Exercise-Induced ST Depression and ST/Heart Rate Index to Predict Triple-Vessel or Left Main Coronary Disease: A Multicenter Analysis

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Long Beach, Calif for 1st; Regensburg, Geneva, Basel and Zurich, Switzerland; Budapest, Hungary; Chicago, Illinois; Rotterdam, The Netherlands; and Milan, Italy

The high mortality rate among patients with triple-vessel or left main coronary artery disease has been a challenge to all methods of heart rate adjustment. ST depression by heart rate is small and confined exclusively to a low exercise heart rate. This lack of superiority cannot be generalized to all methods of heart rate adjustment.

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Coronary angiography

Clinical data

exercise and relieved within 20 min by rest: 2) nonanginal
radiation, neck, shoulders, jaw, or arms and is precipitated by
gangrene, defined as pain that occurs in one of these locations
that is either not precipitated by exertion or not relieved by rest
within 20 min; 3) nonanginal pain, defined as pain that is not
located at any of these sites or if so located, is not related to
exertion and lasts <10 s or >30 min; and 4) asymptomatic,
declared us no pain.

Exercise test variables. All patients underwent symptom-
tlimited upright exercise. A standard 12-lead ECG was re-
corded periodically during exercise, at maximal effort and
during recovery. At all institutions, manual measurements
similar to those previously reported (8) of the ECG lead with
the maximal ST depression related to rest were used for
analysis. In the three U.S. institutions, treadmill protocols
either Bruce or Balke-Ware) were used. In the five Euro-
pean laboratories, a bicycle ergometer was used. The exer-
cise data collected included medications at the time of the
exercise test, duration of the exercise test, heart rate at rest,
maximal achieved heart rate, rest and peak exercise systolic
diastolic blood pressures, exercise-induced angina, ex-
ercise-induced ST depression relative to rest and exercise-
induced ST slope. Measurements of ST depression at rest
during exercise were performed at one institution by an
investigator who, for research purposes (8), was denied
access to all patient data and by the physician supervising
the test at the others. Clinical data and exercise test results
were recorded prior to coronary angiography and therefore
were obtained without knowledge of the angiographic re-

Table 1. Clinical Characteristics of the Study Group of 2,770 Patients From Eight Institutions

<table>
<thead>
<tr>
<th></th>
<th>Chicago</th>
<th>Cleveland</th>
<th>Long Beach</th>
<th>Basel</th>
<th>Budapest</th>
<th>Geneva</th>
<th>Rotterdam</th>
<th>Zurich</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n=1)</td>
<td>122</td>
<td>383</td>
<td>201</td>
<td>79</td>
<td>670</td>
<td>543</td>
<td>295</td>
<td>57</td>
<td>2,770</td>
</tr>
<tr>
<td>Clinical data</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (y)</td>
<td>59 ± 9</td>
<td>54 ± 9</td>
<td>60 ± 8</td>
<td>55 ± 8</td>
<td>48 ± 8</td>
<td>51 ± 9</td>
<td>51 ± 10</td>
<td>54 ± 10</td>
<td>1 ± 10</td>
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<tr>
<td>Men (%)</td>
<td>75</td>
<td>68</td>
<td>94</td>
<td>85</td>
<td>69</td>
<td>81</td>
<td>75</td>
<td>93</td>
<td>78</td>
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<tr>
<td>Typical angina (%)</td>
<td>62</td>
<td>48</td>
<td>72</td>
<td>72</td>
<td>40</td>
<td>61</td>
<td>51</td>
<td>74</td>
<td>34</td>
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<tr>
<td>Stress test</td>
<td>ST 1 &lt; 1 mV</td>
<td>154</td>
<td>45</td>
<td>66</td>
<td>29</td>
<td>37</td>
<td>32</td>
<td>38</td>
<td>49</td>
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<tr>
<td>Peak HR (beats/min)</td>
<td>139 ± 24</td>
<td>150 ± 23</td>
<td>135 ± 22</td>
<td>116 ± 24</td>
<td>137 ± 23</td>
<td>136 ± 22</td>
<td>125 ± 25</td>
<td>136 ± 27</td>
<td>133 ± 25</td>
</tr>
<tr>
<td>Ex angiography (%)</td>
<td>46</td>
<td>33</td>
<td>61</td>
<td>53</td>
<td>29</td>
<td>38</td>
<td>45</td>
<td>28</td>
<td>30</td>
</tr>
<tr>
<td>Beta-blocker use (%)</td>
<td>25</td>
<td>33</td>
<td>33</td>
<td>37</td>
<td>14</td>
<td>37</td>
<td>38</td>
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<td>26</td>
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<td>Protocol</td>
<td>TM</td>
<td>1M</td>
<td>TM</td>
<td>BK</td>
<td>BK</td>
<td>BK</td>
<td>BK</td>
<td>BK</td>
<td>BK</td>
</tr>
<tr>
<td>Ex patients referred for angiography (%)</td>
<td>30</td>
<td>--</td>
<td>76</td>
<td>87</td>
<td>26</td>
<td>40</td>
<td>60</td>
<td>90</td>
<td>--</td>
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<td>Coronary angiography</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 vessel disease (%)</td>
<td>17</td>
<td>46</td>
<td>76</td>
<td>85</td>
<td>39</td>
<td>51</td>
<td>70</td>
<td>74</td>
<td>57</td>
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<tr>
<td>2 vessel disease (%)</td>
<td>52</td>
<td>24</td>
<td>48</td>
<td>58</td>
<td>25</td>
<td>32</td>
<td>40</td>
<td>26</td>
<td>25</td>
</tr>
<tr>
<td>3 vessel or left main disease (%)</td>
<td>26</td>
<td>16</td>
<td>27</td>
<td>30</td>
<td>12</td>
<td>13</td>
<td>21</td>
<td>12</td>
<td>18</td>
</tr>
</tbody>
</table>

