Present Status of Exercise Testing in the Evaluation of Coronary Artery Disease

IWAO SOTOBATA, M.D., TERUO KONDO, M.D.
AND NAOKI KAWAI, M.D.

The present status of exercise testing in coronary artery disease (CAD) was discussed in respect to test protocols, ECG criteria and lead systems, and hemodynamic responses. Advantages of modern multistage protocols over single-stage ones such as Master two-step tests are obvious in diagnostic accuracy and patient's safety. Clinical significance of horizontal and downsloping ST depression has already been established. Diagnostic significance of other exercise-induced ECG alterations such as slow upssloping ST depression, ST elevation, U-wave inversion, and R-wave amplitude changes was discussed. The latter parameter is still controversial as to its clinical significance. Use of an inadequate ECG lead system is one of major causes of false negative tests. Necessity of multiple lead systems was emphasized for higher diagnostic accuracy. From the view point of cost-efficacy relation, we will recommend simultaneous recording of CC5 or CM5, V3 and CL or III in routine exercise testing for screening of CAD. Test results such as exercise time, and heart rate and systolic blood pressure responses are also useful parameters for the evaluation of the severity and prognosis of CAD. It was emphasized that in-exercise monitoring of ECG and blood pressure is indispensable in multistage exercise testing for improvement of diagnostic accuracy as well as patient's safety.

DESPITE certain limitations, exercise testing with a modern multistage protocol has become an indispensable and invaluable tool for noninvasively diagnosing the presence as well as the severity of coronary artery disease. This article presents the present status of multistage exercise testing in coronary artery disease from the electrocardiographic as well as hemodynamic view points. It has been frequently stressed that hemodynamic and symptomatic results of exercise testing are equally as useful.

Key Words:
Multistage exercise testing
ECG criteria of exercise testing
ECG lead system for exercise testing
Hemodynamic monitoring

Superiority of Multistage to Single-stage Exercise Testings

Exercise testing to be used in clinical cardiology should satisfy the following requirements; i) it should employ dynamic exercise involving large muscle groups, e.g., dynamic leg exercise in order to impose stress of sufficient intensity to the heart; ii) it should impose quantifiable workload; iii) it should be reproducible and repeatable; iv) all of the examinees can tolerate the testing; v) the mechanical efficiency of the exercise should be relatively constant throughout the population of the examinees; vi) ECG and blood pressure monitoring must be feasible during exercise not only for safety of the examinee but also for diagnostic improvement of the test. Feasibility of sampling blood and expired gases is also a
desirable feature. Multistage exercise testing using an adequate protocol with a treadmill or a bicycle ergometer can satisfy the above prerequisites although each apparatus has some inherent minor shortcomings. Master test is still widely being used for the diagnosis of coronary artery disease in our country. However, in addition to infeasibility of in-exercise blood pressure measurement and strong dependency of work intensity upon the examinee’s cooperation, Master two-step test has another major demerit inherent to any single-stage exercise testing, which will be discussed below.

Single-stage exercise testing imposes work load of a fixed intensity for a given duration and, therefore, can not quantify the exercise capacity of the examinee but only estimate the capacity as greater or less than the energy expenditure imposed. Quantification of the exercise tolerance capacity is one of the major purposes of the modern exercise testing. Master double two-step test has been the most popular single-stage exercise testing, the energy expenditure being approximately 7 MET’s. It is nearly equivalent in oxygen consumption to the stage II (2.5 mph, 12%) of the Bruce treadmill exercise testing. The oxygen consumption of Master double two-step test and Bruce’s stage II were 25.1 ± 3.8 and 24.0 ± 2.3 ml/kg-min, respectively, for healthy Japanese men. Data of our exercise laboratory shows that some patients with exercise-induced angina due to severe coronary artery disease such as left main trunk or triple vessel disease were unable to enter the stage II of Bruce’s treadmill protocol (Fig. 1). If these patients are forced to perform Master double two-step test without ECG and blood pressure monitoring as is usually done, rapidly developing myocardial ischemia may cause severe hemodynamic deteriorations, engendering even the patient’s life. Clinical importance of blood pressure monitoring during exercise will be discussed later. To the contrary, there existed many patients with significant coronary artery disease who were able to complete Bruce’s stage II without any signs and symptoms of myocardial ischemia and/or hemody-

Fig. 1. Exercise tolerance of patients with angiographically significant coronary artery disease.

