Heart Rate Adjustment of ST Segment Depression and Performance of the Exercise Electrocardiogram: A Critical Evaluation

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Analysis of the rate-related change in exercise-induced ST segment depression using the exercise ST segment/heart rate slope and ST segment/heart rate index can improve the accuracy of the exercise electrocardiogram (ECG) for the identification of patients with coronary artery disease, recognition of patients with anatomically or functionally severe coronary obstruction and detection of patients at increased risk for future coronary events. These methods provide a more physiologic approach to analysis of the ST segment response to exercise by adjusting the apparent severity of ischemia for the corresponding increase in myocardial oxygen demand, which in turn can be linearly related to increasing heart rate. Solid-angle theory provides a model for the linear relation of ST segment depression to heart rate during exercise and a framework for understanding the relation of the ST segment/heart rate slope to the presence and extent of coronary artery disease. False positive and false negative test results of the heart rate-adjusted methods are well known in selected populations and require further clarification. Application of these methods is also highly dependent on the type of exercise protocol, number of ECG leads examined, timing of ST segment measurement relative to the J point and accuracy of ST segment measurement. These methodologic details have been an important limitation to test application when traditional protocols and measurement procedures are required. When applied with attention to required details, the heart rate-adjusted methods can improve the usefulness of the exercise ECG in a range of clinically relevant populations.

©1995 by the American College of Cardiology 0735-1097/95/$9.50 0735-1097(95)00085-I

Methods of Heart Rate Adjustment of ST Segment Depression

Heart rate adjustment is a rational, physiologic approach to interpretation of the exercise tolerance test. ST segment depression recorded on the surface ECG during exercise-induced ischemia results primarily from the separate interactive influences of the extent of coronary obstruction and the magnitude of excess myocardial oxygen demand. In patients with demand-mediated myocardial ischemia due to obstructive coronary artery disease, ST depression will be proportional to exercise work load for any degree of obstruction. Thus, a patient with 1.0 mm (100 μV) of ST depression during exercise might reach 1.5 or 2.0 mm of ST depression with further effort, whereas less effort might provoke only 0.5 mm of ST depression. Because the underlying extent of coronary obstruction is the same in each of these conditions, the ischemia apparent in ST depression alone cannot be directly related to the presence or extent of disease without adjustment for the corresponding myocardial work load.

Physiologic insights result when exercise-induced ST segment depression is plotted against heart rate rather than against time. At higher exercise work loads, myocardial oxygen demand is directly proportional to heart rate and clinical observations suggest that the relation between ST...
heart rate in a patient with three-vessel coronary artery disease. This case illustrates the linear relation of ST segment depression to heart rate as peak exercise is approached. As a result, the slope of the line relating the final three data points by linear regression is higher than the slope of lines incorporating earlier data points. When more than one linear correlation is statistically significant, the greatest value (in this case 10.0) is taken as the test result for that patient. Note that the value obtained by simply dividing the total change in ST segment depression by the total change in heart rate (the ST segment/heart rate index) markedly underestimates the true ST segment/heart rate slope. bpm = beats/min.

Figure 1. Calculation of the ST segment depression/heart rate (ST/HR) slope. Progressive ST segment depression in lead CM5 (shown as a positive magnitude on the vertical axis) is plotted against exercise heart rate in a patient with three-vessel coronary artery disease. This case illustrates the linear relation of ST segment depression to heart rate as peak exercise is approached. As a result, the slope of the line relating the final three data points by linear regression is higher than the slope of lines incorporating earlier data points. When more than one linear correlation is statistically significant, the greatest value (in this case 10.0) is taken as the test result for that patient. Note that the value obtained by simply dividing the total change in ST segment depression by the total change in heart rate (the ST segment/heart rate index) markedly underestimates the true ST segment/heart rate slope. bpm = beats/min.