38.5.9.12. At two institutions (Cleveland and Rotterdam),
data were collected prospectively as well as prospectively
(13). The definitions of clinical and test results were defined
a priori. Each institution was allowed to use its routine
exercise protocol. At three institutions, the same patients
had been described in previous clinical reports (8.14.15).

Clinical variables. Clinical data collected at all institu-
tions included age, gender and chest pain characteristics.
The latter were classified into four categories: 1) typical angina pectoris, defined as pain that occurs in the anterior
thorax, neck, shoulders, jaw, or arms and is precipitated by
exertion and relieved within 20 min by rest; 2) atypical angina, defined as pain in one of these locations that is either
not precipitated by exertion or not relieved by rest within
20 min; 3) nonanginal pain, defined as pain that is not
located at any of these sites or if so located, is not related to
exertion and lasts <10 s or >30 min; and 4) asymptomatic,
declared us no pain.

Exercise test variables. All patients underwent symptom-
timed upright exercise. A standard 12-lead ECG was re-
corded periodically during exercise, at maximal effort and
during recovery. At all institutions, manual measurements
similar to those previously reported (8) of the ECG lead with
the maximal ST depression related to rest were used for
analysis. In the three U.S. institutions, treadmill protocols
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pean laboratories, a bicycle ergometer was used. The exer-
cise data collected included medications at the time of the
exercise test, duration of the exercise test, heart rate at rest,
maximal achieved heart rate, rest and peak exercise systolic
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ercise-induced ST depression relative to rest and exercise-
induced ST slope. Measurements of ST depression at rest
during exercise were performed at one institution by an
investigator who, for research purposes (8), was denied
access to all patient data and by the physician supervising
the test at the others. Clinical data and exercise test results
were recorded prior to coronary angiography and therefore
were obtained without knowledge of the angiographic re-

The ST depression was evaluated as the difference be-
tween the rest and peak exercise ST depression measured
0.08 ms after the J point; it is expressed in mV. Because the
ST/heart rate (HR) index does not utilize information about
the slope of ST depression, we ignored slope in our conven-
tional analysis as well.

The ST/HR index was calculated as the ratio of the dif-
ference between exercise and rest ST depression and the
difference between exercise and rest heart rate as previously
described (8); it is expressed in mV/beat per min.

Referral for coronary angiography. The process of refer-
ral for coronary angiography was complex. Factors affect-
ing the decision to perform an angiogram included age, gender,
clinical symptoms, risk factor profile, exercise test results,
availability of an angiographic suite, method of reimburse-

BK = bicycle ergometer; Ex = exercise; HR = heart rate; ST: = ST segment depression; TM = treadmill.
ment and philosophy and attitudes of patients and physicians. At all eight institutions, clinical symptoms affected the decision to refer patients for exercise testing and coronary angiography. At all institutions except Cleveland, the exercise test result also affected the decision to refer for angiography. In Cleveland, the exercise test was part of a research project and the results were unknown to the physician making the referral decision. Of all eight institutions, only Long Beach and Chicago can be considered primary care facilities for the purpose of this study. At the other institutions, most subjects were referred from outside hospitals for exercise testing and angiography.