The abscissa represents the exercise time in second, and the ordinate the proportion of patients who were able to walk on treadmill for that time indicated on the abscissa. Master double two-step test is approximately equivalent in oxygen consumption to Bruce’s stage II which corresponds to the exercise time from 180 to 360 seconds on the abscissa. Not a few patients with angina pectoris were unable to walk either even into stage II or beyond the first half of the stage. On the other hand, patients were not infrequently able to terminate stage III (360 to 540 seconds). Note that as the severity of coronary artery disease increases, the exercise time tends to be shorter, and that patients with exercise-induced angina tend to have lower exercise tolerance than those without angina.
Fig. 2. Evolution of slow upsloping ST depression at peak exercise into typical ischemic patterns at mid-recovery.
Panel A is the resting ECG recorded from a patient with angina pectoris who had 90% stenosis of LAD (6) and 50% stenosis of dominant RCA (2) and normal LVG. In panel B recorded immediately before the termination of treadmill exercise at moderate angina at 6′30″ of exercise a slow upsloping ST depression was seen in leads V3–6, CM5, CL and Frank X. Two minutes and 30 seconds after the end of exercise (panel C) the slow upsloping pattern evolved into horizontal (V4–6 and CL) and downsloping (CM5 and X) ones. Note that ST depression is deeper in CM5, CC5 and V5, 6 than in Frank leads, with the greatest depth in CM5.

It seems likely for the Master test to fail to provoke myocardial ischemia of diagnostic importance in many of these patients. Insufficient intensity of work load is generally said as one of major causes of false negative tests.

Diagnostic accuracy of exercise testings depends upon many other factors than the intensity of work load, which include the characteristics of the test population (symptomatic or asymptomatic population, men or women, prevalence and severity of coronary artery disease etc.), the ECG lead system employed (the number and the sort of ECG leads), the ECG criteria for a positive test (the sort and the threshold of criteria), presence or absence of in-exercise ECG recording etc. Thus, direct comparison seems almost infeasible among studies using different exercise protocols on different patient populations. However, a survey of 10 reports on Master double two-step test and 13 studies on multistage exercise testing suggested that the multistage testing had a higher diagnostic accuracy than the Master test. Furthermore, the results of three long-term follow-up studies showed that the maximal treadmill testing outperformed the Master test in screening asymptomatic men for coronary heart disease, the sensitivity being about two times greater using the treadmill test.

II Electrocardiographic Criteria for a positive Test

I. Horizontal and downsloping ST depression
Diagnostic importance of classical ischemic ST depression has already been established on the basis of many studies with use of epidemiologic, coronary angiographic, or clinical long-term follow-up techniques. At the present time, horizontal or downsloping ST depression is invariably regarded as a positive test if the ST depression is greater than 0.1 mV at 80 msec after the ST junction in multistage exercise testing. Horizontal and downsloping ST depression are shown in lead CL and leads CM5 and CC5 in panel C of Fig. 2, respectively. When the control ST level is already deviated at rest, a downward ST segment shift of greater than 0.1 mV below the control level is usually regarded as positive.

In general, leads with a tall R wave are more sensitive to ischemic ST depression than leads
Fig. 3. Multiple left precordial unipolar leads recorded during exercise-induced anginal pain.

The patient is a 54-year-old man who had 90% stenosis of LMTA (5) and 50% stenosis of LAD (7) and hypokinesis of LV wall segment 3. The ECG was recorded immediately after the end of modified Bruce treadmill exercise at 5'7'' with moderate chest pain. A slow upsloping ST depression was seen in V4 and V5, while significant horizontal and downsloping ST depression was observed in adjacent unipolar leads with the positive electrode placed 3 to 6 cm above C4 and C5. It is noteworthy that diagnostic ST depression occurs in the high anterolateral leads, not in the standard precordial leads.

with a small one. Bipolar chest leads such as CC5 and CM5 usually show a taller R wave and a greater ST depression than V5 or V6, or Frank lead X although these have a similar lead axis (Fig. 2). However, a uniform threshold (0.1 mV) for ischemic ST depression is being used for all leads. Re-evaluation of the threshold of the ischemic ST depression seems necessary for each lead (or each lead group). Some investigators suggested correction of ST depression by the height of the R wave.

2. Upsloping ST depression

The criteria of the horizontal and downsloping ST depression have been established for post-exercise ECG in single-stage exercise testing. The advent of multistage exercise testing and computer technology promoted the analysis of in-exercise ECG. In Sheffield et al.'s report a slow upsloping ST depression was regarded as abnormal if the slope was less than 1 mV/sec during exercise. Bruce regarded any ST depression of greater than 0.1 mV lasting for at least 0.06 second in the immediate postexercise period as abnormal. McHenry et al. obtained the ST Index (=ST junction depression in mm + ST slope in mV/sec), which was regarded as an abnormal response if the sum was less than zero during exercise or in the immediate postexercise period. They observed that with use of the ST Index the sensitivity was clearly enhanced and the specificity was not impaired.

