Exercise Graded by Heart Rate in Electrocardiographic Testing for Angina Pectoris

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A TYPICAL features of location, quality, time course, radiation, precipitating and ameliorating factors of angina pectoris evoke in the clinician a desire for objective evidence to aid in this sometimes difficult diagnosis. Interest in the electrocardiographic response to exercise of subjects with and without angina pectoris is a manifestation of this difficulty.

The “two-step” test, introduced by Master and Jaffe in 1941, is by far the most widely used procedure of this type, but other investigators prefer an unstandardized test allowing the patient to exercise at his accustomed rate until dyspnea, fatigue, or pain develops. Of greater importance than the mode of exercise is, in our opinion, the reproduction in every subject of a standardized degree of cardiac stress regardless of age or work capacity of the individual undergoing the procedure.

Physiologic Considerations

An exercise test should be graded according to the changes induced in the requirement of the myocardium for oxygen. The available evidence suggests that the coronary blood flow does not necessarily parallel the severity of the work done by the body as a whole. Thus, although there is an excellent parallelism between the external work of the body and its oxygen consumption and the cardiac output, there is considerable variation in the efficiency with which the heart accomplishes the increased output. It has been known since the work of Evans and Matsuoka in 1915 that the oxygen consumption of the heart for a given useful work (pressure times cardiac output) will vary according to the relative values of the pressure and flow components. Saroff and his colleagues showed that the time integral of ventricular pressure during systole (tension-time index) has a much better correlation with the myocardial oxygen consumption per beat than does the stroke volume, peak systolic pressure, or stroke work. This relationship is a useful guide to the oxygen requirement of the heart per beat.

It has long been recognized that the heart size remains essentially constant through exercise. It has also been shown that the tension-time index remains relatively constant during exercise. Therefore, from the Laplace relationship of pressure, cardiac diameter, and tension, it follows that the time integral of myocardial tension is relatively constant during exercise. Since the time integral of tension per beat is relatively constant during exercise, the oxygen consumption of the heart per minute will tend to vary in proportion to the heart rate. It is therefore reasonable to equate the challenge to the coronary circulation with the heart rate during exercise. Even if there is some variation in the oxygen cost per beat during exercise, there is a strong correlation between oxygen consumption per minute and the heart rate.

With these physiologic considerations in mind, the Master two-step tests, single and double, have been compared with the test standardized according to the maximum heart rate achieved during a 4-minute period of exercise. In the standardized procedure, or graded exercise test, the exercise is carried

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out at graded levels of exercise until the heart rate, 85 per cent of the maximal predicted for the subject’s age, is achieved unless the test is terminated at a lower level by pain, “positive electrocardiographic changes,” undue dyspnea, or fatigue. In the development of this test, the following principles relevant to the heart rate’s response to exercise were considered: (1) The maximal heart rate possible during “all-out” exercise in health is primarily determined by the age of the subject, as shown by Robinson.7 The maximal heart rate for healthy children, aged 12 to 15 years, is 198 ± 14; at age 30, healthy adults will have a maximal heart rate of 190 ± 12; and at age 50, 174 ± 12. At age 70, the maximal rate is 146 ± 12. (2) The general effect of physical training is to decrease the heart rate, not only at rest, but also at any given level of exercise. The maximal heart rate possible is not materially affected by training, but the level of effort required to produce it is increased. Lack of regular physical activity tends to have the opposite effect. (3) Since the heart rate varies with the relative severity of the exercise, the end point (85 per cent of maximal) is self-adjusting according to the age and physical fitness of the subject. (4) The type of leg exercise, i.e., stair climbing, treadmill walking, or cycling is not important except as a matter of convenience to the examiner and the familiarity of the subject. (5) The heart rate should be measured during the exercise, not at its conclusion, since the rate declines precipitously as soon as the exercise is terminated. It is obvious that a rare patient will not be able to achieve the desired heart rates without inordinate effort. Reasonable judgment will then determine when the testing should be terminated.

