Quantitative Interpretation of the Exercise Electrocardiogram

Use of Computer Techniques in the Cardiac Evaluation of Aviation Personnel

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The consequences of misdiagnosed coronary heart disease assume a different dimension in aviation medicine than in civilian practice. Death of the pilot from coronary disease has been implicated as the cause of 20 aircraft accidents or incidents, and failure to detect imminent impairment of function due to coronary heart disease is to court disaster. On the other hand, aviators are highly trained personnel and each man represents an exceedingly high investment in training, money, and personal risk. A false-positive diagnosis of coronary disease is also a costly error because of the resulting loss of an individual from duty involving the control of aircraft.

The routine use of the electrocardiogram (ECG) has proven of value in the selection and evaluation of pilots and aircrew, and there is general agreement among cardiologists that exercise stress increases the sensitivity of the ECG as a method of detecting latent coronary disease. However, the diagnostic accuracy of currently accepted exercise stress tests is poor, and equivocal responses occur frequently in cases in which objective information is most needed. Because of this need for a more sensitive and a more specific ECG test for cryptic coronary disease, a testing method has been developed that enables one to quantitatively measure changes in the electrocardiogram after exercise and to express the data in a form that allows rapid statistical analysis. It is the purpose of this report to describe this methodology and to compare findings in normal subjects and patients who have mild angina pectoris.

Methods

Subjects
Electrocardiographic tracings recorded after exercise in 151 persons were used in this study. The subjects and patients comprising the study population were grouped as follows:

Normal Control Group
Those members of the group of 1,000 aviators who were part of the longitudinal study and who returned for re-evaluation during the period July 10, 1964, to May 1, 1965, were included as potential control subjects if they were free from angina pectoris or other cardiac ischemic syndromes in the opinion of the separate medical team assigned to that project. One hundred and forty asymptomatic men were given the exercise stress test, and these men will be followed in an ongoing longitudinal study. Since the present study proposed to compare persons who had a low probability of significant coronary heart disease with a group of patients with a high probability, subjects were eliminated from the normal control group if they exhibited abnormal values of epidemiologically proven risk factors for coronary disease. Frequency distributions of values of blood pressure, cholesterol, S, 20–400 serum lipoprotein, postprandial blood sugar, and uric acid had been determined as part of the primary study, and the eightieth percentile was that value chosen as the upper limit of normal for each of the cardiovascular risk parameters. As a result, 96 asymptomatic men were eliminated from the normal group; the remaining 44 constituted the normal controls for our study. An exercise ECG was not used as a basis for selection of the normal group. If, subsequently, such an ECG was found to be abnormal, the subject was not excluded from the group. The age of the normal control group ranged from 43 to 55 years with the mean age of 47 years.
Abnormal Group

Physicians in the Cardiology Department of the U.S. Naval Hospital, Pensacola, and physicians in the Cardiology Branch of the U.S. Naval Aerospace Medical Institute were asked to refer patients for a vectorcardiographic (VCG) exercise test who met the following criteria: (1) a definite history of angina pectoris or the coronary insufficiency syndrome; (2) normal or essentially normal resting ECG with no evidence of a previous myocardial infarction; and (3) enough cardiac reserve by history to enable the patient to undergo safely exercise stress slightly greater than that of the Master two-step test.

 Eleven patients are included in this group; two of the men were active duty naval aviators, four were chief petty officers, and five were former naval officers. One patient was a Negro. Their ages ranged from 38 to 53 years, with a mean of 46 years.

Exercise Load

In this study a Lanooy* bicycle ergometer was used to supply a work load. A negative feedback system in the unit decreased the magnetic coupling between the flywheel and the pedal axle, thus keeping the rate of work constant when at a speed of 50 to 70 rpm. Each subject was given 2 minutes of exercise at 150 watts (a calculated work load of 18,000 joules). By comparing calculated work, oxygen uptake, pulse rate, and pulse recovery time, it had previously been determined\textsuperscript{12} that this amount of exercise was greater than the double two-step test for all subjects but less than the 3-minute Harvard step test (single 20-inch step at a rate of 20 steps per minute). Only one patient was unable to perform the 2-minute exercise run because of leg fatigue. None of the patients with coronary disease complained of chest discomfort during the test.

