On-line Analysis of the Exercise Electrocardiogram

By L. T. Sheffield, M.D., J. H. Holt, M.D., F. M. Lester, M.D.,
D. V. Conroy, and T. J. Reeves, M.D.

SUMMARY

A computer program has been developed which clarifies the distorted exercise ECG and performs desired measurements of it which are reported in the laboratory almost immediately, so that the program can be used as an aid to exercise test monitoring. We have introduced a new measurement of the ECG, the negative ST (− ST) integral, which while unfamiliar to the eye is readily performed by computer. A − ST integral value of 7.5 μv-sec during exercise served to separate a normal group from a group with angina pectoris. Strenuous exercise was often necessary to elicit positive responses in diseased subjects, and the graded exercise test was found well-suited for this purpose.

Use of a computer program as an investigative instrument in its own right, rather than as a means of duplicating classical human measurements, shows promise for improving the diagnosis of ischemic heart disease.

Additional Indexing Words:
Ischemic heart disease  Submaximal exercise test  Graded exercise test
ST integral  Angina pectoris  Computer analysis

The exercise ECG test for ischemic heart disease recently has undergone extensive modification with increase in knowledge of the disease and progress in medical instrumentation. Recently the main areas of activity directly affecting the exercise electrocardiographic test have included (a) increasing the exercise stress involved,1−5 (b) introduction of ECG monitoring during exercise,6−8 and (c) application of computer technology toward evaluation of the ECG signal.9−12 The present work embodies these three developments. We have developed an on-line computer program for measuring the exercise ECG and will present clinical data which lead toward the establishment of a diagnostic criterion for ischemic heart disease when applied to the computer-measured exercise ECG.

No ECG change has been found entirely specific for the confirmation of angina pectoris. Many criteria have been proposed, including varying degrees of ST-segment depression, T-wave inversion, interval changes, ratios of intervals, and precipitation of arrhythmias during exercise. The precipitation of ST depression during exercise with its return to iso-electric potential during recovery, however, has been the most valuable ECG sign of exertional myocardial hypoxia.3, 18−16 Although ST-segment depression has wide acceptance as a primary indication of myocardial ischemia, the quantity and quality of a minimal positive change vary in the eyes of different electrocardiographers. The range of human variation in interpreting exercise ECGs, as recently reported by Blackburn and colleagues,18 is remarkable. This variation suggests that interpretation is the least precise aspect of the exercise test.

In the development of a computer program

From the Allison Laboratory of Exercise Electrophysiology, Department of Medicine, University of Alabama Medical Center, Birmingham.

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for measurement of the ECG before, during, and after exercise, it was suggested that measurement of the time integral of the depression of the ST segment offered in a single expression information that characterized the ischemic response. Smith and Wherry\textsuperscript{11} reported in 1966 on the usefulness of time-voltage integral recordings of scalar VCG leads in the detection of ischemic heart disease. They used analog recordings, and the visual measurements of them did not specifically quantitate the ST-segment region. Although our program was designed to minimize technical artifacts occurring during exercise and to provide accurate measurements of a number of electrocardiographic variables, the present study was focused on the question of the usefulness of the integral of the ST segment in the clinical recognition of ischemic heart disease. Toward this end we have studied two groups of patients, one clinically normal, the other with unquestioned coronary heart disease manifested by angina pectoris. The usefulness of the other measurements, which in our early studies were less promising in the detection of myocardial ischemia, is being evaluated in a larger group of subjects, both normal and with a variety of diseases.

Methods

The Exercise ECG

Electrode sites were located on the skin, and these sites were prepared by cleansing with acetone followed by abrasion of a 1-mm circle of epidermis with a spherical dental burr in a 25,000 rpm motor tool.\textsuperscript{17} This is painless and helps create a low-resistance ECG signal pathway. Electrodes of the plastic-cup type,\textsuperscript{1} with a stainless steel disk, 1 cm in diameter, located 1 mm below the rim of the cup, are filled with electrolyte paste and held to the skin with double-sided adhesive disks.\textsuperscript{1} The chest electrodes and lead wire are stabilized by a brief garment of elastic mesh.\textsuperscript{8} A patient cable, consisting of individual coaxial cables, 2.5 mm in diameter,\textsuperscript{**} bound together with polyethylene spiral wrap, leads to the ECG preamplifiers which have an input impedance of 5 megohms and a frequency response of 0.1 to 1,000 Hz (time constant, 3.4 sec). There are no shunting resistors across any electrode groups. The patient cable, suspended from the ceiling midway between the examining table and the treadmill, permits freedom of movement without entanglement or tripping. Resting and postexercise recovery records were taken in the sitting position.

