Detection of Anatomically Severe Coronary Artery Disease by the ST/HR Slope*

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Over the past ten years, it has become well recognized that standard exercise electrocardiography has poor sensitivity for the diagnosis of coronary artery disease and poor predictive value for the identification of anatomically extensive disease. Reports of improved survival with coronary artery bypass surgery in patients with three-vessel disease, particularly in those patients with functionally severe exercise-induced ischemia, together with recent observations that coronary artery scoring systems may more effectively stratify prognosis than the number of obstructed vessels, highlight the need for more accurate noninvasive identification of anatomically severe coronary disease in patients with angina pectoris.

The ST/HR slope, which normalizes the amount of myocardial ischemia during exercise (estimated by ST segment depression) for the augmentation in myocardial oxygen demand (estimated by the increase in heart rate), has been shown to improve the diagnostic accuracy of the exercise ECG for the identification of patients with three-vessel coronary disease. Further, the ST/HR slope appears to be relatively independent of the absolute heart rate achieved, allowing the accurate assessment of the anatomic and functional severity of coronary disease even in patients with limited effort tolerance and in patients taking beta-blocking drugs. Exercise test findings in a patient with typical angina due to three-vessel coronary disease, who had a markedly blunted heart rate response to exercise while on therapy with drugs, are presented to illustrate the theoretic basis and practical value of the ST/HR slope for the detection of prognostically important coronary artery disease.

Case Report

The patient is a 56-year-old man who was well until November 1982, when he presented to The New York Hospital-Cornell Medical Center with prolonged epigastric discomfort and ECG changes consistent with an acute inferior wall myocardial infarction. He had an uncomplicated course and was discharged from the hospital on therapy with atenolol and isosorbide dinitrate. He did well, with only rare exertional angina provoked by high levels of activity, until December, 1984, when, with the onset of colder weather, he began to experience more frequent exertional angina with less provocation. With the addition of nifedipine and aspirin to his medical regimen, his anginal pattern stabilized at one to four episodes of exertional angina daily, occurring whenever he walked more than two blocks. To assess the prognostic significance of his coronary disease, and to assist in planning further therapy, he was admitted for elective coronary angiography.

As part of our prospective evaluation of the exercise electrocardiogram in coronary artery disease, the patient had a symptom-limited treadmill exercise test prior to coronary arteriography. He was taking his usual dosages of atenolol, isosorbide dinitrate and nifedipine at the time of study. The test was terminated due to limiting typical anginal chest pain after 2 minutes of stage 2.0 of the Cornell protocol, at which time the heart rate was only 52 beats/min (48 percent of age-predicted maximum) and the blood pressure was 110/60 mm Hg. Slightly less than 0.1 mV of horizontal ST-segment depression was present in the infarolateral leads at end exercise (Fig 1), returning to baseline by 3 minutes of recovery. Although the heart rate at end exercise was low, none of the features often associated with anatomically extensive coronary disease (early test positivity, prolonged ischemic response, or marked ST segment depression) were present in this case.

Calculation of the maximal ST/HR slope was performed by linear regression analysis, relating the amount of ST-segment depression in each lead (except aVR and aVL), measured to the nearest 10 µV at a point 60 msec after the j point, to the heart rate at the end of each stage of exercise. Because the maximal rather than the average ST/
HR slope is sought, linear regression analysis is performed from the end of exercise to earlier intermediate stage points, using heart rate as the independent variable and the magnitude of ST segment depression as the dependent variable. The slope derived from linear regression analysis of the final three data points is then compared with slopes obtained by including progressively earlier data points. The highest ST/HR slope with a statistically significant coefficient of correlation is then taken as the test finding for that lead. After calculation of the maximal ST/HR slope in each lead, the highest ST/HR slope from among all leads is taken as the final test result. The maximal ST/HR slope in this patient was 14.0 \( \mu \text{Volt/beat/min} \) in lead V\(_6\) (Fig 2). This is a strikingly abnormal value, since ST/HR slopes \( \geq 6.0 \ \mu \text{Volt/beat/min} \) have been found to predict anatomically extensive and functionally severe coronary disease.\(^{7-9,34}\)

Cardiac catheterization with coronary arteriography was performed in March, 1985. Ventriculography revealed a left ventricular ejection fraction of 60 percent with inferobasal and anterolateral hypokinesia that improved during post-extrasystolic beats. The left anterior descending coronary artery was totally occluded after the second septal perforator branch; the circumflex coronary artery had a 90 percent proximal stenosis, with an additional 75 percent distal stenosis before a large posterolateral branch and a total occlusion of the third obtuse marginal branch; the right coronary artery was dominant and was totally occluded in its middle third. Coronary artery scoring resulted in a Gensini score\(^{35}\) of 100 and a Duke jeopardy score\(^{36}\) of 10; each is consistent with anatomically extensive disease. The patient subsequently underwent saphenous vein aorto-coronary bypass to the left anterior descending, right coronary and first obtuse marginal branch of the circumflex coronary artery, and remains angina-free 18 months after this procedure.