Coronary angiography. Coronary angiograms were obtained within 60 days after the noninvasive evaluation. They were interpreted as a routine hospital procedure. Because the exercise tests and angiograms were performed in a clinical setting, the results of the former were known to the physicians interpreting the latter. At two institutions the exercise test results were not known to the cardiology angiographers and referring physician so that the decision to perform coronary angiography was not influenced by these results. To assess the influence of the clinical data on the interpretation of the angiograms, 30 angiograms from patients with and 30 from patients without triple-vessel or left main coronary artery disease were randomly chosen for evaluation by an angiographer who had no access to clinical information or to the previous interpretation. In only five cases (8%) was there disagreement between the two interpretations. In one case, the disagreement could be ascribed to the influence of the clinical and exercise variables; the other four disagreements could be explained by interobserver variability.

Triple-vessel or left main coronary artery disease was defined by an obstruction of ≥50% of the normal diameter of at least three major coronary arteries or the left main coronary artery. Major coronary vessels were considered the left anterior descending, left circumflex (including obtuse marginal branches) and the right coronary artery (including the posterior descending branch). The maximal percent diameter narrowing in each major vessel was assessed visually by an experienced angiographer at each institution who based the assessment on views of the vessels in more than one plane.

Statistical analysis. To compare ST and ST/HR index criteria, the usual clinical cut point of 0.1-mV ST depression was adopted as the standard criterion. Sensitivity and specificity at this point regarding the diagnosis of triple-vessel or left main coronary artery disease were calculated according to standard definitions (16). The ST/HR index cut point giving the same specificity of 0.1-mV ST depression was determined and the sensitivity calculated and compared with that of the ST depression of 0.1 mV. The analysis was also performed for the two groups of patients whose peak heart rate was lower or exceeded the median peak heart rate (132 beats/min). The McNemar chi-square test for paired data was used to analyze differences between sensitivities at the same specificity.

To detect differences in the discriminatory power of the two methods, the area under the receiver-operating characteristic curve was used. The false positive ratio (1 - specificity) was plotted on the horizontal axis and the true positive ratio (sensitivity) on the vertical axis at various cut points. The area under the generated curves for each diagnostic method represents the discriminatory power of the method. The method of Hanley and McNeil (17) was used to calculate each area as well as the statistical significance of the difference between the two criteria in the overall study group and in different subgroups of patients.

Continuous variables were expressed as mean values ± SD as a measure of dispersion. In comparing the groups of subjects in which only one or the other criterion correctly classified the patients, t test and chi-square analyses were used.

Results

Patient characteristics. Clinical variables, exercise performance and angiographic results of the eight participating institutions are listed in Table 1. 2,270 patients fulfilled the entry criteria and were considered for analysis. The mean age was 53 ± 10 years; 78% were men and 54% had typical angina according to the previously defined classification.

Forty-three percent of the patients had ≥0.1-mV ST depression. The average peak heart rate was 133 ± 25 beats/min. Exercise-induced angina was present in 38% of patients and treatment with beta-adrenergic blocking agents (continued at the time of testing) was present in 28%.

At coronary angiography, 57% of patients (range 39% to 89% at different institutions) had at least one 50% narrowing in a major coronary artery, 35% of patients (range 25% to 58%) had two-vessel coronary artery disease and 38% of patients (range 12% to 30%) had triple-vessel or left main coronary artery disease.

Referral bias (Table 1). To estimate factors affecting the decision to perform an angiogram, we examined the percent angiographic referrals for each exercise laboratory. This is the percent of patients who underwent exercise testing and also underwent angiography. The importance of age, gender and symptoms for determining referral at each of the eight institutions can be evaluated by examining Table 1. The prevalence rate of disease was higher at institutions where the percent of angiographic referrals from the exercise laboratory was higher. This finding is precisely the opposite of what one would expect if exercise test results strongly affected the decision to perform angiography. On the contrary, the institutions with high prevalence rates of disease were more likely to include many men with typical angina pectoris (Table 1). These findings indicate that pretest angiography referral bias was more important than posttest referral (or diagnostic evaluation [workup]) bias.
Comparison of two criteria (Table 2). Exercise-induced ST depression of 0.1 mV was found to have a specificity of 64% and a sensitivity of 75% for the prediction of triple-vascular or left main coronary artery disease. At the same specificity (64%), the ST/HR index had a sensitivity of 78% (p = 0.08) at a cut point equal to 1.43 beats per min.