The resting ECG was interpreted and found free of any contraindication to testing in each case prior to commencement of exercise.

The volunteers in this study engaged in treadmill exercise sufficient to bring their heart rates to within 90\% of their age-predicted maximum exercise heart rate as shown in table 1, unless clinical or ECG changes dictated earlier termination of exercise.\textsuperscript{18} This rate was attained typically in 2 to 4 minutes of exercise, and in the absence of contraindication they continued to exercise for a minute or two longer while

<table>
<thead>
<tr>
<th>Table 1</th>
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<tr>
<td><strong>Maximum Predicted Heart Rate Fractions with Respect to Age and Physical Training</strong></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>HR</th>
<th>20</th>
<th>25</th>
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<th>35</th>
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<tr>
<td>MHR</td>
<td>120</td>
<td>114</td>
<td>108</td>
<td>102</td>
<td>96</td>
<td>90</td>
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<td>72</td>
<td>66</td>
<td>60</td>
<td>54</td>
<td>48</td>
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</tr>
<tr>
<td>90% MHR</td>
<td>108</td>
<td>102</td>
<td>96</td>
<td>90</td>
<td>84</td>
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<td>72</td>
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<td>60</td>
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<td>36</td>
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</tr>
<tr>
<td>75% MHR</td>
<td>96</td>
<td>90</td>
<td>84</td>
<td>78</td>
<td>72</td>
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<td>36</td>
<td>30</td>
<td>24</td>
<td>18</td>
<td>12</td>
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<tr>
<td>60% MHR</td>
<td>84</td>
<td>78</td>
<td>72</td>
<td>66</td>
<td>60</td>
<td>54</td>
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<td>18</td>
<td>12</td>
<td>6</td>
<td>0</td>
</tr>
</tbody>
</table>

Abbreviation: MHR = maximal heart rate.
treadmill adjustments minimized further increase in heart rate. In some normals the treadmill time was longer due to a much more gradual increase in work rate. After finding no difference in ECG response as a result of this variation, we included their data in this report.

Lead V5 of the ECG and an exercise modification of the Frank VCG were recorded continuously on magnetic tape. Only analyses of lead V5 are reported in this paper. The signal was transmitted by analog data line to the digital computer laboratory. Outputs from the computer were transmitted to a monitroscope, strip chart recorder, and a teletypewriter in the exercise laboratory.

Computer Program

The computer program has two main functions: the elimination of exercise artifact and measurement of specified characteristics of the ECG. Successive heart cycles with attendant muscle noise and other artifact are stored in designated computer memory arrays. Precise recognition of a given point in the QRS complex allows these to be stored in temporal alignment (fig. 1). If they were not well aligned, the resultant signal would be rounded, and the signal at any instant would be smeared into adjacent portions of the tracing.\(^6,10\) Prolonged acquisition of signal tends to increase this undesirable effect, and for this reason we have limited our acquisition to 19 beats or less. We have adopted median computation (the determination of the median value of all stored complexes at 2-msec intervals after the fiducial point) rather than mean or average computation in order to extract a clear signal without requiring an excessive number of heart cycles.