Ellestad et al. observed in a 6-year follow-up study no significant difference in the annual incidence of coronary events between subjects with a slow upsloping ST depression of more than 0.2 mV measured 0.08 second after the J point and those with a horizontal ST depression of the same degree in maximal multistage treadmill exercise testing (9% vs 9%). A downsloping ST depression of more than 0.2 mV showed a significantly higher annual incidence (13%). In a study of near-maximal treadmill exercise testing with 14 ECG leads Chaitman et al. observed an improved sensitivity without decrease in specificity except for using all 14 leads for screening when the slow upsloping ST depression criteria was added to the criteria of classical ischemic ST depression of greater than 0.1 mV. They found that there was always one lead in the 14-lead ECG which showed horizontal or downsloping ST depression when a slow upsloping pattern was observed in another lead(s). Fig. 3 shows multiple left precordial unipolar leads recorded, in a
TABLE I  SENSITIVITY OF MULTISTAGE TREADMILL EXERCISE TESTING OF MODIFIED BRUCE PROTOCOL IN 31 ANGINA PECTORIS PATIENTS WITH SIGNIFICANT CORONARY ARTERY DISEASE DOCUMENTED ANGIOGRAPHICALLY

<table>
<thead>
<tr>
<th>Criteria</th>
<th>CM5</th>
<th>CC5</th>
<th>V3</th>
<th>V5</th>
<th>CM5+CC5</th>
<th>CM5+CC5+V3</th>
<th>CM5+V3+III</th>
<th>12 leads</th>
<th>17 leads</th>
<th>Frank leads</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>61.3%</td>
<td>67.7%</td>
<td>12.9%</td>
<td>58.1%</td>
<td>71.0%</td>
<td>74.2%</td>
<td>64.5%</td>
<td>67.7%</td>
<td>74.2%</td>
<td>35.5%</td>
</tr>
<tr>
<td>1+2</td>
<td>67.7%</td>
<td>67.7%</td>
<td>22.6%</td>
<td>64.5%</td>
<td>74.2%</td>
<td>77.4%</td>
<td>74.2%</td>
<td>71.0%</td>
<td>77.4%</td>
<td>38.7%</td>
</tr>
<tr>
<td>1+2+3</td>
<td>71.0%</td>
<td>67.7%</td>
<td>32.2%</td>
<td>64.5%</td>
<td>77.4%</td>
<td>83.9%</td>
<td>80.6%</td>
<td>83.9%</td>
<td>83.9%</td>
<td>38.7%</td>
</tr>
<tr>
<td>1+2+3+4</td>
<td>80.6%</td>
<td>74.2%</td>
<td>38.7%</td>
<td>74.2%</td>
<td>80.6%</td>
<td>87.1%</td>
<td>87.1%</td>
<td>87.1%</td>
<td>87.1%</td>
<td>48.4%</td>
</tr>
<tr>
<td>1+2+3+4+5</td>
<td>90.3%</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>90.3%</td>
<td>93.5%</td>
<td>-</td>
<td>90.3%</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Criterion 1: horizontal or downsloping ST depression ≥ 0.1 mV. Criterion 2: slow upsloping ST depression ≥ 0.2 mV. Criterion 3: ST elevation ≥ 0.1 mV. Criterion 4: U-wave inversion. Criterion 5: no change or increase in R-wave amplitude measured immediately postexercise in lead CM5.

Fig. 4. Walk-through phenomenon observed in a 55-year-old man with both effort and rest angina pectoris. The patient complained of mild chest pain during exercise, and exercise was terminated at 9.30. After exercise, ECG recorded 30 sec after the end of exercise showed significant ST elevation in V6, CM5, and Frank X. Reproductive ST depression was seen in V4 and V6. (CM5 and Frank X.)
criterion of the slow upsloping pattern was included (Table I). A slow upsloping pattern during exercise usually evolves into a typical ischemic ST depression as the heart rate decelerates in the mid to late recovery phase (Fig. 2). This common clinical observation is compatible with Case et al.’s experimental work demonstrating that early myocardial ischemia in dogs at the onset of anaerobic metabolism is manifested first by junctional ST depression that is followed later by horizontal ST depression.