Calculation of Data

A special-purpose analog computer utilizing operational amplifiers in a configuration for integration was constructed for this project.\textsuperscript{13} Three integrator channels were available for simultaneous display of data from three orthogonal leads. The unit contained a base-line correcting circuit to return the tracer to the same position on the recording paper after each complex and a synchronizing circuit to reset the integrators at a predetermined fraction of the R-R interval. The reset occurred at the same relative time in the cardiac cycle and thus was not disrupted by rate changes unless they were extreme. Initially the scalar ECG traces from three orthogonal leads were fed directly to the integrator, and the scalar ECG for each lead was displayed with its companion integral on Sanborn eight-channel heat-sensitive paper. Later, scalar traces were recorded on an Ampex FR-1300 FM magnetic tape recorder during exercise and for the postexercise period. Integrator analysis of the FM tapes was then performed. A typical recording for a normal subject is shown in figure 1 and a recording from a patient with angina pectoris is shown in figure 2.

Automatic analog-to-digital conversion equipment was not available at the time of this study, and it was necessary to measure manually the height of the integral trace at the time in the cardiac cycle of interest and place these data on IBM punch cards. With this card input, standard spatial trigonometric operations were carried out on a Univac 418 digital computer and vector parameters were automatically calculated. The spatial mean QRS vector, spatial mean T vector, spatial mean ventricular gradient (G), and the angle between the spatial QRS and T vectors were calculated for each patient during a control period prior to exercise, immediately after exercise, 3 minutes after exercise, and 10 minutes after exercise. A fourth parameter representing initial repolarization (TI) was arbitrarily defined as the accumulated area from the junctional point (J point) at the end of the QRS to the midpoint in the T wave. For each control and postexercise period the J-T interval was measured on X, Y, and Z leads, and one half of the longest J-T interval of that period was used to determine the point at which TI was to be measured. This measurement was taken in lieu of the ST segment because of the great difficulty inherent in a quantitative definition of the ST segment (fig. 3). In addition to the conventional VCG measurements, the Cartesian coordinates of each spatial vector were used in the statistical analysis described in “Results” and in the “Appendix.” The digital computer was programmed for this analysis.

Lead System and Electrode Mounting

The lead system for vectorcardiography described by Frank\textsuperscript{14} was used throughout this study. The left, posterior, and inferior electrodes are positive in this system. The skin was prepared by first shaving a small area, then cleansing vigorously with alcohol and acetone. Stainless steel mesh electrodes were used for the initial part of this study, but silver electrodes were later substituted because of their greater durability. Studies prior to the start of this project disclosed that small changes in the anterior chest electrodes caused significant changes in the vector orientation. For this reason, each electrode

*Manufactured by N. V. Godant, Holland.
was mounted separately with a moleskin patch to prevent electrode shift.

**Statistical Model**

If the Cartesian coordinates $(x, y, z)$ of a vector in space of any magnitude are multiplied by a constant $(c)$ defined as

$$ c = \sqrt{\frac{1}{x^2 + y^2 + z^2}}, $$

a new vector in space can be defined with the same direction as the original vector but having the magnitude $(sM)$ of 1.0. Thus,

$$ sM = \sqrt{(cx)^2 + (cy)^2 + (cz)^2} = 1.0. $$

From the Cartesian coordinates of a group of such unity vectors the average coordinates can be defined for the group, and an average unity vector constructed. There will be a distribution of individual vectors about this average central vector. A line drawn from the terminus of the average vector to the terminus of an individual vector forms the third side of an isosceles triangle in space ($d'$ of fig. 4A). As a conceptual model of the statistical analysis, the termini of the unity vectors can be considered to form a cluster of points when projected on the surface of a hypothetical sphere with a radius 1.0 and its center common to the origin of the vectors (fig. 4B). The average vector of the group will have a corresponding point on this surface. The distance ($d'$) between the average point and each individual point can be calculated by an application of the law of cosines. Standard statistical methods can be applied to the frequency distribution of $d'$ values. A more formal proof of

**Figure 1**

*Exercise tracing from a normal subject. Tracings made immediately, 3 minutes, and 10 minutes after exercise.*
the statistical methods appears in "Appendix I" and "Appendix II."