In the group of patients with a peak heart rate below the median peak heart rate (112 beats/min), 0.1-mV ST depression was found to have a specificity of 66% and a sensitivity of 73%. At the same specificity, the ST/HR index had a higher sensitivity (76%) (p = 0.02), in those with a peak heart rate equal to or above the median value, specificity and sensitivity of ST depression and ST/HR index were identical (68% and 80%, respectively, p = 1.0).

Factors affecting increased accuracy of ST/HR index (Table 3). Among the 401 patients with triple-vascular or left main coronary artery disease, the two criteria were discordant (both negative or both positive) 378 times (94.3%). The ST depression was positive and the ST/HR index negative in 7 patients (1.7%) and the ST/HR index was positive and ST depression negative in 16 patients (4%). When the 7 subjects in whom ST depression was the more accurate indicator were compared with the 16 in whom the ST/HR index was superior, by using Student's t test and chi-square analyses, only peak heart rate was found to differ significantly between groups. Heart rate averaged 103 beats/min when the ST/HR index was more accurate compared with an average of 156 beats/min when the standard ST depression was more accurate (Table 3). The number of subjects with discordant results is small and the suggestive though not statistically significant difference in the percent taking a beta-receptor antagonist is worthy of note.

Receiver-operating characteristic curve analysis (Table 4). The receiver-operating characteristic curves for the overall data are plotted in Figure 1. For each false positive value, sensitivity was slightly higher for ST/HR index. The area under the curve for ST/HR index was somewhat larger than that for ST depression (0.76 versus 0.74, p = 0.03). The value of the area under the curves according to ST depression and ST/HR index are reported in Table 4 for the overall study group and for each of the eight participating institutions. As only one institution (Chicago) was the difference in the area statistically significant.

**Discussion**

By the classic interpretation, the value of exercise-induced ST segment depression at 0.08 s after the J point is an index of the severity of coronary artery obstruction. The 0.1-mV cut point has been widely used as an imperfect method for distinguishing patients with from those without coronary artery disease (18-24). Unfortunately, its utility is often

<p>| Table 3. Univariate Analysis Among 401 Patients With Triple-Vessel or Left Main Coronary Artery Disease With Discordant Results by the Two Methods |</p>
<table>
<thead>
<tr>
<th>Best Indicator of Disease</th>
<th>ST Depression (n = 7)</th>
<th>ST/HR Index (n = 16)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>53 ± 7</td>
<td>53 ± 6</td>
<td>NS</td>
</tr>
<tr>
<td>Typical angina (%)</td>
<td>28</td>
<td>69</td>
<td>NS</td>
</tr>
<tr>
<td>Mean METs</td>
<td>5.6 ± 1.4</td>
<td>6.5 ± 2.7</td>
<td>NS</td>
</tr>
<tr>
<td>Mean peak heart rate (bpm)</td>
<td>156 ± 17</td>
<td>103 ± 17</td>
<td>0.0001</td>
</tr>
<tr>
<td>Essential drugs (%)</td>
<td>37</td>
<td>35</td>
<td>NS</td>
</tr>
<tr>
<td>Positive treadmill tests (%)</td>
<td>71</td>
<td>69</td>
<td>NS</td>
</tr>
<tr>
<td>Beta-blockers (%)</td>
<td>56</td>
<td>50</td>
<td>NS</td>
</tr>
</tbody>
</table>

METs = metabolic equivalents.

| Table 4. Receiver-Operating Characteristic Analysis of Area Under the Curve for Each Center |
|-----------------------------------------------|----------------|----------------|---------|
| Study Site | ST Depression (n) | ST/HR Index (n) | p Value |
| Chicago    | 74               | 80             | 0.02    |
| Cleveland  | 76               | 79             | 0.16    |
| Long Beach | 70               | 70             | 0.88    |
| Basel      | 65               | 74             | 0.52    |
| Budapest   | 74               | 50             | 0.03    |
| Geneva     | 68               | 70             | 0.85    |
| Rotterdam  | 72               | 77             | 0.51    |
| Zurich     | 65               | 74             | 0.37    |
| Overall    | 74               | 76             | 0.03    |

HR = heart rate.
limited by false positive and false negative results (25-28). Because heart rate variations are closely related to the changes in myocardial oxygen demand (29,30), it has been suggested (5) that normalizing the amount of ST depression (index of ischemia) by the corresponding change in heart rate (index of oxygen demand) might increase the accuracy of ST depression in predicting the presence of severe coronary artery disease. As the number of occluded coronary vessels increases, the ratio of oxygen supply to demand decreases and ischemia may occur at a lower heart rate. Therefore, the clinician who sees ST depression at a lower heart rate can suspect more severe coronary artery disease.