In Goldschlager et al.’s study a slow upsloping ST depression of greater than 0.15 mV showed an unacceptably high incidence of false positives (32%) in a single bipolar chest lead, and when it was included into the diagnostic criteria, the overall false positive rate increased from 7 to 18% although the overall sensitivity was improved from 64 to 76%. They concluded that slow upsloping ST depression was best considered an “equivocal” response and its interpretation must be placed in context with other clinical data. Presently, we feel that a slow upsloping ST depression ≥ 0.20 mV may be included with limited application to the peak exercise and immediate postexercise period, especially when the number of ECG leads is small. Detailed left precordial mapping seems likely to degrade the significance of the slow upsloping ST pattern.

3. Exercise-induced ST elevation

Exercise-induced ST elevation is a relatively rare phenomenon and was reported to be seen in 6.5% of 720 patients and in 0.5% of asymptomatic healthy subjects in multistage treadmill exercise testing. Its mechanism and clinical significance are still controversial. Some investigators considered it as an electrocardiographic expression of severe myocardial ischemia of probable transmural extent, while the others related it to abnormal left ventricular wall motions. Recently, Waters et al observed exercise-induced ST elevation (≥ 0.1 mV measured at 0.06 second after the J point) in 36 (17.8%) of 202 patients with prior transmural myocardial infarction. In 33 (92%) of these 36 patients ST elevation was seen in leads facing an akinetic or dyskinetic segment of the left ventricular wall. On the other hand, they provoked ST elevation by treadmill exercise in 10 of 33 patients with variant form of angina pectoris who showed no abnormalities in ECG and left ventriculogram at rest. In six such patients they demonstrated a large left ventricular segment of hypoperfusion with stress TI scintigraphy. Figs. 4 and 5 show a similar case of exercise-induced ST elevation in a patient with angina pectoris both on exertion and at rest. Specchia et al angiographically demonstrated coronary arterial spasm provoked by dynamic exercise, which is probably re-
Fig. 6. Isolated U-wave inversion induced by treadmill exercise.

The patient was a 46-year-old man with exertional angina, who had 90% stenoses of LAD (6) and (7) and hypokinesis at LV wall segments 2 and 3 with ejection fraction of 70%. He began to feel mild chest discomfort at 5' of modified Bruce treadmill exercise and terminated treadmill walk at 6'30" because of a moderate chest pain. The control ECG at rest (A) was normal. The immediate postexercise ECG (B) showed definite U-wave inversion in leads V2–5, CM5, CC5 and Frank X. A slow up-sloping ST depression of less than 0.15 mV was seen in V4–6, CM5 and CC5. No diagnostic ST segment abnormalities were found throughout the testing with 17 leads.

responsible for exertional angina with either ST elevation or depression in patients with variant angina.

We observed a significant ST elevation concomitant with chest pain in 3 of 31 angina pectoris patients with significant stenosis of one or more major coronary arteries but without prior transmural myocardial infarction. No significant ST depression was observed in other multiple leads in these three patients. Thus, the sensitivity of exercise testing was improved by inclusion of the ST elevation criterion (Table 1).

Our present attitude to exercise-induced ST elevation is that severe transmural myocardial ischemia should be considered when ST elevation occurs, especially concomitantly with chest pain in patients with a normal resting ECG, but severe segmental abnormalities of left ventricular wall motion such as akinesis or dyskinesis should be considered when ST elevation occurs without chest pain in leads with an abnormal Q waves in patients with prior transmural infarction.

4. T wave changes

In multistage treadmill exercise testing no diagnostic significance is given to exercise-induced T wave changes. Lowering or inversion of positive T waves is generally considered as a physiologic response to exercise and is not associated with a significantly higher long-term mortality. Normalization of inverted T waves may occur in patients with or without ischemic heart disease McHenry and Morris stated that such T wave normalization, which occurs suddenly and at a relatively low heart rate synchronous with the onset of chest pain, suggested an ischemic origin of the chest pain.

5. U-wave inversion

The mechanism of the U wave has not yet been elucidated, and several theories have been proposed. According to McHenry et al., exercise-induced inversion of a positive U-wave strongly suggests the occurrence of myocardial ischemia, especially when the resting ECG is normal. It is generally considered as a relatively rare phenomenon. However, in a recent report by Gerson et al. it was observed as frequently as in 15% of 248 patients who performed multistage treadmill exercise testing. The sensitivity of the criterion of U-wave inversion was very low (21%), but the specificity was as high as 97%. Their observations are noteworthy, from the diagnostic point of view, that U-wave inversion
### TABLE II
VARIABLES OBSERVED DURING EXERCISE TESTING THAT HAVE BEEN CORRELATED WITH MULTIPLE CORONARY ARTERY DISEASE AND AN INCREASED RISK OF SUBSEQUENT MYOCARDIAL INFARCTION OR CARDIAC DEATH**