Results

The digital computer was programmed to calculate the magnitude, azimuth, and elevation of the spatial mean QRS, TI, T, and G vectors as well as the Cartesian coordinates of these parameters. A marked shift in the mean T axis to the right after exercise has been a constant finding in patients referred because of coronary heart disease. This has been true for the patients in this study as well as for patients from disparate populations who had exercise tests performed but were not included in this series. An unexpected finding in the patients with angina pectoris was that the maximum change in the T vector direction usually occurred 3 minutes after exercise, and the best separation of the symptomatic patients and the normal subjects could be made during this time period. The initial portion of the ventricular repolarization vector (TI mean vector), which essentially corresponds to the ST segment vector, has proved to be sensitive to the effects of exercise, but changes occurred in both of our study groups. Changes in the direction of the ventricular gradient also lacked specificity. In table 1 a comparison is made of a normal subject and a patient with mild angina pectoris. In figure 5, the position of the spatial T vector has been diagrammed.
Figure 3
Method of area analysis.

for the 3-minute postexercise period. Although the differences between the normal subject and the patient are readily apparent from the diagram, statistical analysis of direction change expressed in spherical polar coordinates is somewhat unwieldy. For this reason the relative linear distance (d') between the terminus of the average T vector of the normal group and the termini of the spatial vectors of abnormal individuals has been utilized (see "Methods").

The d' of the mean spatial QRS, TI, T, and G vectors has been calculated for each member of the study during the control period and for each of the three periods after exercise. Since the goal of this investigation was individual diagnosis rather than group differentiation, a method which could be used to obtain the probability that a given individual was a member of a "healthy" population was desired. For this purpose a derivation of Student's t-test (Appendix II) was used and a t score was computed from the following equation:

\[
t_i = \frac{d'_i - \bar{d}'_n}{S_{d'n}} \cdot \sqrt{\frac{N - 1}{N + 1}},
\]

degrees of freedom = N - 1
where d'_i is the distance between individual i's unity vector terminus and the terminus of the average unity vector of the normal group,

\[
\bar{d}'_n = \text{the mean } d' \text{ of the normal group (independent of } i)\]

\[
S_{d'n} = \text{the biased standard deviation of } d' \text{ values of the normal group (independent of } i)\],

\[
N = \text{the number of cases } \bar{d}'_n \text{ and } S_{d'n}\]

are based on.

The calculated t scores of the 11 patients appear in table 2. For the T vector d' 3 minutes after exercise, the t scores were greater than 1.85 (P > 0.05) for the 11 patients with angina pectoris, and greater than 2.76 (P >
Table 1

Comparison of VCG Items in a Normal Individual and a Patient with Angina Pectoris

<table>
<thead>
<tr>
<th>Resting and time after exercise</th>
<th>Magnitude</th>
<th>QRS</th>
<th>T</th>
<th>G</th>
<th>Mean spatial vectors in a normal individual*</th>
<th>Direction</th>
<th>Spatial angle</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>QRS</td>
<td>T</td>
<td>G</td>
<td>azQRS</td>
<td>azTI</td>
<td>azT</td>
</tr>
<tr>
<td>Resting</td>
<td>28</td>
<td>25</td>
<td>62</td>
<td>74</td>
<td>-25</td>
<td>73</td>
<td>53</td>
</tr>
<tr>
<td>Immediate</td>
<td>32</td>
<td>17</td>
<td>33</td>
<td>18</td>
<td>-88</td>
<td>97</td>
<td>61</td>
</tr>
<tr>
<td>3 min</td>
<td>27</td>
<td>17</td>
<td>50</td>
<td>54</td>
<td>-44</td>
<td>88</td>
<td>56</td>
</tr>
<tr>
<td>10 min</td>
<td>25</td>
<td>21</td>
<td>61</td>
<td>70</td>
<td>-37</td>
<td>67</td>
<td>50</td>
</tr>
</tbody>
</table>

*Mean spatial vectors in a normal individual.
†Mean spatial vectors in a patient with mild angina pectoris.