Method

Subjects not receiving digitalis or long-acting coronary vasodilators, after being found free from subjective or objective evidence of fresh or impending infarction, were tested 2 hours or more after meals. A 12-lead electrocardiogram was taken at rest and examined initially to exclude subjects with contraindications to testing and to select a chest lead for monitoring during exercise (lead manifesting clearest positive QRS and T waves, typically V5). This lead and three other chest leads were established with use of disposable self-adhering electrodes, and the limb electrodes were attached securely with tape. A long patent cable containing four chest lead conductors was employed, and a switch at the cable terminal permitted selection of V6, V5, V4, and V2, plus the possibility of recording differentially between V2 and V6 if limb electrode contact was lost during exercise. The electrocardiogram was displayed on an oscilloscope and recorded, either continuously on magnetic tape or periodically with a clinical electrocardiograph at 50 mm./sec. After termination of each exercise period, leads V6, V5, V4, V2, I, aV5, and aVF were recorded immediately, without any delay required for changing of chest electrode positions. These leads were repeated at 2, 4, and 6 minutes.

Three exercise levels were employed. The first and second were as described by Masteri for the single and double “two-step” tests, respectively, and similar steps were used.

The third, or graded exercise test level was defined as that producing a heart rate of 85 per cent of the mean predicted maximal heart rate for the subject’s age, as determined by Robinson.7 Heart rate was determined from the electrocardiogram at 30-second intervals. Exercise levels were performed in order, after recovery of resting levels of heart rate and respiration. Unless terminated by moderately severe pain, weakness, or electrocardiographic changes during exercise, the series of exercise levels was completed on each subject. It will be seen that the “two-step” levels and the graded exercise test level are not mutually exclusive; and frequently the second level of exercise qualified as a graded exercise test level as well. In this case testing was terminated upon recovery.

Electrocardiographic records thus obtained were evaluated for confirmation of maximal heart rate during exercise, R-ST junction (J) depression, slope and contour of ST segment, and T-wave changes. Rhythm, conduction, and measurements of wave amplitude and duration not herein reported were also made. Responses were classified as positive if ST-segment depression of 1 mm. or more (−0.1 mV) appeared, beginning with J depression and continuing flat or down-sloping for a duration at least equivalent to QRS duration before beginning its return to the isoelectric line, arbitrarily defined as the P-R junction.

Results

Two hundred sixteen individuals, with ages from 15 to 94 years, were studied: 104 were patients having an initial diagnosis of possible
angina pectoris (table 1). At least two experienced cardiologists examined each patient without knowledge of exercise electrocardiographic response, and classified each into one of the following groups: patients without previous myocardial infarction were with undoubted angina pectoris (34 patients); with probable angina pectoris (14); and with improbable angina pectoris (21). Those with evidence of previous infarction were with angina pectoris (26) and without current angina (9). One hundred twelve normal subjects were also studied.

Nearly all subjects, both normal and patients, if they were free from obvious musculoskeletal defects, could complete the work prescribed by the single and double Master-test tables, and could, by means of "two-step" climbing, chair mounting or running in place, reach 85 per cent of their age-predicted maximal heart rate (the graded exercise test rate). The great majority achieved their "target rate" by "two-step" climbing.

Characteristics of electrocardiographic responses in normal subjects were the following:

1. No subject developed flat or sagging ST depression of 1 mm. or more. (Lesser degrees of depression were seen).
2. J depression occurred in many, but by no means in all subjects. In a few subjects J depression exceeded 3 mm., but was followed by a proportionately steep, upsloping ST segment (fig. 5A).
3. Minor atrioventricular conduction changes were found in some subjects, but no intraventricular conduction disturbances were produced.
4. Subjects frequently exhibited a few premature atrial and ventricular beats in the first 2 minutes of recovery, but not during exercise.
5. No subject developed angina pectoris during testing.