<table>
<thead>
<tr>
<th>A. Onset of ischemic ST depression* at low heart rate (&lt; 130/min or 70% of predicted maximal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B. Pronounced ST depression at low heart rate or work load</td>
</tr>
<tr>
<td>i. Ischemic ST depression &gt; 0.2 mV</td>
</tr>
<tr>
<td>ii. Downsloping ST depression</td>
</tr>
<tr>
<td>iii. Postexercise ST depression* persisting more than 5 minutes</td>
</tr>
<tr>
<td>C. Abnormal systolic blood pressure response with progressive exercise</td>
</tr>
<tr>
<td>i. Flat response (SBP rise &lt; 10 mmHg for two stages)</td>
</tr>
<tr>
<td>ii. Sustained decrease in SBP &lt; 10 mmHg</td>
</tr>
<tr>
<td>D. Increase in diastolic blood pressure &gt; 15 mmHg</td>
</tr>
<tr>
<td>E. Frequent or complex ventricular arrhythmias at a low exercise heart rate or work load</td>
</tr>
<tr>
<td>F. Reduced peak heart rate or work load</td>
</tr>
<tr>
<td>i. Inability to complete Bruce stage II (2.5 mph, 12%) or equivalent</td>
</tr>
<tr>
<td>ii. Peak heart rate &lt; 70% of predicted maximal</td>
</tr>
</tbody>
</table>

* refers to 0.1 mV or greater horizontal or down sloping ST segment depression  
** modified from Table II by Morris and McHenry

was the only exercise-induced abnormality in 4.8% of 166 patients with significant coronary artery disease, and 92% of patients with exercise-induced U-wave inversion had significant stenosis of either the left anterior descending artery or the left main trunk.

Our observations on U-wave inversion in multistage treadmill exercise testing are compatible with the study by Gerson et al. Exercise-induced U-wave inversion occurred most frequently in leads CC5, CM5, V4, V5 and Frank lead X (33–37%) and less frequently in V6 (17%). It is noteworthy that Frank lead X is as sensitive to U-wave inversion as bipolar or unipolar C5 leads in spite of a remarkably lower sensitivity to ischemic ST depressions (Table I). In one patient (3%) U-wave inversion was the sole abnormality provoked in exercise testing with the 17-lead ECG system (Fig. 6). We have seen no instances of exercise-induced U-wave inversion in normal subjects. Thus, inclusion of the U-wave inversion criterion seems to slightly improve the sensitivity without a decrease in specificity.

### 6. Exercise-induced QRS changes

Exercise-induced QRS changes have long been recognized, but little attention has been paid to their diagnostic significance. In 1978 Bonoros et al24 studied a group of false ST responders to treadmill exercise testing (33 false positives and 96 false negatives) and observed that diagnostic accuracy was significantly improved by use of the R-wave criterion in addition to the criteria of the ischemic and slow upsloping ST depression in a single lead (CMS). They regarded an increase or no change in the R-wave amplitude as abnormal in the immediate postexercise period. They also proposed another new criteria; the ΔRST index > 0, which was the sum of the increment of the R amplitude (mV) and the deviation of the ST segment (mV). In the analysis of modified 12-lead ECG of 230 patients with chest pain syndrome undergoing Bruce exercise testing, Berman et al25 showed that, when added to the classic ischemic ST depression criteria, the criterion Σ R ≥ 0 significantly improved the predictive value for coronary artery disease from 92 to 99% and for multivessel disease from 72 to 85%. The Σ R was defined as the R waves in aVL, aVF and V3 to V6 plus the S waves in V1 and V2. In their conclusion the mechanism for an exertional increase in Σ R in patients with coronary artery disease was assumed to be related to abnormalities in left ventricular function. Our preliminary study also showed that the R-wave amplitude criteria applied to CMS lead improved the sensitivity (Table I).

Diagnostic use of the ST segment response to exercise is still controversial in intraventricular conduction defects. Most investigators26–28 agree that the classic ST segment criteria are not reliable in these abnormalities. Uhl et al29 stud-
ied 44 asymptomatic men with acquired left bundle branch block who underwent maximal treadmill exercise testing and concluded that the exertional increase in R-wave amplitude in lead CM5 appeared to be a sensitive test in identifying coronary artery disease in such a population.

On the other hand, Battler et al.\textsuperscript{30} claimed, in their study with equilibrium radionuclide angiography, that R-wave amplitude changes had little diagnostic value and were not related to exercise-induced changes in left ventricular function and volume. Similarly, Wagner et al.\textsuperscript{31} concluded that exercise-induced QRS amplitude changes in lead V5 were unreliable predictors of presence, absence or severity of coronary artery disease. Others\textsuperscript{32} observed that the R-wave criteria improved sensitivity but accompanied a concomitant reduction in specificity. In healthy subjects R-wave amplitudes showed no change or a slight increase until the heart rate reached 150 beat/min and then decreased with a further increase in heart rate.\textsuperscript{33} We feel that further studies are obviously needed to elucidate the diagnostic and prognostic significance of exercise-induced R-wave amplitude changes.

