Recovery-Phase Patterns of ST Segment Depression in the Heart Rate Domain
Identification of Coronary Artery Disease by the Rate-Recovery Loop

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Although the time course of ST segment depression after exercise has been related to the presence and severity of coronary artery disease, recovery-phase patterns of ST segment depression with reference to changing heart rate have not been quantified. We have found distinct recovery loop patterns of ST segment depression that distinguish subjects without coronary disease from patients with coronary artery disease when ST segment depression is examined in the heart rate domain. Continuous plots of ST segment depression and heart rate were constructed throughout treadmill exercise and recovery in 100 clinically normal subjects, in 124 patients with coronary artery disease proven by catheterization, and in 17 patients with no significant coronary disease at catheterization. Among clinically normal subjects, 95% (95 of 100) had normal (clockwise) rate-recovery loops, and 5% (five of 100) had abnormal (counterclockwise) rate-recovery loops. In these normal subjects, the resulting 95% specificity of a normal rate-recovery loop was similar to the 93% (93 of 100) specificity of standard end-exercise ST segment depression criteria. Among patients with coronary disease proven by angiography, 93% (115 of 124) had abnormal (counterclockwise) rate-recovery loops, and 7% (nine of 124) had normal rate-recovery loops. In contrast was the significantly lower 74% (92 of 124) sensitivity of standard ST segment criteria (p<0.001 vs. the rate-recovery loop).

Specificity of a normal rate-recovery loop (71%, 12 of 17) and standard ST segment depression criteria (71%, 12 of 17) were similar in the patients with normal coronary arteries at angiography. We conclude that the pattern of ST segment depression as a function of heart rate during exercise and recovery can markedly enhance the accuracy of the exercise electrocardiogram for the identification of coronary artery disease. (Circulation 1989;80:533–541)

Exercise electrocardiography remains the most widely used method for assessing the presence and severity of coronary artery disease.1–4 Because of the poor sensitivity of standard ST segment depression criteria at end exercise alone for the identification of coronary disease,5,6 additional diagnostic information has been sought from the time course and magnitude of ST segment depression during the postexercise recovery phase.2,7–14 Simple evaluations of the duration of ischemic ST segment responses into recovery,8–12 as well as complex algorithms that depend on the magnitude, slope, and duration of ST segment depression throughout exercise and recovery,2,7,13,14 have been reported to enhance test accuracy.

Recent work has also shown the ability of heart rate–adjusted indexes of ST segment depression during exercise to improve the accuracy of the exercise electrocardiogram for identifying coronary disease and assessing its severity.15–23 Although patterns relating ST segment depression to heart rate during exercise and recovery were described in early reports from Bruce and colleagues,24–28 the potential diagnostic value of heart rate–dependent behavior of ST segment depression during recovery has not been quantified.29 Based on these observations, we examined whether or not distinct recovery-phase patterns of ST segment depression, in relation to heart rate rather than time, could separate patients with and without coronary disease more accurately than standard end-exercise criteria or time-dependent ST segment changes during recovery.

Methods

Study Population

The records of 241 patients who underwent exercise electrocardiography at The New York Hospital-
Cornell Medical Center were reviewed. Clinical data and exercise-phase electrocardiographic findings of a smaller subset of these patients have previously been reported in detail.21,23

The first group (clinically normal) consisted of 100 consecutive, asymptomatic, unmedicated subjects referred by their physicians for exercise electrocardiography as part of a comprehensive screening evaluation or as a precautionary evaluation before beginning an exercise program.23 There were 81 men and 19 women whose mean age was 47±13 (SD) years. Each had normal findings on cardiac examination and resting electrocardiogram before exercise; no subject was included in this group if exercise systolic blood pressure exceeded 210 mm Hg or if exercise was limited by chest pain.

The second group (stable angina) consisted of 141 consecutive patients with effort-related chest pain referred to The New York Hospital-Cornell Medical Center for diagnostic coronary arteriography, who underwent exercise testing at the time of hospital admission as part of a prospective evaluation of the ST segment/heart rate slope for the identification of anatomically extensive coronary obstruction.21 Patients with coexisting valvular heart disease, left bundle branch block, myocardial infarction within 8 weeks of arteriography, or unstable angina were excluded from this group. There were 111 men and 30 women in this group whose mean age was 57±9 years; 124 had coronary disease, and 17 had no significant coronary disease (by 50% luminal obstruction criteria). In this group, 28% (40 of 141) had a history of remote myocardial infarction, and 16% (23 of 141) had electrocardiographic evidence of a previous Q wave myocardial infarction. There were 23 patients in this group who were not receiving medications; among the remaining 118 patients, 92 were taking β-blocking drugs, 79 were taking nitrates, 76 were taking calcium channel blocking drugs, and only five were taking a digitalis preparation at the time of exercise evaluation.