Two related but distinct methods of heart rate adjustment of the magnitude of ST segment depression occurring during exercise have evolved: the linear regression-based ST segment/heart rate slope and the simpler ST segment/heart rate index. The ST segment/heart rate slope is calculated from the maximal rate of change of ST depression relative to heart rate during the period of active ischemia that accompanies exercise. The ST segment/heart rate index represents the maximal ST segment/heart rate slope because it includes a large change in heart rate before any ischemia occurs. Both of these methods specifically do not consider any ST segment depression that occurs during the postexercise recovery period (10,11,31,37,39).

Regression-based ST segment/heart rate slope calculation. Accurate measurement of the ST segment/heart rate slope is determined by linear regression analysis to relate the measured amount of ST segment depression in each lead to the heart rate at the end of each stage of exercise and at peak exercise (10–12,31–33,37,40). Because the maximal rather than the average rate of change is sought, linear regression analysis is performed from the end of exercise to progressively earlier intermediate stage data using heart rate as the independent variable and ST depression as the dependent variable. The highest ST segment/heart rate slope with a statistically significant correlation coefficient is taken as the test finding for that lead (in μV/beat per min), as illustrated in Figure 1. After calculation of the maximal ST segment/heart rate slope in each lead, the highest ST segment/heart rate slope with a statistically significant correlation coefficient among all the leads (including bipolar CM5 but excluding aVR, aVL and V1) is taken as the final test result (10–12,31–33,37,40).

Although a major goal of exercise electrocardiography is improved sensitivity for coronary disease, new tests must also perform with high specificity in general populations. Accordingly, an ST segment/heart rate slope partition of 2.4 μV/beat per min with 95% specificity in clinically normal subjects correctly identified 90% of patients with nonanginal chest pain and a predictably lower 72% of patients with normal coronary arteries at catheterization (37). This criterion for identification of coronary disease was found to have a sensitivity of 95% in our first series of patients at catheterization and also 95% in patients with stable angina, compared with only 68% for standard criteria in these same subgroups (37).

For assessment of the severity of coronary obstruction, perhaps for evaluation of potentially high risk symptomatic patients for coronary angiography, high test sensitivity is a more critically important feature of test performance than is high specificity. An ST segment/heart rate slope partition of 6.0 μV/beat per min, observed in early studies (10–12,27) to be at the upper range of values in patients with two-vessel disease was found to identify 93% of patients with three-vessel or left main coronary artery disease, with a specificity of 57% (34),
thus providing a usefully sensitive, if imperfect, marker for extensive obstruction in this important subgroup.

**Simple ST/HR index calculation.** This simplification of the ST segment/heart rate slope method, which evolved from separate observations by Detrano et al. (20), is derived by dividing the maximal change in ST segment depression during exercise by the total change in heart rate from rest to peak effort (20,33,37). An ST segment/heart rate index partition of 1.6 μV/beat per min with 95% specificity in clinically normal subjects had a specificity of 88% in patients with nonanginal chest pain but a specificity of only 61% in patients with normal coronary arteries at catheterization (37). The 93% and 88% sensitivity of this partition for identification of coronary disease in our initial series of patients with catheterization-proved disease and patients with stable angina (37) was similar to the 95% sensitivity of the ST segment/heart rate slope and significantly greater than the 68% sensitivity of standard criteria in these groups. However, for identification of three-vessel or left main coronary artery disease, an ST segment/heart rate index partition of 3.3 μV/beat per min, at a specificity of 57% matched to the ST segment/heart rate slope partition, identified anatomically severe disease with a sensitivity of only 77%, a value between the 66% sensitivity of a markedly positive standard test and the 93% sensitivity of the ST segment/heart rate slope for this purpose (34). Thus, the simple ST segment/heart rate index appeared to approach the performance of the ST segment/heart rate slope for identification of coronary disease only, not for assessment of its anatomic severity.