*A 42-year-old aviator from 1000-aviator evaluation. All cardiovascular tests were negative.
†A 42-year-old aviator from the abnormal group. Patient 97 in table 2.
Table 2

The t-Test Scores of d' Values of Spatial Vector Directions for Eleven Patients with Coronary Heart Disease Measured prior to Exercise, and Immediately, Three Minutes, and 10 Minutes after Exercise (P<0.05 = 1.68; P<0.01 = 2.42; P<0.001 = 3.55)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Resting and time after exercise</th>
<th>ORS</th>
<th>TI</th>
<th>T</th>
<th>G</th>
</tr>
</thead>
<tbody>
<tr>
<td>46</td>
<td>Resting</td>
<td>-0.696</td>
<td>-1.621</td>
<td>0.106</td>
<td>-0.229</td>
</tr>
<tr>
<td></td>
<td>Immediate</td>
<td>-0.489</td>
<td>-0.653</td>
<td>1.297</td>
<td>1.074</td>
</tr>
<tr>
<td></td>
<td>3 min</td>
<td>-0.575</td>
<td>0.477</td>
<td>3.735</td>
<td>2.538</td>
</tr>
<tr>
<td></td>
<td>10 min</td>
<td>-0.358</td>
<td>-0.844</td>
<td>1.069</td>
<td>1.492</td>
</tr>
<tr>
<td>50</td>
<td>Resting</td>
<td>0.789</td>
<td>0.894</td>
<td>2.879</td>
<td>-1.244</td>
</tr>
<tr>
<td></td>
<td>Immediate</td>
<td>-0.102</td>
<td>0.841</td>
<td>3.941</td>
<td>1.252</td>
</tr>
<tr>
<td></td>
<td>3 min</td>
<td>0.583</td>
<td>1.466</td>
<td>4.555</td>
<td>1.441</td>
</tr>
<tr>
<td></td>
<td>10 min</td>
<td>0.944</td>
<td>0.984</td>
<td>3.529</td>
<td>-1.254</td>
</tr>
<tr>
<td>68</td>
<td>Resting</td>
<td>0.049</td>
<td>-1.368</td>
<td>-0.552</td>
<td>0.062</td>
</tr>
<tr>
<td></td>
<td>Immediate</td>
<td>0.498</td>
<td>-0.660</td>
<td>0.553</td>
<td>1.724</td>
</tr>
<tr>
<td></td>
<td>3 min</td>
<td>-0.487</td>
<td>1.087</td>
<td>3.384</td>
<td>1.684</td>
</tr>
<tr>
<td></td>
<td>10 min</td>
<td>-0.338</td>
<td>-0.260</td>
<td>-0.774</td>
<td>0.286</td>
</tr>
<tr>
<td>70</td>
<td>Resting</td>
<td>0.227</td>
<td>0.695</td>
<td>0.519</td>
<td>-1.528</td>
</tr>
<tr>
<td></td>
<td>Immediate</td>
<td>-1.066</td>
<td>0.568</td>
<td>-0.169</td>
<td>-0.393</td>
</tr>
<tr>
<td></td>
<td>3 min</td>
<td>-0.420</td>
<td>1.001</td>
<td>4.713</td>
<td>0.316</td>
</tr>
<tr>
<td></td>
<td>10 min</td>
<td>0.122</td>
<td>-1.215</td>
<td>0.294</td>
<td>-1.465</td>
</tr>
<tr>
<td>78</td>
<td>Resting</td>
<td>-0.785</td>
<td>2.816</td>
<td>2.476</td>
<td>0.360</td>
</tr>
<tr>
<td></td>
<td>Immediate</td>
<td>0.913</td>
<td>0.229</td>
<td>1.862</td>
<td>2.858</td>
</tr>
<tr>
<td></td>
<td>3 min</td>
<td>0.737</td>
<td>0.909</td>
<td>4.242</td>
<td>4.043</td>
</tr>
<tr>
<td></td>
<td>10 min</td>
<td>-1.475</td>
<td>2.129</td>
<td>4.479</td>
<td>1.511</td>
</tr>
<tr>
<td>85</td>
<td>Resting</td>
<td>0.108</td>