Exercise Electrocardiography

Exercise electrocardiograms were performed on a treadmill with a Computer Assisted System for Exercise (CASE II) (Marquette Electronics, Milwaukee, Wisconsin), modified by the addition of a bipolar CM5 lead to the standard 12-lead recording system. All patients exercised according to the Cornell protocol, our more gently graded modification of the Bruce protocol that produces small heart increments between stages, with alternate stages of the Cornell protocol directly comparable with standard Bruce protocol workloads.29 Age-adjusted target heart rates were sought as the exercise endpoint for all studies, but tests were terminated when necessary because of limiting chest pain, dyspnea, or fatigue. As is customary in our laboratory, all patients walked at 1.7 mph at 0% grade for the first 3 minutes of recovery and remained upright through-out the remainder of the postexercise recovery period.

Exercise tests were evaluated with standard electrocardiographic criteria measured from the raw intracardiac tracings in each study.2 The test was considered positive in the presence of either 0.1 mV or more of additional downsloping or horizontal ST segment depression, or 0.15 mV or more of additional upsloping ST segment depression, measured between 60 and 80 msec after the J point, at the end of exercise.

ST Segment Depression in Relation to Heart Rate and Time

In addition to standard electrocardiographic output during exercise, the CASE II provides continuously updated, computer-based measurement of ST segment levels in each lead, based on incremental averaging of normal complexes during exercise. Computer-calculated ST segment amplitudes (both depression and elevation), measured to the nearest 10 μV at a point 60 msec after the J point with the end of the PR segment as a reference, were obtained in each lead after each stage of exercise, at peak effort, and after each minute of recovery. Accuracy of this measurement has been previously validated in our laboratory.30

The recovery-phase patterns of ST segment depression with reference to changing heart rate were examined by constructing continuous plots of absolute ST segment deviation and heart rate throughout treadmill exercise and recovery, with both ST elevation and depression values used for analysis. Analysis was performed in the lead with the most ST segment depression at end exercise, but leads aVR, aVL, and V1 were ignored. When no ST segment depression was present, the lead with the least amount of ST segment elevation at end exercise was selected for analysis. ST segment depression was plotted in the upward direction, and ST segment elevation was plotted in the downward direction (Figure 1).

The behavior of ST segment depression during recovery with reference to time was evaluated by constructing similar plots of ST segment deviation as a function of the time (in minutes) before and after peak exercise (Figure 2). The time-dependent behavior of ST segment depression in recovery was further analyzed for the presence of persistent ST segment depression 0.1 mV or more at 1 minute into recovery.8–10

Definition of Recovery-Phase Patterns of ST Segment Depression

Preliminary observations revealed that clinically normal subjects with ST segment depression at end exercise often exhibited a distinct pattern of recovery-phase ST segment depression as a function of heart rate (Figure 1). Because ST segment depression was lower at early recovery-phase heart rates than at corresponding exercise heart rates,
there was a clockwise loop of ST segment depression as a function of the heart rate during exercise and recovery. This pattern was defined as a normal rate-recovery loop.

In contrast, patients with coronary artery disease often exhibited the opposite pattern of ST segment depression in relation to heart rate: ST segment depression was greater at recovery-phase heart rates than at corresponding exercise heart rates, producing a counterclockwise loop of ST segment depression as a function of the heart rate during exercise and recovery. This pattern was defined as an abnormal rate-recovery loop (Figure 1).

As a function of time, rather than heart rate, the recovery-phase pattern of ST segment depression in clinically normal subjects was also generally in a clockwise pattern (Figure 2). This pattern was defined as a normal time-recovery loop. As will be shown, no distinct behavior of ST depression in the time domain emerged for patients with coronary disease. Patients with coronary disease exhibited both clockwise and counterclockwise loops of ST segment depression as a function of the time in exercise and recovery (Figure 2). For comparison with findings in the heart rate domain, counterclockwise time-recovery loops were defined as abnormal.