Patients with angina pectoris uncomplicated by myocardial infarction demonstrated ST depression with flat or sagging ST segments in 27 cases (79 per cent); of this number the "two-step" exercise test levels produced 22
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Figure 1
Percentages of positive responses in each clinical class are indicated by the horizontal bars. The dotted portions of bars indicate the percentages of positive responses detected with Master’s test exercise levels. Shaded portions of bars indicate percentage of positive responses detected only by graded exercise test (GXT) levels. Figures directly above bars indicate over-all incidence of positive responses to GXT procedure in each class.

positive responses (65 per cent), and the graded exercise test uncovered five (14 per cent) additional positive responses (fig. 1).

Of the “probable angina” group, “two-step” exercise produced four positive responses (28 per cent) and the complete graded exercise test raised this figure to seven (50 per cent). Only one positive response was found among the 21 patients classified “angina improbable,” and this response was following a double “two-step” exercise.

Patients with old myocardial infarction but without current angina yielded one electrocardiographic positive (11 per cent). This occurred following a double “two-step” exercise. Those with angina pectoris demonstrated 10 positive responses associated with “two-step” tests (38 per cent), increasing to 14 (54 per cent) with the graded exercise tests.

In all, there were 50 positive electrocardiographic responses and the addition of the graded exercise test level of stress accounted for 12 (24 per cent) of this number, which would otherwise have been undetected.

Examination of heart rate responses to the “two-step” test (fig. 2) shows that, in providing a standardized work challenge to the legs, a wide variation in cardiac stress results. Some subjects are strained but little, and do not develop sufficient tachycardia to unmask mild angina; on the other hand, some patients developed heart rates within a few beats per minute of their maximal predicted heart rate. This could represent a potential hazard. Thirty-five per cent of all positive responses occurred at heart rates at least 90 per cent of the graded exercise test rate (fig. 3). A distinctive characteristic of the graded test level of exercise is the “excess” heart rate after 6 minutes of recovery, in angina patients as well as in normal subjects (fig. 4). This finding, which is proportional to the relative severity of cardiac stress during exercise is inconstantly observed after the “two-step” tests.

In the course of testing, no circulatory arrests or myocardial infarctions occurred during or immediately after the procedure. Brief episodes of ventricular tachycardia or mild pulmonary edema occurred occasionally, relieved within a few moments by sitting up.

Discussion

The physician using an exercise electrocardiographic test is continuously confronted with the question of which criteria to apply. It is generally agreed that the original criteria of Master are excessively sensitive, resulting in a high percentage of “false positive” responses (fig. 5B). Because of our doubt regarding the accurate reproducibility of 0.5-mm. ST-segment displacement measurements, particularly in the presence of induced tachycardia and tachypnea, we have for the present adopted 1.0 mm. as a conservative and widely accepted critical magnitude for recognition of “ischemic ST-segment depression” in any lead in which the segment was isoelectric prior to exercise. This is our only current electrocardiographic criterion for angina pectoris.

It is recognized that ischemic heart disease may produce diverse electrocardiographic changes. These include ventricular premature beats and ventricular tachycardia, atrial premature beats, left bundle-branch block, atrioventricular block, R-ST elevation, alterations in the ST-T period, as reflected in the “QX-QT ratio” (see legend, fig. 5, for explanation of terms). Applied to the diagnosis of ischemic heart disease, these criteria fail to distinguish
Maximal heart rate during single and double two-step tests in relation to age.

Relation to age of maximal heart rate during positive exercise test.
clearly between normal and abnormal populations, and all of the above changes may at times be caused by disease other than angina pectoris. Their occurrence indicates to us the need for further diagnostic study.

Since there is evidence that patients exhibiting J depression without flat or sagging ST segment do not have an increased mortality rate in long-term follow-up but actually have a lower mortality than an average population, this measurement in particular is excluded as a criterion for angina.