<td>-0.615</td>
<td>1.605</td>
<td>-0.700</td>
</tr>
<tr>
<td></td>
<td>Immediate</td>
<td>0.702</td>
<td>1.133</td>
<td>3.930</td>
<td>3.655</td>
</tr>
<tr>
<td></td>
<td>3 min</td>
<td>-0.264</td>
<td>1.524</td>
<td>4.824</td>
<td>3.129</td>
</tr>
<tr>
<td></td>
<td>10 min</td>
<td>0.420</td>
<td>1.034</td>
<td>4.822</td>
<td>0.873</td>
</tr>
<tr>
<td>97</td>
<td>Resting</td>
<td>-1.264</td>
<td>-1.406</td>
<td>-0.478</td>
<td>-0.317</td>
</tr>
<tr>
<td></td>
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<td>-0.090</td>
<td>-0.314</td>
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</tr>
<tr>
<td></td>
<td>3 min</td>
<td>0.521</td>
<td>1.958</td>
<td>4.318</td>
<td>3.322</td>
</tr>
<tr>
<td></td>
<td>10 min</td>
<td>-0.513</td>
<td>0.604</td>
<td>1.772</td>
<td>1.870</td>
</tr>
<tr>
<td>113</td>
<td>Resting</td>
<td>1.148</td>
<td>1.054</td>
<td>2.415</td>
<td>-0.506</td>
</tr>
<tr>
<td></td>
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<td>-0.073</td>
<td>0.455</td>
<td>3.378</td>
<td>-0.085</td>
</tr>
<tr>
<td></td>
<td>3 min</td>
<td>-0.239</td>
<td>0.592</td>
<td>3.662</td>
<td>2.081</td>
</tr>
<tr>
<td></td>
<td>10 min</td>
<td>0.094</td>
<td>0.694</td>
<td>3.808</td>
<td>0.856</td>
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<tr>
<td>118</td>
<td>Resting</td>
<td>-1.296</td>
<td>-0.223</td>
<td>-0.720</td>
<td>-1.172</td>
</tr>
<tr>
<td></td>
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<td>-0.417</td>
<td>-0.979</td>
<td>0.068</td>
<td>0.065</td>
</tr>
<tr>
<td></td>
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<td>1.145</td>
<td>4.283</td>
<td>3.316</td>
</tr>
<tr>
<td></td>
<td>10 min</td>
<td>-0.866</td>
<td>-0.909</td>
<td>1.141</td>
<td>0.851</td>
</tr>
<tr>
<td>168</td>
<td>Resting</td>
<td>1.885</td>
<td>-0.173</td>
<td>-0.571</td>
<td>0.008</td>
</tr>
<tr>
<td></td>
<td>Immediate</td>
<td>1.849</td>
<td>1.310</td>
<td>0.791</td>
<td>0.231</td>
</tr>
<tr>
<td></td>
<td>3 min</td>
<td>1.572</td>
<td>1.384</td>
<td>1.850</td>
<td>0.457</td>
</tr>
<tr>
<td></td>
<td>10 min</td>
<td>1.723</td>
<td>-0.244</td>
<td>-0.035</td>
<td>-0.512</td>
</tr>
<tr>
<td>296</td>
<td>Resting</td>
<td>0.797</td>
<td>-1.017</td>
<td>-0.219</td>
<td>0.175</td>
</tr>
<tr>
<td></td>
<td>Immediate</td>
<td>0.624</td>
<td>1.327</td>
<td>1.302</td>
<td>0.921</td>
</tr>
<tr>
<td></td>
<td>3 min</td>
<td>0.357</td>
<td>2.304</td>
<td>2.769</td>
<td>0.774</td>
</tr>
<tr>
<td></td>
<td>10 min</td>
<td>0.029</td>
<td>2.340</td>
<td>3.673</td>
<td>0.803</td>
</tr>
</tbody>
</table>

because of the difference in size of the three groups.