**Coronary Angiography**

Selective coronary cineangiography was performed by means of the Judkins technique in all stable angina patients. Multiple views were obtained in all patients, with the left anterior descending and left circumflex coronary arteries visualized in at least four views and the right coronary artery in at least two views. The results were interpreted separately from the original report, specifically for the purpose of our exercise test studies, by a single experienced angiographer using calipers, without knowledge of clinical or exercise test data as previously reported in detail.21,23

![Figure 1](image1.png)

**Figure 1.** Plots of ST segment deviation plotted as a function of heart rate during exercise and recovery, with ST segment depression shown in the upward direction and ST segment elevation shown in the downward direction. Typical rate-recovery loops are shown for a clinically normal subject (left panel) and for a patient with coronary artery disease (right panel). Despite similar heart rates and magnitude of ST segment depression at peak exercise, the clinically normal subject had a clockwise pattern of ST segment depression relative to heart rate during recovery, whereas the patient with coronary disease has the opposite, counterclockwise pattern of recovery. 2v-CAD, two-vessel coronary artery disease.

![Figure 2](image2.png)

**Figure 2.** Plots of ST segment deviation plotted as a function of time before and after peak exercise in the same clinically normal subject (left panel) and patient with coronary artery disease (right panel) in Figure 1. Although the clinically normal subject had clockwise behavior of recovery-phase ST segment depression in relation to time, the patient with coronary disease also showed a similar clockwise time-recovery loop. 2v-CAD, two-vessel coronary artery disease.
TABLE 1. Group Characteristics and Exercise Performance

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Clinically normal (n=100)</th>
<th>CAD by catheterization (n=124)</th>
<th>No CAD by catheterization (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>47±12</td>
<td>58±9</td>
<td>54±10</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>81/19</td>
<td>NS</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Exercise duration (min)</td>
<td>18±3</td>
<td>9±4</td>
<td>11±4</td>
</tr>
<tr>
<td>Proportion of target rate</td>
<td>93±7</td>
<td>66±10</td>
<td>76±15</td>
</tr>
<tr>
<td>Maximum heart rate (beats/min)</td>
<td>164±16</td>
<td>112±18</td>
<td>132±28</td>
</tr>
<tr>
<td>Maximum systolic pressure (mm Hg)</td>
<td>177±21</td>
<td>157±22</td>
<td>161±19</td>
</tr>
<tr>
<td>Maximum double product (×10⁻³) (mm Hg×[beats/min])</td>
<td>29±5</td>
<td>18±4</td>
<td>21±6</td>
</tr>
</tbody>
</table>

Data are mean±SD.
*Clinically normal subjects vs. CAD by catheterization; †CAD by catheterization vs. no CAD by catheterization; ‡no CAD by catheterization vs. clinically normal subjects.

Degree of stenosis was defined as the greatest percent reduction of luminal diameter in any view compared with the nearest normal segment. For classification of the number of obstructed coronary arteries, disease was considered significant when 50% luminal obstruction was present. Left main narrowing of 50% or greater was scored as the equivalent of two-vessel disease. According to these criteria, there were 17 patients with no significant disease, 34 with one-vessel disease, 43 with two-vessel disease, and 47 with three-vessel coronary disease. Ten patients had left main coronary disease, including four with additional two-vessel disease and six with additional three-vessel disease. Of note, 96% (119 of 124) of the patients with coronary disease defined by 50% stenosis also had at least 75% luminal obstruction of one or more major vessels.

Data Analysis

Sensitivity and specificity were calculated according to standard definitions. Test specificity was tested separately in the 100 clinical normal subjects and in the 17 patients with no significant coronary disease at angiography. Test sensitivity was assessed in the 124 patients with angiographically proven coronary disease. Comparison of test performance of standard exercise test criteria and the time-recovery loop with outcome based on the rate-recovery loop was performed in each group by McNemar's modification of the χ² method for paired proportions. In addition, sensitivity of each method was compared for patients with demonstrated coronary disease subgrouped by the number of obstructed coronary arteries. Sensitivity of the rate-recovery loop was further assessed with patients subgrouped by medication usage and by a history of or electrocardiographic evidence of previous myocardial infarction.