Measurements are received in the exercise laboratory by teletype. Each line of measurement is typed 3 to 5 sec after a given set of heart cycles has been acquired and consists of the time of acquisition, followed by the heart rate, QRS duration, amplitude of the QRS complex, ST junction, or J point, the depressed ST area or integral in microvolt seconds (\(\mu\text{V-sec}\)) the T-wave area, two measurements of ST-segment slope, and the amplitude of the R wave in millivolts. The ST-segment time-voltage integral (\(-\int \text{ST}\)) which we have investigated warrants explanation (fig. 2). On a conventional ECG tracing, one small horizontal unit equals 0.1 mv (100\(\mu\text{V}\)) and a small horizontal unit equals 0.04 sec (40 msec). The area of one small square is then equal to the product of these two sides or \(4\mu\text{V-sec}\). It is apparent that the ST integral reflects the entire behavior of the ST segment in a way that one or two measurements of this region could not accomplish. This measurement, although difficult for the human eye, is readily approximated by the computer, since it only requires the summation of the values of all measurements, with respect to the Q onset base line, from the J point to the crossing of the base line (fig. 3). Measurement of T-wave area is accomplished in the same way. Other points recognized and measured by computer include onset of QRS, R-wave peak, S-wave nadir, and T-wave peak amplitudes.

Clinical Evaluation

To test the possible value of this computer measurement, we processed exercise ECGs

\[\text{Figure 1}\]

On the left from above downward is illustrated the storage of successive heart cycles in temporal alignment, based upon identification of the maximum R-wave downslope. All of the stored complexes are superimposed in the upper right. The representative median ECG complex has been computed and plotted in the lower right.
from two distinct groups of men (table 2). The first group was free of historical, symptomatic, or physical findings of cardiovascular disease. There were 41 of them with a mean age of 56 years and the age distribution as indicated. The second group of 31 volunteers was determined by two or more of the investigators at different times to have angina pectoris beyond reasonable doubt. In this group 17 had electrocardiographic evidence of healed myocardial infarction, and 14 did not. Healed infarction of the inferior wall was diagnosed in 14 instances, anterior wall in two, and lateral wall in one. Patients not classified as having had prior infarction had normal tracings in 10 instances and borderline ST-T changes in three. These patients were free of valve lesions or hypertension, were not in congestive heart failure, and had not been receiving digitalis or other drugs known to affect the ECG. Their mean age was 48 years. If the higher mean age of the normal group

**Table 2**

*Exercise Test Subjects*

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean age</th>
<th>Age distribution (yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (yr)</td>
<td>30-39</td>
</tr>
<tr>
<td>Normal</td>
<td>41</td>
<td>56</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>31</td>
<td>48</td>
</tr>
</tbody>
</table>
ON-LINE ANALYSIS OF EXERCISE ECG

Measurements performed on the median ECG. Q onset is identified from the first time derivative as the beginning of the first major deflection of the QRS complex. The R peak and the S nadir are identified at their inflection points. QRS offset (Iₚ) is identified on the first time derivative as its last major deviation in the QRS complex which is significantly smaller than deviations appearing within the ST segment. Depressed ST integral (−fST) is the summation of measurements occurring from Iₚ to the crossing of the base line (Iₑ) referred to the amplitude of Qₑ. T peak is measured at its inflection point. T-wave integral (fT) is measured similarly to −fST.

has any effect on the study, it is to bias against, rather than in favor of, the separating power of the computer measurements, because of the recognized increase in incidence of asymptomatic coronary artery disease with advancing age.

Coronary arteriograms were made on 10 patients (32% of the angina group). In eight the examination occurred during the same admission as the exercise test; in the remaining two the examination was performed within 3 months of exercise testing (table 3). All 10 patients developed ECG abnormality during exercise testing; in eight it was ST-segment depression with negative ST-integral values exceeding 7.5 μv-sec. In two others atypical abnormalities were found as tabulated. All 10 subjects were found to have moderate to severe coronary artery disease. Although there

is complete qualitative agreement between exercise test and arteriographic data in this small group, the quantitative relationship between the exercise ECG and degree of demonstrated coronary occlusive disease is not statistically significant.

The greatest ST-segment deviation during exercise, represented by the largest measured −fST value, was plotted for each normal and abnormal volunteer with respect to a heart rate function. This function, in which 100% equals the predicted maximum heart rate for each individual, gives a standardized (or normalized) indication of the relative cardiac stress to each person in producing the observed ST change (fig. 4).