**Theoretic and Experimental Background for Heart Rate Adjustment of ST Segment Depression**

Experimental evidence (62–75) provides a theoretic framework for a model that relates measured ST segment depression to heart rate during exercise (51). According to solid-angle theory (65), the magnitude of ST depression recorded at a surface electrode can be related to the product of spatial and nonspatial determinants as defined by the following relation:

\[
\Delta \text{ST} = (\Omega/4\pi)(\Delta V_m)K,
\]

where \(\Delta \text{ST} = \) magnitude of ST segment depression; \(\Omega = \) solid angle subtending the boundary of the ischemic territory; \(\Delta V_m = \) difference in transmembrane voltage between the ischemic and adjacent nonischemic regions; and \(K = \) correction term for the differences in intracellular and extracellular conductivity and changes in gap junctional conductance (63–67). As a consequence, during the transient ischemia associated with exercise, the magnitude of ST depression recorded by a surface electrode will be proportional to the area of ischemic territory subtended by the recording electrode (63–69) and to the local transmembrane potential difference, which reflects the electrical consequences of the metabolic severity of ischemia at the level of the myocardial cell (62–67). This relation remains proportional under conditions in which major changes in gap junctional conductance do not occur (63–68).

During exercise the severity of ischemia is directly proportional to changes in myocardial oxygen demand (70,71), which in turn can be linearly related to increasing heart rate (AHR) (72–75). As an arithmetic consequence, the ratio \(\Delta V_m/\Delta \text{HR} \) should remain constant when the changing severity of ischemia is equilibrated with changing heart rate (51) and under conditions in which changes in conductance are proportional or small:

\[
\Delta \text{ST}/\Delta \text{HR} = (\Omega/4\pi)(c),
\]

where \(c = \) a new constant of proportionality (51). Thus, during exercise-induced transient subendocardial ischemia due to increased work load, the instantaneous ratio of changing ST segment depression to changing heart rate should be directly proportional to the area of ischemic boundary when the severity of ischemia is steadily related to progressive demand. Further, this ratio should remain independent of the metabolic effects of ischemic severity on transmembrane potential differences across the ischemic boundary. The relations inherent in equation 2 provide a strong theoretic basis for the practical application of heart rate adjustment to analysis of the ST segment response to exercise, whereas equation 1 offers further insight into the poor performance of traditional exercise test criteria that are based solely on the magnitude and configuration of ST segment depression (1–9,76–78), particularly in the presence of limited effort tolerance or beta-adrenoceptor blockade (77–79). Of course, many factors relating to changing coronary flow might alter these relations (80–88).

**Clinical Applications of Heart Rate Adjustment**

Like standard exercise tolerance test criteria, the ST segment/heart rate slope and ST segment/heart rate index can each be applied to the identification of coronary obstruction and separately to the assessment of the anatomic and functional severity of disease (2,3,6,10–12,34,37). Test performance of each method and the performance of each method relative to standard test criteria will vary with these different major diagnostic purposes of exercise testing, so that the clinical application of the exercise tolerance test must be considered in interset comparison of these methods (2,6,7).

**Exercise testing for identification of coronary artery disease.** False positive and false negative responses of the heart rate-adjusted methods are well recognized in selected populations, which require further clarification, but both the ST segment/heart rate slope and the simple ST segment/heart rate index can improve the identification of coronary disease in clinically relevant populations. In addition to early reports from Leeds (10–12), findings from Europe (15,16,26), Japan (21) and several centers in the United States (19,37,41,46,50).
Table 1. Summary of Studies of ST Segment/Heart Rate Slope for Identification and Quantification of Coronary Artery Disease in Relation to Test Performance and Methodologic Variables