Statistical Analysis

Mean values for all findings are reported with the standard deviation (SD) as the index of dispersion. Comparison of mean values among groups was performed by one-way analysis of variance, with post hoc testing of individual group differences by Scheffe's method. Comparison of subgroup proportions was performed by χ² analysis with correction for continuity. For tests of proportion and for post hoc testing of mean values, a p value less than 0.05 was required for rejection of the null hypothesis.

Results

Group Characteristics and Exercise Performance

Group characteristics and exercise performance are shown in Table 1. Patients with coronary disease were similar to clinically normal subjects with respect to sex distribution, but there was a higher proportion of women among the catheterized patients with no significant coronary obstruction. Maximum predicted heart rate achieved, peak exercise heart rate, and maximum double product were higher in clinically normal subjects than in the patients without coronary disease, and these were higher in patients with no demonstrated disease at angiography than in those with coronary disease. Patients with coronary disease were older and exercised for a shorter period of time and to lower peak systolic pressures than clinically normal subjects, but they were similar to stable angina patients shown to have no coronary disease by these findings.

Test Performance of the Rate-Recovery Loop

Test performance for the rate-recovery loop is compared with performance of standard test criteria and time-dependent recovery-phase criteria in Table 2. Among clinically normal subjects, 95% (95 of
100) had normal (clockwise) rate-recovery loops, and 5% (five of 100) had abnormal (counterclockwise) rate-recovery loops. Of the 95 subjects with clockwise rate-recovery loops, 51 had end exercise ST segment depression, 35% (44/124) had abnormal ST segment depression, and 51% (63/124) had abnormal rate-recovery loops. Of these subjects, 95% (95/100) had ST segment depression ranging from 10 to 180 μV, and 44 had no ST segment depression in any lead at end exercise. Despite the absence of end exercise ST segment depression, all 44 of these subjects had a clockwise pattern of abnormal ST segment deviation when changing amounts of ST segment elevation were examined as a function of heart rate during exercise and recovery.

In these normal subjects, the resulting 95% specificity of a normal rate-recovery loop was similar to the 93% specificity of standard test criteria, the 96% specificity of a normal (clockwise) time-recovery loop, and the 99% specificity of ST depression persisting at least 1 minute into recovery. Specificity of the rate-recovery loop was 71% (12 of 17) in patients with stable angina who had normal coronary arteries at angiography; specificity was similarly low in this subgroup for both standard and time-dependent recovery criteria (Table 2).

In patients with angiographically proven coronary disease, 93% (115 of 124) had abnormal (counterclockwise) rate-recovery loops (Table 2), and all nine patients with false-negative rate-recovery loops had clockwise loops. In contrast was the significantly lower 74% sensitivity of standard test criteria, 35% sensitivity of an abnormal (counterclockwise) time-recovery loop, and 51% sensitivity of an abnormal test persisting at least 1 minute into recovery (all \( p < 0.001 \) vs. the rate-recovery loop).

### Test Sensitivity in Relation to Extent of Coronary Artery Disease

Test sensitivities of the rate-recovery loop pattern, standard test criteria, the time-recovery loop pattern, and abnormal ST depression persisting at least 1 minute into recovery are shown in relation to anatomic extent of coronary disease in Table 3. Of note, the rate-recovery loop identified 98% of patients with three-vessel disease, and 93% (84 of 90) of patients with multivessel disease. In contrast, standard test criteria identified only 83% of patients with three-vessel disease and only 82% (74 of 90) of patients with multivessel disease (\( p < 0.05 \) vs. rate-recovery loop). For each test, there was a trend toward increased sensitivity with increasing numbers of obstructed arteries. However, this trend was only modest for the rate- and time-recovery loop criteria. Within each subgroup defined by extent of obstruction, detection of coronary disease by the rate-recovery loop was significantly greater than for the other test criteria, except for similar sensitivity of standard test criteria in patients with two-vessel disease.

### Table 2. Sensitivity and Specificity of the Rate-Recovery Loop, Time-Recovery Loop, and Standard ST Segment Criteria

<table>
<thead>
<tr>
<th>Criteria*</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CAD by catheterization (( n = 124 ))</td>
<td>Clinically normal (( n = 100 ))</td>
</tr>
<tr>
<td>Rate-recovery loop</td>
<td>93% (115/124)</td>
<td>95% (95/100)</td>
</tr>
<tr>
<td>Standard ST segment</td>
<td>74% (92/124)</td>
<td>93% (93/100)</td>
</tr>
<tr>
<td>Time-recovery loop</td>
<td>35% (44/124)</td>
<td>96% (96/100)</td>
</tr>
<tr>
<td>ST depression at 1 min recovery</td>
<td>51% (63/124)</td>
<td>99% (99/100)</td>
</tr>
</tbody>
</table>

CAD, coronary artery disease.