Historical perspective (Table 5). To have a historical perspective on the debate, all published reports utilizing heart rate adjustment of exercise results were analyzed. The list of reports was obtained from the bibliographies from two recent reviews (31,32) and from each bibliography of the original reports. Abstracts and letters were excluded from this analysis. Since 1977, 28 original reports have been published (4-10,15-33-35) and are listed in Table 5 according to the date of journal acceptance (when stated).

Table 5. Studies of Heart Rate Adjustment of ST Segment Depression

<table>
<thead>
<tr>
<th>First Author</th>
<th>City</th>
<th>Date of Acceptance on Year of Publication</th>
<th>No. of Patients</th>
<th>Exercise Protocol</th>
<th>Beta Blocker Use Included</th>
<th>Myocardial Infarction Included</th>
<th>Coronary Artery Disease (14)</th>
<th>3-Vessel or Left Main Disease (4)</th>
<th>Criterion</th>
</tr>
</thead>
<tbody>
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<td>Somers (4)</td>
<td>Rotterdam</td>
<td>1977</td>
<td>138</td>
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<td>NS</td>
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<td>62</td>
<td>...</td>
<td>ST/HR slope</td>
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<td>Barens (5)</td>
<td>Balatonfured</td>
<td>1979</td>
<td>25</td>
<td>BK</td>
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<td>Yes</td>
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<td>Elam (6)</td>
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<td>1980</td>
<td>64</td>
<td>BK</td>
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<td>Yes</td>
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<td>Yes</td>
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<td>Yes</td>
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<td>Yes</td>
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<td>21</td>
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<td>Lakhani (10)</td>
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<td>Yes</td>
<td>100</td>
<td>5</td>
<td>ST/HR slope</td>
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<tr>
<td>Lakhani (11)</td>
<td>Leeds</td>
<td>10/1/83</td>
<td>46</td>
<td>BK</td>
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<td>Yes</td>
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<td>28</td>
<td>ST/HR slope</td>
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<td>No</td>
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<td>Rocky (13)</td>
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<td>Yes</td>
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<tr>
<td>Balcon (14)</td>
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<td>41</td>
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<td>...</td>
<td>96</td>
<td>4</td>
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<td>Okazaki (15)</td>
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<td>50</td>
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<td>Yes</td>
<td>Yes</td>
<td>92</td>
<td>36</td>
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<tr>
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<td>New York</td>
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<td>Yes</td>
<td>100</td>
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<td>Kiefer (17)</td>
<td>New York</td>
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<td>Yes</td>
<td>57</td>
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<td>ST/HR slope</td>
</tr>
<tr>
<td>Thawley (18)</td>
<td>London</td>
<td>7/20/85</td>
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<td>BK</td>
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<td>Yes</td>
<td>72</td>
<td>14</td>
<td>ST/HR slope</td>
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<td>Edmonton</td>
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<td>No</td>
<td>94</td>
<td>37</td>
<td>Sum ST/HR</td>
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<tr>
<td>Fisk (20)</td>
<td>Cleveland</td>
<td>12/12/86</td>
<td>64</td>
<td>TM</td>
<td>Yes</td>
<td>Yes</td>
<td>58</td>
<td>9</td>
<td>ST/HR slope</td>
</tr>
<tr>
<td>American (21)</td>
<td>New York</td>
<td>3/11/86</td>
<td>113</td>
<td>TM</td>
<td>Yes</td>
<td>Yes</td>
<td>28</td>
<td>28</td>
<td>ST/HR slope</td>
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<tr>
<td>Okazaki (22)</td>
<td>New York</td>
<td>1/12/86</td>
<td>130</td>
<td>TM</td>
<td>No</td>
<td>No</td>
<td>...</td>
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<td>5/12/86</td>
<td>300</td>
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<td>No</td>
<td>45</td>
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<td>1987</td>
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<td>Yes</td>
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<td>31</td>
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<td>Yes</td>
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<td>Bagiordi (29)</td>
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<td>6/4/89</td>
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<td>Robbins (32)</td>
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... = not stated; abbreviations as in Tables 1 and 2.
The Leeds group (5,34–38) found a perfect separation of single, double and triple-vessel coronary artery disease using a variation of the previous approach in six consecutive studies. However, two investigations (40,41) at two different institutions in London were not able to reproduce these results. The Cornell group (6,42,43,46,47) and others (7,45) showed improved accuracy using the same approach, although some false positive and false negative results were encountered.