<table>
<thead>
<tr>
<th>Study*</th>
<th>No. of Patients</th>
<th>ST Segment Measurement Point (ms)</th>
<th>ST Segment Measurement Precision (µV)</th>
<th>Method of ST Segment Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved Performance: Identification of Disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kardash et al. (12)</td>
<td>60</td>
<td>J + 80</td>
<td>10</td>
<td>Magnifying graticule</td>
</tr>
<tr>
<td>Sievanen et al. (26)</td>
<td>156</td>
<td>J + 60</td>
<td>NR</td>
<td>Computer average</td>
</tr>
<tr>
<td>Ameisen et al. (29)</td>
<td>135</td>
<td>J + 70</td>
<td>25</td>
<td>Magnifying graticule</td>
</tr>
<tr>
<td>Ameisen et al. (30)</td>
<td>113</td>
<td>J + 70</td>
<td>25</td>
<td>Magnifying graticule</td>
</tr>
<tr>
<td>Okin et al. (42)</td>
<td>130</td>
<td>J + 60</td>
<td>10</td>
<td>Computer average</td>
</tr>
<tr>
<td>Okin and Kligfield (46)</td>
<td>254</td>
<td>J + 60</td>
<td>10</td>
<td>Computer average</td>
</tr>
<tr>
<td>Improved Performance: Quantification of Disease</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Okin et al. (27)</td>
<td>50</td>
<td>J + 70</td>
<td>25</td>
<td>Magnifying graticule</td>
</tr>
<tr>
<td>Okin et al. (34)</td>
<td>128</td>
<td>J + 60</td>
<td>10</td>
<td>Computer average</td>
</tr>
<tr>
<td>Kligfield et al. (48)</td>
<td>172</td>
<td>J + 60</td>
<td>10</td>
<td>Computer average</td>
</tr>
<tr>
<td>Improved Performance: Identification and Quantification of Disease</td>
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<td></td>
</tr>
<tr>
<td>Elamin et al. (10)</td>
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<td>J + 80</td>
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<td>Magnifying graticule</td>
</tr>
<tr>
<td>Elamin et al. (11)</td>
<td>206</td>
<td>J + 80</td>
<td>10</td>
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</tr>
<tr>
<td>Finkelhor et al. (19)</td>
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<td>J + 80</td>
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<tr>
<td>Sato et al. (21)</td>
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<td>J + 60</td>
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<tr>
<td>Kligfield et al. (37)</td>
<td>300</td>
<td>J + 60</td>
<td>10</td>
<td>Computer average</td>
</tr>
<tr>
<td>No Significant Improvement in Performance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quyyumi et al. (53)†</td>
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<td>J + 80</td>
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<tr>
<td>Balcon et al. (54)†</td>
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<td>Thwaites et al. (55)</td>
<td>60</td>
<td>J + 80</td>
<td>10</td>
<td>Magnifying graticule</td>
</tr>
</tbody>
</table>

*Numbers in parentheses are reference numbers. †Probably no improvement; no direct comparison made with standard ST depression criteria. NR = not reported.

have demonstrated greater accuracy of the ST segment/heart rate slope than of standard ST segment depression criteria for the detection of significant coronary obstruction (Table 1). Improved sensitivity of the ST segment/heart rate slope relative to standard ST segment depression criteria has been most evident among population groups in which false negative standard test responses are common, including patients with anatomically modest disease (37) and those with submaximal effort tolerance and parallel submaximal heart rate increases during exercise, a group in which exercise ECGs are frequently considered “nondiagnostic” because of limited effort tolerance. Additional value of the ST segment/heart rate slope for identification of coronary disease is highlighted by 1) similar test outcomes in patients with and without beta-adrenergic blocking agents (12,48); 2) its ability to accurately detect coronary disease among subjects with upsloping ST depression >1 mm (100 µV) (37) (frequently considered an “equivocal” test response); and 3) the similar performance of this method in men and women (46). Improved accuracy for the detection of coronary disease has also been found for the simple ST segment/heart rate index in most (20,24,25,35,37,42,46) but not all studies (56,57,59,61) (Table 2).

Exercise testing for prediction of cardiovascular risk. In a totally nonreferred group of asymptomatic subjects within the Framingham offspring cohort (44), an abnormal ST segment/heart rate index significantly concentrated the risk of future cardiovascular events. Improved risk stratification with heart rate adjustment was independent of age, gender and multiple additional cardiac risk factors (44), but coronary event risk was not significantly concentrated among subjects with a positive
Table 2. Summary of Studies of ST Segment/Heart Rate Index for Identification of Coronary Artery Disease in Relation to Test Performance and Methodologic Variables