*See text for definitions of test criteria.

\( t p < 0.001 \) vs. rate-recovery loop.

### Table 3. Sensitivity of the Rate-Recovery Loop, Time-Recovery Loop, and Standard ST Segment Criteria According to the Extent of Coronary Disease

<table>
<thead>
<tr>
<th>Criteria*</th>
<th>One vessel</th>
<th>Two vessel</th>
<th>Three vessel</th>
<th>Total CAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate-recovery loop</td>
<td>91% (31/34)</td>
<td>88% (38/43)</td>
<td>98% (46/47)</td>
<td>93% (115/124)</td>
</tr>
<tr>
<td>Standard ST segment</td>
<td>53% (18/34)</td>
<td>81% (35/43)</td>
<td>83% (39/47)</td>
<td>74% (92/124)</td>
</tr>
<tr>
<td>Time-recovery loop</td>
<td>35% (12/34)</td>
<td>30% (13/43)</td>
<td>40% (19/47)</td>
<td>35% (44/124)</td>
</tr>
<tr>
<td>ST depression at 1 min recovery</td>
<td>24% (8/34)</td>
<td>58% (24/43)</td>
<td>64% (30/47)</td>
<td>51% (63/124)</td>
</tr>
</tbody>
</table>

CAD, coronary artery disease.

*See text for definitions of test criteria.

\( t p < 0.05 \) vs. rate-recovery loop; \( t p < 0.01 \) vs. rate-recovery loop; \( t p < 0.001 \) vs. rate-recovery loop.
TABLE 4. Effect of Medications on Sensitivity of the Rate-Recovery Loop for Coronary Disease

<table>
<thead>
<tr>
<th>Medication</th>
<th>Medication present</th>
<th>Medication absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-Blockers</td>
<td>95% (84/88)</td>
<td>86% (31/36)</td>
</tr>
<tr>
<td>Nitrites</td>
<td>93% (69/74)</td>
<td>92% (46/50)</td>
</tr>
<tr>
<td>Calcium blockers</td>
<td>94% (66/70)</td>
<td>91% (49/54)</td>
</tr>
</tbody>
</table>

Effect of Medications and Previous Infarction on Sensitivity of the Rate-Recovery Loop

Test sensitivity of the rate-recovery loop in relation to medications used, presence of a Q wave infarction on the resting electrocardiogram, and history of a remote myocardial infarction are shown in Tables 4 and 5. There was no significant difference in the ability of the rate-recovery loop to identify coronary disease among patients who were taking or were not taking β-blockers, long-acting nitrates, or calcium channel blockers. Neither electrocardiographic evidence of previous Q wave myocardial infarction nor a history of infarction had a significant effect on the sensitivity of the rate-recovery loop, whereas there was a trend toward lower test sensitivity of standard ST segment criteria among patients with a previous infarction. Of note, among patients with coronary disease and negative standard exercise tests, the rate-recovery loop identified 92% (12 of 13) of patients with a history of a myocardial infarction and 100% (seven of seven) of patients with a previous Q wave infarction.

Discussion

Early observations by Bruce and colleagues24-29 suggest that different heart rate-related postexercise patterns of ST segment depression may occur in individuals with and without coronary disease. Our present data provide quantitative evidence of improved diagnostic performance of these patterns for identifying coronary artery disease.

TABLE 5. Effect of Previous Myocardial Infarction on Sensitivity of the Rate-Recovery Loop and Standard ST Segment Criteria for Coronary Disease

<table>
<thead>
<tr>
<th>Electrocardiographic</th>
<th>Rate-recovery loop</th>
<th>Standard ST criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q wave infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present (n=22)</td>
<td>95% (21/22)</td>
<td>68% (15/22)</td>
</tr>
<tr>
<td>Absent (n=102)</td>
<td>92% (94/102)</td>
<td>75% (77/102)†</td>
</tr>
<tr>
<td>History of remote infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present (n=39)</td>
<td>90% (35/39)</td>
<td>67% (26/39)*</td>
</tr>
<tr>
<td>Absent (n=85)</td>
<td>94% (80/85)</td>
<td>78% (66/85)†</td>
</tr>
</tbody>
</table>

*p<0.05 vs. rate-recovery loop; †p<0.01 vs. rate-recovery loop.