**DISCUSSION**

This case illustrates the practical and theoretic advantages of the ST/HR slope method for the identification of prognostically important coronary disease\(^{7-9,34}\) and highlights limitations of standard exercise test methodology in some patients with typical angina.\(^{34}\) Considerable experimental and clinical evidence suggests that the ST/HR slope should more accurately reflect the anatomic and functional extent of myocardial ischemia than do standard exercise test criteria alone.

Strong correlation has been found between myocardial oxygen demand and the change in heart rate with exercise in experimental animals, normal subjects and in patients with coronary artery disease.\(^{35,36}\) It is not surprising therefore that Detre et al\(^{37}\) found ST segment depression to be directly related to changes in heart rate in patients with coronary obstruction. Although the magnitude of ST segment depression with exercise has been related to the extent of myocardial ischemia caused by underlying coronary artery dis-
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Figure 2. Calculation of the maximal ST/HR slope. Cumulative ST-segment depression in lead V<sub>6</sub> is plotted against exercise heart rate in this patient with three-vessel coronary artery disease. Initially, there is no change in ST-segment level with exercise. However, at a heart rate of 77 beats/min there is the rapid onset of ST-segment depression, becoming 70 μVolts by end exercise at a heart rate of 82. The slope of the line relating the three data points by linear regression is statistically significant, and is consistent with the presence of anatomically extensive coronary disease.

Thus, the ST/HR slope may be relatively independent of either the heart rate achieved during exercise or the magnitude of ST-segment depression alone. In the present case, the patient was limited by increasing angina after 10 minutes of exercise, but the heart rate was only 82 beats/min due to a beta-adrenergic blocking drug. Even though ST segment depression did not reach 0.1 mV at end exercise, it is obvious, in context, that the lesser ST depression observed is a reflection of important ischemia, “masked” by the blunted heart rate response. However, none of the standard exercise test criteria often used to identify anatomically severe coronary disease<sup>4</sup> (stage 1 positive response, prolonged ischemic response, markedly positive response) were present to indicate the extent of coronary obstruction found at catheterization. In contrast, the rate of change in ST-segment depression with exercise indicated by the ST/HR slope method suggests the presence of anatomically and functionally important coronary disease (Fig 2). Even though the absolute amount of ST-segment depression in lead V<sub>6</sub> is small (70 μVolts), this change occurs between a heart rate of 77 and 82 beats/min. Thus, the modest amount of ST segment depression, when adjusted for the small augmentation in myocardial oxygen demand, is consistent with the presence of extensive coronary disease in this patient.

As illustrated by this case, estimation of the severity of coronary disease by the ST/HR slope is not markedly affected by the use of beta-blocking drugs.<sup>28,29</sup> So long as ischemia occurs, since the slopes of lines relating myocardial oxygen consumption to heart rate during exercise do not appear to significantly differ from those in unmedicated subjects.<sup>31</sup> In a previous study,<sup>30</sup> no difference in ST/HR slopes was found when patients taking beta-blockers were compared with patients with a similar extent of coronary disease who were not taking these drugs, despite significantly less ST-segment depression and lower maximal heart rates in the patients on beta-blockers. Further, no difference in ST/HR slopes was found in patients tested both with and without beta-blocker therapy.<sup>28</sup> Thus, in the presence of beta-blockade, a decrease in ST-segment depression may be effectively normalized by a corresponding decrease in heart rate response to exercise, to result in ST/HR slope values that accurately reflect the extent of disease. However, as might be expected, the sensitivity of standard exercise test criteria that depend on the attainment of a certain magnitude of ST-segment depression are often quite poor in patients on beta-blockers.<sup>28</sup>

Since bicycle or treadmill exercise testing are easily available to most clinicians, the ST/HR slope may provide a widely accessible technique for the identification of patients with anatomically extensive coronary artery disease. This may improve the cost-effectiveness of evaluation strategies in patients with chest pain, and the improved accuracy of the method may increase the reliability of decisions based on exercise electrocardiograms alone. However, the possibility that the ST/HR slope may independently stratify patients according to risk requires further evaluation.
and the method requires confirmation by careful analysis in other laboratories.

REFERENCES

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