<table>
<thead>
<tr>
<th>Study*</th>
<th>No. of Patients</th>
<th>ST Segment Measurement Point (ms)</th>
<th>ST Segment Measurement Precision (µV)</th>
<th>Method of ST Segment Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Improved Performance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detrano et al. (20)</td>
<td>303</td>
<td>J + 80</td>
<td>10</td>
<td>Magnifying graticule</td>
</tr>
<tr>
<td>Deckers et al. (22)</td>
<td>189</td>
<td>J + 80</td>
<td>NR</td>
<td>Computer average</td>
</tr>
<tr>
<td>Deckers et al. (23)</td>
<td>345</td>
<td>J + 80</td>
<td>NR</td>
<td>Computer average</td>
</tr>
<tr>
<td>Robert et al. (25)</td>
<td>135</td>
<td>J + 60</td>
<td>NR</td>
<td>Computer average</td>
</tr>
<tr>
<td>Kligfield et al. (37)</td>
<td>300</td>
<td>J + 60</td>
<td>10</td>
<td>Computer average</td>
</tr>
<tr>
<td>Okin et al. (42)</td>
<td>130</td>
<td>J + 60</td>
<td>10</td>
<td>Computer average</td>
</tr>
<tr>
<td>Okin and Kligfield (46)</td>
<td>254</td>
<td>J + 60</td>
<td>10</td>
<td>Computer average</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No Significant Improvement in Performance</td>
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<td></td>
</tr>
<tr>
<td>Lachterman et al. (56)</td>
<td>328</td>
<td>J point</td>
<td>NR</td>
<td>NR</td>
</tr>
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<td>Herbert et al. (57)</td>
<td>200</td>
<td>J point</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Moreau and Duval (59)</td>
<td>420</td>
<td>J + 80</td>
<td>NR</td>
<td>Visual estimation</td>
</tr>
</tbody>
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*Numbers in parentheses are reference numbers. NR = not reported.

Relationship of Test Performance to Methodologic Variability

ST segment/heart rate slope and ST segment/heart rate index calculations are performed in our laboratory by a computerized ECG system that measures ST segment depression below the isoelectric baseline to the nearest 10 µV at a point 60 ms after the J point from a 12-lead recording system modified by the addition of bipolar lead CM₅ (excluding leads aVR, aVL, and V₁ from all analyses), with exercise according to the Cornell protocol. These methodologic details are required for test accuracy, but they have also been an important limitation to test application where traditional protocols and measurement procedures are standard practice. Seemingly small variations of these details can have large effects on test outcome. Therefore, the relative performance of standard and heart rate-adjusted criteria among different studies must be examined in context of the separate effects of methodologic variables that are known to change the performance of exercise test criteria (Table 4).

Effect of ST segment measurement timing. The timing of ST segment depression measurement relative to the J point can have a profound effect on relative test performance of standard and heart rate-adjusted ST depression criteria. Traditionally, ST depression has been measured either at the J point or 60 to 80 ms after the J point (2,7,13,14,17,23,42,49,56,61). Performance of standard ST depression criteria will vary with the timing of ST segment measurement relative to the J point, but measurements made at 60 ms after the J point have generally outperformed J-point measurements for the identification of coronary disease (13,14,17,23,42,49). Performance characteristics of both the ST segment/heart rate slope and ST segment/heart rate index are also optimized when ST segment depression is measured precisely at 60 ms after the J point (42). Use of J-point measurements reduces performance of heart rate-adjusted criteria to the level of standard test criteria (42). These findings provide a partial, reasonable

Table 3. Summary of Studies of ST Segment/Heart Rate Index for Identification of Anatomically Severe Coronary Artery Disease in Relation to Test Performance and Methodologic Variables