Recovery-Phase Behavior of ST Segment Depression in the Heart Rate Domain

Physiologic correlates of rate-recovery loop patterns can be found in previous observations that compare myocardial ischemia during exercise and recovery. Detry and colleagues28 found a close linear relation of ST segment depression during exercise to myocardial oxygen demand, as reflected by tension-time index, in patients with coronary disease. During recovery, however, this relation was nonlinear, with similar ST segment depressions observed at lower tension-time indexes than during exercise. Also, exercise- or pacing-induced subendocardial ischemia has been well recognized to continue into the recovery phase as shown by persistent ST segment depression associated with continued abnormal lactate production,32,33 regional wall motion abnormalities,34 and diminished subendocardial blood flow to the affected area.35,36 Although these electrocardiographic, metabolic, performance, and perfusion abnormalities may be less severe during early recovery than at peak pacing or exercise,32-36 they remain greater relative to heart rate during early recovery than during the development of ischemia.32,33,36

Although the magnitude of ST segment depression during exercise can be directly related to the level of myocardial workload (as reflected by heart rate) in patients with myocardial ischemia, ST segment depression during early recovery remains greater than expected for the rapidly decreasing myocardial oxygen demand that results from an abrupt lowering of exercise load. In effect, relative to heart rate, recovery-phase resolution of ST segment depression lags behind its exercise-phase development when coronary disease is present. This results in the counterclockwise pattern of ST segment depression in the heart rate domain found in our patients with coronary obstruction. In contrast, rate-related resolution of repolarization change exceeds its exercise phase development in normal subjects, resulting in a clockwise pattern despite ST segment depression at peak effort.

Because the rate-recovery loop is based on ST segment changes surrounding peak effort, the direction of rotation is independent of the absolute magnitude of ST depression at end exercise. Therefore, in most cases, the recovery-phase pattern cannot be reliably predicted from exercise-phase data alone. Over half of our normal subjects with clockwise loops had measurable ST depression at the end of exercise that was often similar in magnitude to that found at the onset of the counterclockwise loop pattern in patients with coronary disease. However, all subjects with absolutely no ST depression in any lead at end exercise had clockwise recovery-phase loop patterns when examined in the context of changing amounts of ST segment elevation 60 msec after the J point. Whether or not complete absence of ST depression at end exercise
alone might simply be interpreted as a normal test response remains to be established, but a normal pattern may occur even in cases with later recovery phase ST depression if early recovery-phase behavior in these subjects initiates a clockwise pattern of rotation.

Also of note, counterclockwise rate-recovery loops in patients with coronary disease are not simply markers for an increase in ST segment depression during recovery as has been reported in some patients with negative end exercise tests by standard criteria. An increase in absolute magnitude of ST depression during recovery was seen in only nine of our 124 patients with coronary disease, including one patient who had ST segment depression that exceeded 0.1 mV only during recovery. In these cases, early recovery-phase augmentation of ST depression during heart rate slowing is an obvious indication of counterclockwise rotation. On the other hand, ST depression was less during recovery in the large majority of patients with coronary disease, which was similar to the recovery-phase behavior of ST depression in normal subjects, and distinct rotation only became apparent by construction of the rate-recovery loop.

Recovery-Phase Behavior of ST Segment Depression in the Time Domain

Unlike the patterns that result from reference to heart rate, distinct recovery-phase behavior of ST segment depression was not found in the time domain. Nearly two thirds of patients with coronary disease had clockwise time-recovery loops that were indistinguishable from the time-recovery loops of most normal subjects. The diagnostic value of recovery loops in the rate domain, but not in the time domain, highlights differences between heart rate and time as estimates of myocardial work in the period surrounding peak exercise. Heart rates at matched times before and after peak exercise are different. If the rate-recovery loop examines ST segment depression during recovery and exercise at approximately matched workloads, as reflected by similar heart rates, it follows that the time-recovery loop relates ST segment depression during exercise and recovery at varying levels of myocardial oxygen demand. Our findings therefore indicate that the time course of ST depression may be an indirect and potentially inaccurate method for evaluating myocardial ischemia.