We found that normal persons demonstrated on the average a modest increase in −fST with increasing heart rate. At the maximum observed heart rate the mean value of −fST was 4.3 μv-sec with a standard deviation of 2.9 μv-sec (fig. 5). They did not manifest any recognized ECG abnormalities.
Coronary Arteriographic Correlation

<table>
<thead>
<tr>
<th>Subject</th>
<th>Coronary arteriogram (grade*)</th>
<th>Resting ECG</th>
<th>Exercise ECG</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Right</td>
<td>Left main</td>
<td>Ant. desc.</td>
</tr>
<tr>
<td>1. L.B.</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>2. J.C.</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>3. C.G.</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>4. C.J.</td>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>5. J.O'H.</td>
<td>4</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>6. B.P.</td>
<td>5</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>7. D.T.</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>8. T.W.</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>9. C.T.</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>10. J.B.</td>
<td>2</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>

* Coronary cineangiograms were graded according to the following schedule: 0 = no abnormality; 1–4 = progressively increasing degrees of narrowing; 5 = total obstruction.
† A 2 to 3 month interval separated the exercise studies from the coronary arteriographic studies in these two subjects.
‡ This subject manifested an atypical "giant T-wave" reaction coinciding with clinical angina pectoris, but without significant ST depression.
§ ST-segment elevation, anteriorly directed (Prinzmetal type), was the characteristic ECG response to exercise in this subject.

Abbreviations: Inf. MI = inferior myocardial infarction; ant. = anterior; EHR/MHR = exercise heart rate/maximum predicted heart rate.

The patients with angina pectoris developed much larger \(-\text{fST}\) values and developed them at significantly lower heart rate fractions before exercise was interrupted by the supervising physician. Maximum \(-\text{fST}\) measurements from the angina group had a mean of 15.3 \(\mu V\)-sec, with a standard deviation of 8.2 \(\mu V\)-sec. Two of these angina volunteers developed other ECG abnormalities; one showed anteriorly directed ST elevation similar to that seen in the type of angina described by Prinzmetal and associates\(^7\) and the other developed an intraventricular conduction defect and multifocal ventricular premature beats. Within the abnormal group there was no significant difference in \(-\text{fST}\) measurements on subjects with healed myocardial infarction and those without.

There was little overlap between the \(-\text{fST}\) values of the normal group and of the angina group. Thirty-nine of the 41 normals have maximum \(-\text{fST}\) values of \(-7.5\ \(\mu V\)-sec or less, and 25 of the 31 angina patients had \(-\text{fST}\) values greater than this. Separating the test results into normal or abnormal on the tentative assumption that the normal range is zero to \(-7.5\ \(\mu V\)-sec, results in a calculated test sensitivity of 81% and a specificity of 95% \((P<0.001)\) using the clinical diagnosis as a standard of comparison.

The extreme range of ST-segment behavior in the abnormal group is apparent, since values for the great majority of the normals fall well above those from the normals. Five measurements from the abnormal group,
ON-LINE ANALYSIS OF EXERCISE ECG

ON-LINE ANALYSIS OF EXERCISE ECG

Heart Rate, ST Segment and T Wave Response to Exercise in Two Subjects

Figure 6
Behavior of $-\Delta ST$, $\Delta T$, and heart rate in a typical normal subject and in a patient with angina pectoris in response to graded exercise test (GXT).

however, overlap the normals. Three of these, including the one at the far right on the graph, may be regarded as legitimate failures of detection. The other two, however, resulted from incomplete tests in which exercise was interrupted prematurely because of arrhythmia or ST elevation.

The time course of the ST integral showed interesting differences between normal and abnormal (fig. 6).

A typical normal demonstrates low measured $-\Delta ST$ values and some fluctuation at peak exercise. In a representative angina patient this value rises steeply as the patient achieves his programmed heart rate and progresses further with slight fluctuation while heart rate is constant. Upon stopping exercise the heart rate declines promptly, but $-\Delta ST$ remains large for a short time thereafter. This indicates a hysteresis effect on the $-\Delta ST$ which may be illustrated by plotting $-\Delta ST$ versus

Figure 7
Examples of $-\Delta ST$ versus heart rate plots in normals. The solid lines represent measurements during exercise, and the dotted lines, measurements after exercise.
heart rate (fig. 7). Values from normals range from virtually flat loops to others which develop modest $-\Delta ST$ values. Conversely, figure 8 contains comparable plots from patients with angina pectoris, which vary from a well-formed hysterisis loop, that during recovery returns to normal and remains there, to loops showing the familiar postexercise deterioration of ST segment following an initial improvement. In either case it is apparent that while there is occasional variation from one measurement to another, a consistent trend is recognized when the measurements are observed in context. The rapidity with which these trends sometimes take place illustrates the necessity for measuring the ECG over a fairly brief interval.