III Optimal ECG Lead System

The ECG lead system optimal for exercise testing in terms of the cost-efficiency relationship still remains controversial. Four different types of lead systems are currently in clinical use: i) one or more bipolar precordial leads, ii) modified 12-lead system with the limb electrodes placed on the trunk, iii) orthogonal three-lead system, and iv) multiple unipolar precordial leads covering the left anterolateral thorax. Selection of the ECG lead system greatly influences the diagnostic accuracy of exercise testing in coronary artery disease.

1. High sensitivity of bipolar precordial leads to ischemic ST depression

It is generally accepted that unipolar or bipolar precordial leads with the positive electrode at the position C5 are the most sensitive to the ischemic ST depression, CM5 and CC5 being usually more sensitive than V5\textsuperscript{5,34} Our data was compatible with these observations (Table I). Although bipolar precordial leads such as CM5 and CC5 gained a wide popularity because of less artifacts and simpler electrode placement than the modified 12-lead and orthogonal lead systems, many investigators\textsuperscript{5,8,11,35,36} claimed that multiple lead systems were superior in diagnostic accuracy to single lead systems. Our preliminary study showed that the combination of CM5 and CC5, which is currently in clinical use in some other laboratories, had a higher sensitivity (74%) than either lead alone (67%) and was, surprisingly, comparable to the 12-lead system in sensitivity when the ST criteria alone were used (Table I).

2. Importance of lead V3 for detection of anterior wall ischemia

Waters et al.\textsuperscript{11} studied 47 patients with exercise-induced ST elevation, who consisted of 36 patients with prior transmural infarction and 11 patients with variant angina. In patients of the latter group ST elevation was invariably detected by the combination of leads III, CL, and V3. Isolated recording of CM5 or CC5 showed a low incidence of detection of ST elevation (19% and 28% respectively). Recently, MacAlpin\textsuperscript{37} analysed the lead distribution of ST elevation produced by severe spasm of major coronary arteries in patients with variant angina. The most sensitive and specific lead for ST elevation during left anterior descending arterial spasm was V3. In right coronary and left circumflex arterial spasm leads III and aVF showed ST elevation most frequently. He recommended simultaneous recording of leads III and V3 in addition to aVL for detection of ST elevation in variant angina. The former two detected 98% of 333 cases of ST elevation. In our study with multistage treadmill exercise testing on 31 angina pectoris patients without prior myocardial infarction a significant ST elevation concomitant with anginal pain was induced in leads V2–4 or V2, 3 in 3 patients (9.7%), in one of whom it was the sole abnormality induced by exercise. Since exercise-induced ST elevation is suggested to be strongly related to severe myocardial ischemia in some patients especially with a normal resting ECG, its recognition is of clinical importance in spite of its low incidence. On the other hand, a diagnostic ST depression was observed in V3 or V2, 3 in 7 patients (22.6%), one of whom showed no electrocardiographically diagnostic findings in other leads. Thus, the combination of CM5, CC5 and V3 gave an improved sensitivity of 84% with the criteria of both ST depression and elevation and of 87% with the addition of the U-wave inversion criterion (Table I).
Panel Discussions on Present Status and Future of Clinical ECG

### TABLE III
RESULTS OF ANGINA-LIMITED MULTISTAGE TREADMILL EXERCISE TESTING IN PATIENTS WITH CORONARY ARTERY DISEASE DOCUMENTED ANGIOGRAPHICALLY

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Systolic Bp (mmHg)</th>
<th>HR (beats/min)</th>
<th>PRP ( \times 10^{-2} )</th>
<th>Exercise duration (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVD</td>
<td>27</td>
<td>155.9 ± 22.3</td>
<td>122.0 ± 17.4</td>
<td>192.0 ± 42.2</td>
<td>390.3 ± 160.4</td>
</tr>
<tr>
<td>DVD</td>
<td>12</td>
<td>141.8 ± 15.0</td>
<td>111.0 ± 19.7</td>
<td>158.0 ± 36.3</td>
<td>324.5 ± 62.3</td>
</tr>
<tr>
<td>TVD</td>
<td>19</td>
<td>157.6 ± 19.6</td>
<td>103.9 ± 26.0</td>
<td>172.5 ± 31.3</td>
<td>292.7 ± 125.3</td>
</tr>
<tr>
<td>LMTD</td>
<td>8</td>
<td>138.4 ± 15.8</td>
<td>108.1 ± 17.4</td>
<td>149.5 ± 28.6</td>
<td>223.4 ± 107.4</td>
</tr>
</tbody>
</table>

