924, 1981.
34. Berger BC, Abramowitz R, Park CH, Desai AG, Madsen MT, Chung EK, Brest AN: Abnormal thallium-201 scans in patients with chest pain and angiographically normal coronary arteries. Am J Cardiol **52**:365, 1983.
35. White CW, Wright CB, Doty DB, et al: Does visual interpretation of the coronary arteriogram predict the physiologic importance of a coronary stenosis? N Engl J Med **310**:819, 1984.
36. Hoffman JIE: Maximal coronary flow and the concept of coronary vascular reserve. Circulation **70**:153, 1984.
37. Ransohoff DF, Feinstein AR: Problems of spectrum and bias in evaluating the efficacy of diagnostic tests. N Engl J Med **299**:926, 1978.

Value of two-dimensional echocardiography, electrocardiography, and clincial signs in detecting right ventricular infarction

Noninvasive tests for the diagnosis of right ventricular (RV) infarction—two-dimensional echocardiography (2DE), ST elevation in V_4R, and clinical parameters—were compared with equilibrium gated blood pool study (GBPS) in 50 patients after acute inferior myocardial infarction. Twenty-two of 50 patients had RV wall motion abnormalities on GBPS and 20 of 50 on 2DE. Sensitivity and specificity of 2DE was 82% and 93%, ST elevation in V_4R was 50% and 71%, elevation of venous pressure was 77% and 85%, and a positive Kussmaul's sign was found in 59% and 89% for the detection of RV infarction compared to GBPS. Patients with RV infarction had higher peak creatine kinase levels and lower left ventricular ejection fractions than patients without RV infarction. Three patients died and all had significant left ventricular damage. At 20 weeks' follow-up, two thirds of the patients had no residual RV wall motion abnormalities, and all but two patients showed some recovery. (Am Heart J 112:304, 1986.)

Gregory R. Bellamy, F.R.A.C.P., Helge H. Rasmussen, F.R.A.C.P., Fred N. Nasser, F.R.A.C.P., Josephine C. Wiseman, F.R.A.C.P., and Robert A. Cooper, F.R.A.C.P. *St. Leonards, New South Wales, Australia*

Various noninvasive techniques are currently being used for the diagnosis of right ventricular (RV) myocardial infarction. Studies describing clinical, ECG, and two-dimensional echocardiographic (2DE) findings in RV infarction have used a variety of other independent techniques to verify the diagnosis. However, the verification has often not occurred at the time the technique in question was performed and patients for some studies were selected after the diagnosis had been confirmed by other means.[1-10] It would appear desirable to establish the diagnostic accuracy of these noninvasive techniques, since they can easily be performed at the bedside. A

From the Departments of Cardiology and Nuclear Medicine, Royal North Shore Hospital.

Received for publication July 8, 1985; revision received Nov. 18, 1985; accepted Dec. 30, 1985.

Reprint requests: Dr. Gregory R. Bellamy, Department of Cardiology, Royal North Shore Hospital, St. Leonard's, New South Wales 2065, Australia.