With the digital computer the groups arbitrarily defined as "normal" and "abnormal" can be easily rearranged. For example, if all asymptomatic men (140 subjects) were taken as the normal group and the 11 patients with angina pectoris compared to this group, all of

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the 11 patients will have \( t \) scores greater than 1.69 \((P \geq 0.05)\), but the \( t \) scores will be lower than when the "normal" group is more stringently defined by eliminating subjects with positive-risk factors. Fewer members of the group of 44 men with no risk factors present had significant \( d' \) scores 3 minutes after exercise when compared to the entire group of 140 asymptomatic individuals. If the 44 normal subjects with average age of 47 years were individually compared to a group of healthy young subjects with average age of 22 years, 12 of the 44 older subjects will have significant \( T \) directional change 3 minutes after exercise. This indicates that the response to this exercise test changes with age and illustrates the importance of using a peer group in defining normal standards.

Although our greatest interest was to determine whether an individual was a member of the normal group, the inverse possibility of whether the subject was a member of the group of patients with angina pectoris should be considered. The \( d' \) values of the VCG parameters of each individual in the abnormal group have been compared to the distribution of \( d' \) values of the other 10 members of the group. For the \( d' \) of the \( T \) vector 3 minutes after exercise, 10 of the 11 men had \( t \) scores less than 1.81 \((P \geq 0.05)\) and a single individual had a \( t \) score of 3.23 \((P \geq 0.02)\).

The finding that the \( T \) vector \( d' \) 3 minutes after exercise gave better separation of patients from normals than that immediately after exercise or 10 minutes after exercise suggests the possibility that even better separation might be obtained at 2 or 4 minutes after exercise. However, the 3-minute postexercise period was selected prior to the statistical analysis and sampling at 2 and 4 minutes was not done regularly. The other VCG parameters (magnitude and spatial direction of QRS, TI, and G) were examined for diagnostic potential, but these parameters did not afford
the sensitivity and specificity comparable to the T wave vector 3 minutes after exercise. The magnitude of the spatial T vector had diagnostic value when the normal group and the abnormal group were compared in the control period, immediately after exercise, and 10 minutes after exercise. Although there was a group difference with this parameter, the magnitude values of the patients overlapped those of normal individuals to some extent. These parameters will be assessed on a later follow-up evaluation.

Discussion

The classical treatise by Wilson and co-workers13 contains the theoretical basis for mean vector analysis. The fact that area analysis of the ECG is a sensitive method of displaying the small, long-acting potentials which are characteristic of the repolarization process justifies its clinical use although the microvolt-second unit is a hybrid electrical term to the physicist. Other authors16–20 have proposed quantitative and semi-quantitative methods of measuring postexercise ECG changes. Winsor and associates18 have described a linear display of instantaneous cardiac vectors which has been used with exercise stress. Changes in normal individuals were not compared or discussed. Giusti and co-workers10, 29 measured postexercise area change in the conventional ECG by planimetry and plotted spatial mean vectors. Measurements were done during a control period and immediately after maximum exercise. In the normal patients the average vector change was to the right and superiorly; the patients with coronary heart disease had a similar directional change but a more marked response to exercise. The exercise was not standardized and the postexercise changes were not statistically analyzed in either group. Simonson and Keys16 studied vectorcardiographic changes after exercise in a group of healthy, middle-aged business and professional men. Spatial vector magnitude was calculated from the maximum scalar amplitude of complexes from conventional leads and vector direction approximated by using a manual plotting device. The actual area of the scalar complex was not measured. Significant changes in the spatial T direction were noted immediately after exercise. For men of normal weight in this age group, the authors defined the limits of normal postexercise T vector change as +45° and −15° azimuth.