In 20% of our patients changes in the ST segment were greater during recovery than they were during exercise. However, in this 20%, the values measured during exercise exceeded the tentative normal range, and in no case was an abnormal value found only in the postexercise period.

**Exercise Severity**

Examination of the ECG findings in figure 4 reveals that one-half of our patients with angina pectoris developed critical ST abnormality at heart rates between 70% and 90% of their age-predicted maximum. Thus employment of this graded exercise test (GXT) "stress level" permits detection of angina pectoris which would not have been detected by milder exercise tests. This finding is consistent with the results of our earlier study comparing the GXT with the two-step test.20 It would appear that the 90% heart rate level,
which was chosen because it is the highest exercise level which we have found to be well tolerated by nearly all of our volunteers, is a reasonable target for such testing.

Discussion

The results presented in this study show clearly that patients with angina pectoris vary widely in the degree of exercise stress and degree of exercise tachycardia required to provoke -/ST abnormality. The amount of ST depression is also highly variable, with some measured values being more than five times greater than the values from other patients with angina pectoris. Therefore, it is hardly reasonable to limit to a strictly qualitative interpretation, normal or abnormal, the evaluation of a condition which all available evidence characterizes as a continuous spectrum. In the severe and very severe range of disease it has been shown that there is correspondence between degree of ECG change and patient survival; one might reasonably expect a quantitative relationship between ECG response and mild to moderate degrees of coronary flow restriction.

There is a choice in the ECG diagnostic approach to this range of abnormality. One may attempt to establish a quantitative relationship between the effects of a fixed stress on the circulation and the degree of resultant ECG changes. Or one may cause the stress to increase until a standard, diagnostic level of ECG change is manifested, and thus seek a quantitative correspondence between the required stress level and the degree of abnormality present in the coronary circulation. Our experience indicates that low levels of exercise are inadequate to provoke ECG changes which may be recognized with diagnostic precision in persons with mild to moderate coronary artery disease. It is also our medical conviction that unnecessary discomfort and risk to the patient would result from requiring him to continue exercise well past the development of recognizable myocardial hypoxia. Therefore, we introduce the function, heart rate fraction (EHR/MHR), as an index of relative stress upon the coronary circulation, since its numerator, exercise heart rate, is an effective index of myocardial O_2 requirement in the normotensive subject, and its denominator, age-predicted maximal exercise heart rate, is therefore an index of maximal normal myocardial O_2 requirement. The heart rate fraction associated with development of a certain degree of ECG abnormality thus offers a potential index of coronary impairment in individuals with lesser degrees of ischemic heart disease.

Computer measurement of exercise ECGs, after median computation to reduce artifact, eliminates observer variability in interpreting tracings and permits the development of objective ECG criteria which are generally applicable. The availability of precise numerical ECG measurements should facilitate exchange of information and advance the application of statistical methods to electrocardiography in large scale population studies. Computer measurement makes practical for the first time the development of ECG criteria involving whatever changes are found useful in disease differentiation, such as measurement over the entire length of the depressed ST segment by integration, similar measurement of the T wave, and the combination of these and other amplitude and duration functions which may be shown to characterize a particular clinical entity. Smith and Wherry's findings indicate that spatial analysis of the VCG contributes additional diagnostic information. Our program, with automatic recognition and measurement of the ST region, is presently being adapted to VCG signals for this reason.

Acknowledgment

Dr. William B. Jones performed the coronary cineangiographic examinations and kindly permitted use of his findings. The authors thank Mrs. Juanita Brasher and Mrs. Florence Driskill for assistance in all phases of the preparation of this report. Dr. David

*This statement applies to diagnostic testing only.

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References