SVD: single vessel disease  
DVD: double vessel disease  
TVD: triple vessel disease  
LMTD: left main trunk disease

### TABLE IV
RESULTS OF MULTISTAGE TREADMILL EXERCISE TESTING IN NON-ANGINAL PATIENTS WITH PRIOR MYOCARDIAL INFARCTION

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Systolic Bp (mmHg)</th>
<th>HR (beats/min)</th>
<th>PRP ( \times 10^{-2} )</th>
<th>Exercise duration (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVD</td>
<td>24</td>
<td>162.8 ± 25.9</td>
<td>138.0 ± 16.8</td>
<td>226.1 ± 46.0</td>
<td>578.5 ± 154.3</td>
</tr>
<tr>
<td>DVD</td>
<td>9</td>
<td>146.9 ± 20.6</td>
<td>139.0 ± 11.3</td>
<td>204.8 ± 44.7</td>
<td>532.8 ± 217.8</td>
</tr>
<tr>
<td>TVD</td>
<td>7</td>
<td>134.3 ± 56.0</td>
<td>121.4 ± 7.3</td>
<td>180.1 ± 30.4</td>
<td>406.4 ± 75.0</td>
</tr>
</tbody>
</table>

SVD: single vessel disease  
DVD: double vessel disease  
TVD: triple vessel disease

3. Importance of vertical leads in detection of inferior wall ischemia

Mason et al. observed that 4 (6%) of 56 patients showed positive responses only in lead II or III in exercise testing with the modified 12-lead system. In our study a significant ischemic ST depression was observed in II, III, or aVF in 8 patients (26%), all of whom, however, showed a deeper ischemic ST depression in CM5 which is often referred to as a semivertical lead. No ST elevation was seen in these vertical leads. However, in view of the reports by MacAlpin and Mason et al. described above, one of vertical leads should be included. In Chaitman et al.'s study with multiple leads including lead CL similar to lead II in waveforms, no increase in sensitivity was obtained by recording of the modified limb leads. They recommended simultaneous recording of leads CM5, CC5 and CL. Lead CL has the positive electrode at the left flank and the negative one at the manubrium. Unipolar leads at the level of the left costal margin seem to be selectively sensitive to inferior wall ischemia due to isolated involvement of the right coronary artery. Further studies are needed to determine which lead is to be used in clinical practice to detect inferior wall ischemia.

4. ECG leads for detection of ischemia localized at the high lateral wall

In our preliminary study there were no instances in which significant ST segment changes occurred at aVL. However, lead aVL or a unipolar lead(s) at the left high lateral region may be essential to detect ischemia confined to the high lateral VL wall as suggested by MacAlpin and Fox et al. McHenry and associates reported a very low sensitivity of a modified bipolar V5 lead system in patients with isolated left circumflex artery disease, which may induce localized ischemia at the high lateral LV wall.

5. Precordial mapping systems

Fox et al. developed a 16-point precordial mapping system for exercise testing, the sensitivity of which was significantly greater than that of the modified 12-lead system (96 vs 80%) with a similar specificity for both systems (90%). They claimed that the mapping system was especially more sensitive to isolated single vessel disease as compared to the modified 12-lead system (74% vs 42%). Although body-surface isopotential ST segment maps are also being investigated during exercise testing for research purposes, inexpensive scalar analysis of multiple unipolar precordial leads seems sufficient for diagnostic exercise.
testing and quite promising in improvement of the diagnostic accuracy.

6. Frank lead system

The Frank orthogonal lead system is less sensitive to ST segment deviation than bipolar or unipolar chest leads, and the sensitivity was less than 40% when ischemic ST depression of \( \geq 0.1 \text{ mV} \), slow upsloping ST depression of \( \geq 0.2 \text{ mV} \), and ST elevation of \( \geq 0.1 \text{ mV} \) were used in combination (Table I). However, the specificity seems quite high. In our previous study the sensitivity was markedly improved from 37 to 77% with no decrease in specificity when the threshold of ischemic ST depression criteria was lowered from 0.1 to 0.05 mV.

At present, we would recommend simultaneous recording of at least three leads, for example CC5 (or CM5), V3 and CL (or a unipolar lead at the left anterior costal margin) in routine exercise testing for screening coronary artery disease. When a six-channel electrocardiograph is available, additional recording of unipolar precordial leads at high left anterior and high left lateral regions would be desirable. If a false negative test is suspected, detailed left precordial mapping should be tried. In rehabilitation program the monitoring ECG system should be individually designed to include the lead which showed the most significant changes in the previous exercise testing with multiple leads.