The systems discussed differ significantly in methodology from that described in the present report. In this system the area of the ECG items is measured electronically, a corrected orthogonal lead system is used, three time periods after exercise are examined, and a method of statistically expressing spatial vector change is utilized. The combination of analog and digital computer methods in this study is quite economical as compared to a completely automatic system employing digital equipment. However, the limiting factor in data collection with the present system is the manual measurement of the analog record and placing these data on IBM cards. An automatic analog-to-digital conversion system is planned for the near future.

The need for improvement of the criteria for defining the abnormal exercise electrocardiogram is evident if the diagnostic accuracy of currently accepted clinical methods is critically assessed. Of the exercise stress tests employing the conventional ECG, the Master two-step test21 and the double two-step test are the most favored in this country.3 These tests are easily administered and are safe for coronary disease suspects if reasonable precautions are observed. Regardless of their general acceptance, a high rate of diagnostic error has been found to be associated with these tests if both false-positive and false-negative errors are considered.3, 6, 22 Mattingly and associates4 used the double two-step test in the evaluation of 836 military patients suspected of having coronary disease. Most of these patients had chest pain, and 68% were older than 40 years of age. Seven years later, follow-up information was available on 778 members of the original group. Based on Master's interpretive criteria, a correct diagnosis was made in 564 patients and an incorrect diagnosis in 214 patients. Of the positive tests, 41% were falsely positive, and of the

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negative tests, 21% were missed diagnoses or false-negative errors. An even higher error rate was present in a similar longitudinal study of 600 asymptomatic Royal Air Force volunteers given an exercise test with a greater work load than the double Master test although the test did identify a group with a higher incidence of coronary symptoms. The group at the U. S. Naval Aerospace Medical Institute has found that it is often necessary to exceed the standard double two-step exercise load when evaluating aviators. The necessity for greater exercise stress is assumed to be related to the better muscle tone and the greater lean body mass of this group than is ordinarily found in the coronary disease suspect from the civilian population. When criteria similar to Master’s criteria for an abnormal response have been used, the authors’ clinical impression has been that, as exercise stress is increased, the false-negative error rate decreases, but at the cost of increasing false-positive and equivocal responses.

In this preliminary study, the definition of “normal” and “abnormal” is a clinical one and is subject to physician error. It will be necessary to establish normal standards for the d′ parameter from data obtained with longitudinal study of these subjects and from a consideration of the false-positive and false-negative error rate. A large prospective study is in progress at the U. S. Naval Aerospace Medical Institute in which the mean spatial vector analysis will be assessed critically by actuarial methods.

Summary and Conclusions

This report describes a system of quantitating ECG changes after exercise which utilizes a special purpose analog computer (integrator) and calculation of mean VCG parameters by digital computer. Synchronizing circuitry automatically adjusts the period of integration for changes of heart rate. The vectorcardiographic response to stress of a group of patients with mild symptomatic coronary disease is compared to a normal control group. Highly significant changes in the direction of the T vector appear 3 minutes after exercise and allow separation of normal subjects from patients with coronary disease. The quantitative output of this system is being used in an epidemiological approach to the problem of coronary disease in the aviator.

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Appendix I

Statistical Proof of the Unity Vector Analysis

The average direction from the origin (o) of a group of points in a k-dimensional space may be found by first separating each point (i) into its k-reference location (x1i, x2i, ..., xki). The distance of point i from the origin will equal the square root of the sum of the squares of their reference locations. Thus,

\[ d_{oi} = \sqrt{\sum_{k=1}^{k} x_{ki}^2} \]  

If each reference location of point i is now divided by its doi, new reference locations may be obtained for each point which will be at a distance of 1.00 from the origin. Thus,

\[ x_{1i}' = x_{1i}/d_{oi}, \]  
\[ x_{2i}' = x_{2i}/d_{oi}, \]  
\[ x_{3i}' = x_{3i}/d_{oi}, \ldots \]  
\[ x_{ki}' = x_{ki}/d_{oi}, \]  

and

\[ d_{oi}' = \sqrt{\sum_{k=1}^{k} x_{ki}'^2} = \sqrt{\frac{x_{1i}^2}{d_{oi}^2} + \frac{x_{2i}^2}{d_{oi}^2} + \frac{x_{3i}^2}{d_{oi}^2} + \cdots + \frac{x_{ki}^2}{d_{oi}^2}} \]  

\[ = \sqrt{\frac{\sum_{k=1}^{k} x_{ki}^2}{d_{oi}^2}} = \sqrt{\frac{\sum_{k=1}^{k} x_{ki}^2}{\sum_{i=1}^{N} x_{ki}^2}} = 1.00. \]