Magnitude of the ischemic ST-segment depression is of prognostic significance according to the same study by Robb and Marks. Their subjects were followed for an average of 5 years. When ST depression was 1 mm. to 1.9 mm., the mortality rate was increased nearly five times, and ST depression exceeding 2.0 mm. was associated with a mortality about 20 times that of the standard population.

Proponents of an exercise test more strenuous than that currently in use must face the possible objection that such exercise may produce "abnormal" changes in normal individuals, even athletes. Our experience, however, suggests that if such false-positive results occur in normal subjects, they occur only rarely. A more difficult problem is the finding of significant ST depression in an individual who, while not having angina pectoris, suffers from some functional disorder, perhaps of the sympathetic nervous system. While uncommon, these changes are known to occur, and appropriate care must be taken in the final translation of test results for treatment of the individual patient.

Indications and contraindications of exercise testing remain a highly individualized clinical consideration. The contraindications we observe include (1) evidence suggesting a recent myocardial infarction; a complete electrocardiogram recorded and interpreted immediately before exercise is a necessary, integral part of the test; (2) evidence of "impending myocardial infarction," i.e., frequent and prolonged episodes of angina, especially if occurring at rest or if of recent onset; and (3) lack of direct, continuous physician supervision of the exercise test.

Indications for testing are many. We regard the graded exercise test as desirable in the evaluation of every patient considered possibly to have angina pectoris. If, with a negative graded exercise test, there is impressive nonelectrocardiographic evidence supporting the diagnosis of angina, further individualized measures designed to increase the likelihood of a positive response are carried out. These may include postprandial and cold-room testing, and the heart rate in the graded exercise test may be deliberately exceeded by more vigorous exercise. Under these conditions special precautions are observed. Two or more physicians and appropriate resuscitative equipment including an external direct-current defibrillator, are immediately available. It should be noted, however, that no deaths, cardiac arrests, or episodes of ventricular fibrillation have occurred during or soon after such testing in more than 5 years, involving more than 1,000 studies.

The graded exercise test is of value in routine examination of asymptomatic individuals who have an increased likelihood of coronary disease by virtue of family history, age, sex, hypercholesteremia, or diabetes mellitus. It also aids in the evaluation of patients following recovery from a myocardial infar-
An electrocardiogram after exercise of a normal subject. At heart rates in excess of 160 per minute the P wave frequently begins before termination of the preceding T wave, masking any U wave and preventing registration of an isoelectric T-P segment. For this reason, the isoelectric line is constructed by connecting the P-Q junctions of two successive cardiac cycles for which the baseline is flat. The J-point is depressed but the slope of the ST segment is steeply upward (note that 50 mm./sec. chart speed is employed). The X point represents the crossing of the isoelectric line by the ST-T portion of the tracing. B, lower. This tracing is from a subject with angina pectoris. The J-point is depressed at least 0.1 mV, followed by a depressed ST segment which fails to slope upward initially. The QX/QT ratio is increased (greater than 0.5). (The QT ratio = QTc/40, where QTc = QT/R-R interval seconds.)

Summary

Standardization of an exercise electrocardiographic test for myocardial ischemia is desirable. Standardization of exercise should be based upon a standardized challenge to the coronary circulation, not upon a standardized challenge to the skeletal muscles, for the stresses upon the heart are not identical.

With the use of heart rate during exercise...
as an index of cardiac stress, the levels of exercise prescribed on the basis of age, sex, and weight in standard "two-step" test tables produce widely varying levels of cardiac stress —sometimes too low to induce significant ST-segment depression in patients with angina pectoris and, occasionally, much greater than necessary to produce such diagnostic electrocardiographic changes.

The graded exercise test, using 85 per cent of the maximal age-predicted heart rate that may be induced by exercise, produces a closer approximation of a standardized cardiac stress, regardless of age, sex, or body build. Its use with angina pectoris patients and normal subjects results in increased sensitivity (fewer false negatives) and increased specificity (fewer false positives).

Use of the graded exercise test as described is considered not to increase the hazard of testing, and perhaps even to decrease it.

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