IV Necessity of ECG Monitoring during Exercise

In a modern exercise testing with a multistage protocol, continuous ECG monitoring throughout the test is essential not only for improvement of diagnostic accuracy but also for patient's safety. Significant ST depression is said to appear only during exercise in 5 to 10% of patients. U-wave inversion or a diagnostic slow upsloping ST depression may also occur only in exercise or in the immediate postexercise period. In rare instances a walk-through phenomenon is seen, in which anginal pain and typical ischemic ST deviation or U-wave inversion transiently appear and then disappear in spite of continuation of exercise (Fig. 4). The phenomenon seems to be due to exercise-induced coronary spasm, the presence of which has already been demonstrated by coronary angiography. Marked ST depression may appear during exercise with a very mild chest oppression or sometimes without any chest discomfort. Ischemic ST depression of greater than 0.4 mV is one of objective exercise endpoints in our laboratory although it is not regarded as an endpoint by some other investigators. Serious arrhythmias such as ventricular tachycardia may be provoked during exercise. A decrease in heart rate during exercise rarely occurs. These are, of course, one of major exercise endpoints and should be carefully watched for.

V Evaluation of Severity and Prognosis of Coronary Artery Disease

The evaluation of the severity and prognosis of coronary artery disease is another facet of exercise testing. Table II lists results of multistage exercise tests which were reported in the literature to be related to multivessel disease or poor prognosis in patients with coronary heart disease.

Results from our exercise laboratory show that as the severity of coronary artery disease increases, the treadmill exercise time in the modified Bruce protocol tends to be shorter, and the peak heart rate, systolic blood pressure and pressure rate product tend to be lower (Tables III and IV). Remarkable findings are that exercise tolerance capacity as well as peak systolic blood pressure is significantly lower in patients with left main trunk disease.

In another study from our laboratory on 31 patients with prior transmural infarction the treadmill exercise time (TMET) and peak systolic blood pressure (PSBP) showed a significant multiple correlation with ejection fraction (EF) determined ventriculographically at rest (R = 0.64, p < 0.002), giving a multiple regression equation of \( EF = 0.038 \times \text{TMET} + 0.28 \times \text{PSBP} - 1.09 \) with a standard error of estimate of 12.3.

In our previous study the clinical significance of the systolic blood pressure (SBP) response to near-maximal multistage treadmill exercise was evaluated. The response was classified into 3 types A, B and C. In type A SBP progressively rises up as exercise continues on and rapidly falls down after the cessation of exercise (unimodal response). In type B SBP progressively goes up with exercise as in type A but decreases during peak exercise or in the immediate postexercise period, with a subsequent transient elevation of SBP during the early phase of recovery.
(bimodal response). In type C SBP rather goes down with exercise or does not rise more than 10 mmHg above the control level (flat response). The incidence of Type B response was significantly higher in those with exercise-induced anginal pain than in those without. There were 11 type B or C responders in whom anginal pain was not provoked during the exercise testing. All of these patients had multivessel disease. On the other hand, type A responders without prior infarction had a very low incidence of left main trunk disease when anginal pain was provoked.

It is emphasized that additional analysis of parameters other than electrocardiographic measurements will give more information of both diagnostic and prognostic importance.

VI Importance of Blood Pressure Monitoring during Exercise

Irving and Bruce reported five patients with exercise-induced ventricular fibrillation in maximal treadmill exercise testing. All these patients, who had either prior myocardial infarction or angina pectoris, showed a marked fall of systolic blood pressure below the control level in the standing position. The incidence of ventricular fibrillation in their study was 2.2% of 228 coronary artery disease patients with exertional hypotension but was zero in 1300 patients without exertional hypotension. In our exercise laboratory a fall of systolic blood pressure of more than 10 mmHg below the peak pressure during exercise is one of the objective signs of exercise endpoint, and no instance of ventricular fibrillation or death was observed in more than 1,500 near-maximal multistage treadmill exercise tests. Thus, blood pressure monitoring is an indispensable procedure for safety in exercise testing.

REFERENCES

2. STARKE H, ELIOT RS: Assessment of available stress testing techniques (treadmill, bicycle ergometer, etc). In, Stress and the Heart, Eliot RS editor, Futura, 1974, p335


37. MACALPIN RN: Correlation of the location of coronary arterial spasm with the lead distribution of ST segment elevation during variant angina. *Am Heart J* 99: 555, 1980