If the average direction of N points is desired, one may then average the new reference locations (x')s for each dimension separately; thus,

\[ \bar{x}_1 = \frac{\sum_{i=1}^{N} x_{1i}'}{N}, \]  
\[ \bar{x}_2 = \frac{\sum_{i=1}^{N} x_{2i}'}{N}, \]  
\[ \vdots \]  
\[ \bar{x}_k = \frac{\sum_{i=1}^{N} x_{ki}'}{N}. \]
These average reference points may likewise be "normalized" by dividing each average reference location by the square root of the sum of the squares of the $\bar{x}$s; thus,

$$x'_1 = \frac{x_1}{\sqrt{\sum x_1}}$$

$$x'_2 = \frac{x_2}{\sqrt{\sum x_2}}$$

$$x'_k = \frac{x_k}{\sqrt{\sum x_k}}$$  (4)

The angular deviation ($\alpha_i$) of a given point from the average of all points may be found by the following equation:

$$\alpha_i = \arccos \left[ \frac{2 - \sum (x'_j - x'_i)^2}{2} \right]$$  (5)

$$\approx \arccos \left[ \frac{k}{\sum x'_j x'_i} \right]$$  (6)

**Appendix II**

The general form of the equation used to compute the $t$ scores is

$$t = \frac{\bar{x}_1 - \bar{x}_h}{S_h} \sqrt{\frac{n-1}{n+1}}$$

where $x_1$ is a single case

$\bar{x}_h$ = the mean of a group of $n$ scores

$S_h$ = the biased standard deviation ($S_h = \sqrt{\sum x^2/n}$), and

$n$ = the number of cases $\bar{x}_h$ and $S_h$ are based on

and is directly derived from the usual sample versus sample $t$-test where the variance of the populations from which the two samples are drawn are unknown but assumed equal.

$$t = (\bar{x}_1 - \bar{x}_2) \sqrt{\frac{n_1 + n_2}{n_1 n_2} \left( \frac{n_1}{n_1} + \frac{1}{n_2} \right)}$$

degrees of freedom $= n_1 + n_2 - 2$.

**References**


300 Years Ago
Intravenous Opium and Human Experimentation

...wherein at several times, upon several Doggs, Opium & the Infusion of Crocus Metallorum were injected into that part of the hindlegs of those Animals, whence the larger vessel, though that carry the Blood, are most easy to be taken hold of: whereof the success was, that the Opium being soon circulated into the Brain, did within a short time stupify, though not kill the Dog; but a large Dose of the Crocus Metallorum, made an other Dog vomit up Life and all: All which is more amply and circumstantially delivered by Mr. Boyle in his Excellent Book of the Usefulness of Experimental Philosophy, Part 2. Essay 2. pag. 53. 54. 55. Where 'tis also mention'd, that the fame of this Invention and of the succeeding Tryals being spread, and particularly coming to the knowledge of a foreign Ambassadour, that was Curious, and then resided in London, it was by him tried with some Crocus Metallorum, upon a Malefactor, that was an inferior Servant of his; with this success, that the Fellow, as soon as ever the Injection began to be made, did, either really or craftily, fall into a swoon; whereby, being unwilling to prosecute so hazardous an Experiment, they desisted, without seeing any other effect of it, save that it was told the Ambassadour, that it wrought once downwards with him.—Sir Christopher Wren: In Albert Faulconer, Jr., and Thomas E. Keys: Foundations of Anesthesia, vol. 2. Springfield, Illinois, C. C Thomas, p. 959.
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