In relatively small groups of patients, the Cornell group compared the ST-heart rate (STIHR) index, used in the present investigation, with their variation of the Leeds method (43,46). The STIHR index was almost as accurate as the ST/HR slope for predicting any angiographic narrowing in one of their studies (9), but was significantly inferior for predicting triple-vessel or left main coronary artery disease in the other (45). These investigators recently reported (50) significant superiority of the STIHR index over standard ST depression for predicting any significant angiographic disease. However, Lachterman et al. (12) recently found no significant difference in accuracy when the STIHR index and standard ST depression were used to predict any significant coronary artery disease in 328 subjects undergoing cardiac catheterization.

The STIHR index method as used in the present study has the advantage of simplicity of calculation, does not require a computer, can be used for screening purposes and can be applied to large groups of patients for retrospective analysis of available data (52). However, the STIHR slope method does present certain theoretic advantages and it is possible that significant improvement over the ST/HR index could be achieved with the slope method. In light of the scanty comparative data for the slope and index methods (12,45) and the contradictions between the results of Lachterman et al. (12) and the Cornell group (9,45), no conclusive proof of this theoretic advantage is available.

Referral bias. In all studies involving coronary angiography as a standard to define disease, the bias incurred in the referral process can be problematic. This bias can be divided into two types: pretest referral bias involving age, gender, symptoms and risk factors and posttest referral bias (or workup bias) involving stress test results (53). To reduce posttest bias, exercise tests in the Cleveland group were performed for research purposes and the results were not used in the decision to perform angiography. Despite the resulting reduction in the amount of workup bias, the Cleveland results were similar to the results at the other seven institutions where workup bias was presumably more important.

Further assessment of the effect of referral bias can be achieved by examining the referral patterns from the exercise laboratories. In Table 1, we have displayed the percent of angiographic referrals at each laboratory. If workup bias was an important determinant of the difference in accuracies, one would expect to see corresponding differences in the areas under the receiver-operating characteristic curves for the two methods. No such differences were found. We therefore see no reason to consider referral bias as an important determinant of the apparent failure of the ST/HR index in our study. Furthermore, a recent meta-analysis (54), treating 157 consecutive published reports that compared exercise-induced ST depression with coronary angiography, found no significant effect of referral bias on test accuracy when controlling for 28 other variables.

Comparison with previous studies. Past studies have restricted the application of the heart rate-adjusted ST depression to patients of only one laboratory. In the present study, 2,370 patients from eight institutions in three countries were analyzed. Data were collected according to an international collaborative protocol. In most of the studies listed in Table 5, patients were selected according to several characteristics that would reduce the number of false positive and false negative findings (the so-called avoidance of a limited challenge group (53)). This factor may partially account for the disparity between the results of these studies and our own.

Limitations. Many cardiologists consider the slope of ST segment depression as well as its magnitude. Upshirling depressions are assigned less diagnostic importance than those that are horizontal or downward. Had we used this modification to conventional ST depression, its accuracy might have improved sufficiently to make it superior to the ST/HR index.

The comparison we made involves the case of predicting triple-vessel or left main coronary artery disease. Our results for predicting coronary artery disease in one or two vessels are similar and will be published soon (55).

Conclusions. As shown by the analysis of discordant cases, the ST/HR index performs better at a lower peak heart rate. From the clinical point of view, a small ST depression at a low heart rate could be misleadingly interpreted as negative, thus raising the false negative rate. By adjusting the small ST depression at low heart rates, the ST/HR index could reach the cut point of 1.43 μV/heats per min. Accordingly, the superior performance of the ST/HR index in patients receiving beta-blocker therapy (Table 3) could be ascribed to the lower heart rate reached during exercise. The differences in accuracy of the ST/HR index found at different institutions could be partially explained by the different heart rates achieved. Thus, the routine use of heart rate adjustment of exercise-induced ST depression provides only minimal improvement in test accuracy. However, this method may be used for individuals who fail to achieve the anticipated increase in heart rate.

The editorial assistance of Barbara Vahle and Jeanette Phillips is deeply appreciated.

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