<table>
<thead>
<tr>
<th>Study*</th>
<th>No. of Patients</th>
<th>ST Segment Measurement Point (ms)</th>
<th>ST Segment Measurement Precision (µV)</th>
<th>Method of ST Segment Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Improved Performance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detrano et al. (20)</td>
<td>303</td>
<td>J + 80</td>
<td>10</td>
<td>Magnifying graticule</td>
</tr>
<tr>
<td>Watanabe et al. (24)</td>
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<td>J + 80</td>
<td>10</td>
<td>Magnifying glass</td>
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<td>No Significant Improvement in Performance</td>
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<td>Okin et al. (34)</td>
<td>128</td>
<td>J + 60</td>
<td>10</td>
<td>Computer average</td>
</tr>
<tr>
<td>Kligfield et al. (48)</td>
<td>172</td>
<td>J + 60</td>
<td>10</td>
<td>Computer average</td>
</tr>
<tr>
<td>Lachterman et al. (56)</td>
<td>328</td>
<td>J point</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Herbert et al. (57)</td>
<td>454</td>
<td>J point</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Bobbio et al. (60)</td>
<td>2,270</td>
<td>J + 80</td>
<td>NR</td>
<td>NR</td>
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</table>

*Numbers in parentheses are reference numbers. NR = not reported.
performance of both ST segment/heart rate slope and ST elevation criteria (1,38,77). In concordance with these observations, reduced relative performance of the ST segment/heart rate index in these patients would be expected to lower test accuracy of both standard and heart rate-adjusted ST depression criteria (31,37), particularly when the amount of ST depression can change test outcome (31,37). Because heart rate-adjusted criteria are calculated as continuous variables, even small differences in the measured magnitude of ST depression can change test outcome (31,37), particularly when the amount of ST depression is small. In contrast, standard exercise ECG criteria traditionally are interpreted as discrete variables, so that precise measurement of ST depression when it is <100 μV (1.0 mm) has no consequence for the routine definition of test outcome (31,37). Because much of the improvement in test sensitivity offered by heart rate-adjusted criteria is found in their ability to accurately identify coronary disease in patients with <100 μV of ST depression (37,42,44), less precise measurement or visual underestimation of the magnitude of ST depression in these patients would be expected to lower test accuracy. Indeed, it can be shown that use of ST segment measurements less precise than 10 μV can reduce sensitivity of the simple ST segment/heart rate index for detection of coronary artery disease by as much as 10% (43). These findings suggest possible additional methodologic explanation for the reduced relative performance of the ST segment/heart rate index in some studies (Tables 2 and 3).

Effect of lead selection and lead number. Differences in the number and position of ECG leads used can also affect the accuracy of both standard and heart rate-adjusted ST depression criteria (1,38,77). In concordance with these observations, performance of both ST segment/heart rate slope and ST segment/heart rate index for detection of coronary disease has been found to be reduced when fewer than the standard 12-leads plus lead CM5 are used, whereas the relative difference in performance between standard and heart rate-adjusted criteria appears to narrow with the use of fewer ECG leads (38). These considerations provide an additional explanation for the smaller difference in test accuracy found between the ST segment/heart rate index and standard test criteria when alternative leads are used for heart rate–adjusted analyses (59). Further investigation is required to establish the contribution of specific leads to test performance and the value of lead-specific criteria during exercise testing.

### Effect of exercise protocol

Differences in the type of exercise test protocol used can also have a profound effect on accuracy of the ST segment/heart rate slope (31,32,38). Calculation of the ST segment/heart rate slope is highly dependent on small heart rate increments between exercise stages, which ensures detection of the maximal rate of ST segment depression as a function of heart rate that occurs during peak exercise–related ischemia (10,11,31,38). Because the average change in heart rate between stages of the Cornell protocol is 10 beats/min (32), whereas heart rate increments between stages of the Bruce protocol are two to three times larger (38), test accuracy of the ST segment/heart rate slope decreases, and in many instances the ST segment/heart rate slope may not be calculable when patients exercise according to the Bruce protocol (33,38). These factors may in part explain the relatively lower test accuracy of the ST segment/heart rate slope in at least one early study (55). Other exercise protocols that produce a graded heart rate response to exercise (89–91) might also allow accurate calculation of the ST segment/heart rate slope, but this must be validated because exercise test performance can vary when different treadmill methods are used (31,32,38).