Although the time-dependent pattern of ST segment depression during recovery was not a sensitive criterion for coronary disease in the present study, other methods that incorporate the pattern of ST segment changes as a function of time during the postexercise period have been shown to improve the ability of the exercise electrocardiogram to identify coronary artery disease. Whether or not accuracy of these methods might be further enhanced by correction for rate, rather than time, throughout exercise remains to be examined.

Improved Identification of Coronary Disease

The sensitivity of the rate-recovery loop for coronary disease is similar in magnitude to the improved accuracy of other methods based on heart rate correction of ST segment depression during exercise only, However, these new methods are different in principle and may provide different types of information. The nonlinear and complex behavior of ST segment depression with respect to heart rate during recovery indicates that this relation may be more difficult to quantify than the linear rate-related changes in ST segment depression that occur during exercise in patients with coronary disease. Thus, although the ST segment/heart rate slope is a continuous variable that can be related to the anatomic and functional severity of coronary obstruction, translation of recovery-phase data to a complementary continuous variable may prove difficult.

Or the findings support the idea that the rate-recovery loop provides diagnostic information distinct from ST segment criteria based on exercise-phase findings. Sensitivity of the rate-recovery loop appears to be relatively independent of the extent of coronary artery disease (Table 3), unlike the performance of standard ST segment criteria and heart rate–adjusted ST segment criteria that are derived from exercise-phase data alone. The strong dependence of the test sensitivity of other electrocardiographic methods on the anatomic extent of coronary disease results from threshold criteria that are directly related to the severity of ischemia induced by exercise. In contrast, the direction of the rate-recovery loop is not dependent on any threshold magnitude of ST segment depression at peak exercise; it may thus be less affected by the anatomic and functional severity of underlying coronary artery obstruction than are standard test criteria.

Similar reasoning may explain the absence of an effect of cardiac medications or previous myocardial infarction on sensitivity of the rate-recovery loop. β-Blockers, by blunting the heart rate response to exercise, have been found to reduce the magnitude of ST segment depression at peak exercise but do not markedly affect the rate-dependent pattern of ST segment depression during recovery. Previous myocardial infarction may also result in a diminished magnitude of ST segment depression with exercise, leading to reduced sensitivity of partition-based standard electrocardiographic criteria. Remote myocardial infarction does not adversely affect sensitivity of the rate-recovery loop in the present population, but test performance may vary in patients with recent infarction who were excluded from this study.

Limitations and Clinical Implications

Although the present data show that the rate-recovery loop is highly sensitive for detecting cor-
Coronary artery disease in patients with stable angina, these findings should not be extrapolated to other populations without caution. Test sensitivity may be lower in asymptomatic subjects with coronary disease, and overall test performance may vary in patients with other chest pain syndromes, such as atypical angina. Test specificity may be lower in patients with other causes of nonischemic ST segment depression than in our clinically normal subjects. These important possibilities require careful evaluation. Further, it must be appreciated that predictive value of a positive rate-recovery loop, like all imperfect diagnostic tests, will vary with the population prevalence of disease. However, even with potential limitations, the rate-recovery loop appears to represent a useful and easily performed method for improving the diagnostic value of the exercise electrocardiogram.

Although our data show that the counterclockwise rate-recovery loop is a sensitive marker for coronary artery disease, the relation of these findings to prognostically important myocardial ischemia remains to be clarified. Because we did not measure myocardial ischemia per se, the mechanisms governing the direction of rate-recovery loops in our patients with angina can only be speculated. Further evaluation is required to examine whether or not the rate-recovery loop can separate myocardial ischemia in patients with coronary disease from abnormal repolarization during exercise in patients with noncoronary heart disease. Expansion of the loop method from a simple vector analysis to a more complex continuous variable that incorporates a magnitude term would be required for comparison with independent measures of the extent of exercise-induced myocardial ischemia. Thus, at present, the rate-recovery loop may best serve as a simple screen for the presence or absence of underlying coronary obstruction. Additional quantitative exercise-phase findings, such as the ST segment/heart rate slope, may be useful in confirming the diagnosis and may be required to estimate the extent and severity of disease in these patients.

Acknowledgments

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Identification of coronary artery disease by the rate-recovery loop.
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