### Relation of Test Performance to Population Selection

Beyond issues of methodologic variability, population selection can have separate and important effects on the relative sensitivity and specificity of exercise ECG criteria (50,92–95). As a consequence, exercise test performance must be related to and adjusted for the populations in which criteria are defined and in whom the test is to be used (50,92–94). It is unlikely that normalization of ST segment depression by heart rate alone should completely eliminate inaccurate exercise test findings in groups characterized by the occurrence of marked repolarization abnormalities that are known to be disproportionate to the presence or extent of coronary obstruction. Thus, because factors other than discrete coronary obstruction, such as exercise-provoked epicardial vasoconstriction (87), as well as valvular and myopathic heart disease, can result in exercise-induced subendocardial ischemia and ST segment depression, false positive ST segment/heart rate slope and ST segment/heart rate index values in the absence of coronary disease are predictable in these patients (29,96).
Heart Rate Adjustment in the Postexercise Recovery Period

Additional applications of heart rate adjustment of ST segment depression can be found in the Hollenberg treadmill exercise score (5,100) and the rate-recovery loop (39,44). Both of these methods incorporate work load or heart rate into an evaluation of the ST segment response to exercise that extends into the postexercise recovery phase. The Hollenberg method has been shown (5) to improve sensitivity of the exercise ECG for detection and quantification of coronary disease and to improve specificity when screening healthy young men (100).

Analysis of the behavior of ST segment depression as a function of heart rate during both exercise and recovery using the rate-recovery loop (39,44) provides additional insight into the value of heart rate-adjusted and standard methods. The Hollenberg method correlates of rate-recovery loop patterns can be found in earlier observations that compared myocardial ischemia during exercise and recovery (76,101–103). Rate-recovery loops are constructed by plotting ST segment deviation with reference to changing heart rate throughout treadmill exercise and recovery (Fig. 2). Normal subjects typically exhibit a clockwise loop of ST depression as a function of heart rate during exercise and recovery, whereas patients with coronary artery disease most commonly exhibit a counterclockwise loop of ST depression as a function of heart rate (39). The rate-recovery loop improves sensitivity of the exercise ECG for the detection of coronary artery disease with no loss in specificity compared with that for standard ST segment depression criteria (39). In contrast to standard ST depression criteria and heart rate-adjusted criteria that are derived from exercise phase data alone, sensitivity of the rate-recovery loop appears to be relatively independent of the extent of coronary artery disease (39). Alone and in combination with the ST segment/heart rate index, the rate-recovery loop can improve the prediction of future cardiovascular risk over that with standard ST depression criteria (44).

Clinical Implications and Future Directions

The limitations of exercise electrocardiography require reevaluation and reconsideration. We suggest that sensitivity and specificity of the exercise tolerance test can be increased in clinically important populations by the ST segment/heart rate slope and ST segment/heart rate index when careful attention is paid to the methodologic criteria that have been found to influence test performance. At the same time, simple demonstration of imperfection of these methods does not obviate their value within clinically relevant, context-sensitive diagnostic strategies. The selected populations in which the heart rate-adjusted methods have been derived and tested to date represent only a segment of the possible clinical populations in which exercise testing can be applied, and it is clear that new test criteria must be developed and test performance examined in the precise population subgroups in which the test will be used (50,92–95). As a consequence, application of these criteria requires further evaluation in other important subsets of patients who frequently undergo exercise testing, such as those with atypical angina or nonanginal chest pain syndromes. Additional areas of test applicability that require further clarification include the modulating effects of drugs, circulating hormones and additional forms of noncoronary heart disease on the heart rate–adjusted methods and criteria.
Conclusions
At present, heart-rate-adjusted methods can be useful in evaluating the ST segment response to exercise, and we believe that the ST segment/heart rate slope is a valuable marker for the presence and severity of coronary artery disease. Applied carefully, with use of context-sensitive criteria in clinically relevant populations and attention to important methodologic details, these methods can improve the clinical utility of the exercise ECG in the 6 to 8 million exercise ECGs that are performed annually in the United States.

References


