Evaluation of R Wave Amplitude Changes versus ST-Segment Depression in Stress Testing

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SUMMARY Exercise ECGs and coronary angiograms were reviewed in 266 patients (81 normals and 185 with significant coronary artery disease). Thirty-three false positive and 96 false negative ST responses to stress testing were purposely chosen to determine if the R wave could reduce the number of false ST responses. R wave amplitude changes were measured in the control and in the immediate postexercise period. An increase or no change in R wave was taken as evidence of an abnormal response, while a decrease in the R wave was a normal response. The sensitivity by ST segment was 48% and the specificity was 59%. These values were low because of the large number of false positive and negative ST responses in the study. It was our purpose to determine if these lowered values could be significantly improved by the R wave. Using R wave criteria, the sensitivity was 63% (P < 0.01) while the specificity was 79% (P < 0.01). The sensitivity and specificity of stress testing can be significantly improved using R wave changes.

EXERCISE STRESS TESTING is undoubtedly one of the most common noninvasive methods for detecting coronary artery disease. However, it is known that stress testing fails to accurately distinguish all cases and because of this some criticism has been directed at the test. Sensitivity and specificity are dependent on the prevalence of disease in most studies. It has been shown that as the specificity increases the sensitivity decreases, the values also being dependent on the degree of ST depression used to denote disease. McConahay, using the double Master's test for ST depression of ≥0.75 mm, reported a sensitivity of 42% and specificity of 91%, but when he used ST ≥1 mm, the sensitivity was 35% and the specificity 100%. Mason et al., using a near-maximal exercise test for ST depression ≥0.75 mm, reported a sensitivity of 84% and a specificity of 83%, and when they used ST depression of ≥1 mm found the sensitivity to be 78% and the specificity 89%.

This study was undertaken to test two new criteria for exercise ECG evaluation.

Materials and Methods

A retrospective study was done reviewing the records of 266 consecutive patients with a treadmill stress test (TST) and a coronary angiogram in a two-year period from 1974 to 1976. Thirty-three false positive and ninety-six false negative ST responses to treadmill stress testing were purposely chosen sequentially from a computer printout of patients in our files who satisfied the restrictions cited.

The 266 patients were analyzed in four groups as follows: normal patients, patients with coronary artery disease (CAD) without previous myocardial infarction, patients with previous transmural diaphragmatic infarction (DMI), and patients with previous transmural anterior infarction (AMI). Criteria for previous infarction were Q waves of 0.04 sec or more in leads III, aVF or in V3-V6.

In the normal group were 51 males whose ages ranged from 25 to 72 (mean 48.6) and 30 females with ages from 31 to 69 (mean 49.2). In the CAD group were 63 males with ages ranging from 37 to 72 (mean 55.8) and 15 females whose ages ranged from 40 to 70 (mean 56.6). The DMI group constituted 53 males with ages from 29 to 66 (mean 51.3), and eight females with ages from 40 to 74 (mean 53.6). The AMI group consisted of 39 males 39 to 74 years of age (mean 53.4) and seven females whose ages ranged from 27 to 64 with a mean of 53.2.

Another group of 53 apparently healthy subjects, 39 males and 14 females, underwent maximal treadmill stress testing for screening evaluation. Their ages ranged from 19 to 38 with a mean of 30. Their history and physical examination revealed no evidence or symptoms of heart disease. These patients were volunteers, with no known risk factors for coronary artery disease, in a Long Beach Heart Association study of risk factors and had not undergone angiography.

Patients with hypertension, cardiomyopathy, conduction defects, valvular diseases or who had been taking digitalis in the last two weeks, or beta-blockers, diuretics or nitrates within 48 hours were excluded.

The interval between the treadmill stress test and coronary angiography ranged from the same day to 4 months with an average of one week.

Treadmill Stress Test

Patients underwent a progressive maximal treadmill stress test (TST) according to the Ellestad protocol, using the maximal predicted heart rate as a target end point. Three leads (CMs, a vertical bipolar lead, and a unipolar V1 lead) were monitored continuously and recorded in the sitting position (control) and in the standing position immediately after exercise. The mean difference between the R-wave sitting and standing was 0.5 mm. The R wave control measurement was taken in the sitting position for comparison with ST changes which we routinely measure sitting for the control value. The CMs lead was used for all measurements. ST depression > 1 mm below the resting level 60 msec from the J point if horizontal or downsloping and > 1.5 mm of depression at 80 msec upsloping, in the immediate postexercise period, was defined as positive (ischemic). R wave amplitude was measured from the isolectric line to the peak of the R wave in mm for an average of 12 consecutive beats. The average value was used in the study so the respiratory variation, if any, was
minimized. An increase in R wave amplitude or no change immediately after exercise was defined as evidence of abnormality, while a decrease in the amplitude was defined as evidence of a normal response. In a previous study, we noted that R wave increase correlated with coronary disease while a decrease correlated with no or minimal disease. As the normal patient exercises, tachycardia and catecholamine release result in a reduced left ventricular volume and by the Brody effect a decrease in R wave, while the patient with coronary disease, as exercise progresses and ischemia develops, increases his left ventricular volume and R wave increases.

An index (ΔRST) was formed from the algebraic summation of the R wave and ST-segment changes. ST depression was taken as a positive value. The R wave was taken as positive if there was an increase and negative if a decrease (fig. 1). An index of 0 or a positive value was taken to represent abnormality, while a negative index was taken as evidence of a normal response.

Treadmill stress tests were evaluated in each group using three criteria: ST depression, change in R wave amplitude, and the index (ΔRST). Specificity and sensitivity for each criterion were determined and compared each with the other criteria. Specificity and sensitivity in each criteria were compared to determine if the index or the R wave changes could significantly reduce the number of false positive and negative responses by ST criteria. The numbers of false positive and negative responses were purposely large numbers and therefore resulted in a low sensitivity and specificity. However, it was our purpose to see if these lowered values could be improved by the R wave or index.

Heart Catheterization

Left and right heart catheterization and coronary angiography were performed using the Sones or Judkins technique. Coronary angiography was performed on 35 mm film with multiple views. Left ventricular angiography was performed in the RAO position. Occlusion of 70% or more of luminal diameter in one or more coronary arteries was defined as significant, while normal coronary angiograms were defined as no occlusion or less than 30% cross sectional narrowing. Patients with obstruction of 31% to 69% were arbitrarily excluded from the study. Coronary arteries were divided into branches according to the reporting system of the American Heart Association. The coronary anatomy was examined by two independent observers without knowledge of the treadmill stress test and any discrepancies were resolved by a third observer.

Results

Angiographically Normal Group

Treadmill Stress Test

The ST segments were normal in 48 (59%) and positive in 33 (41%) of the 81 patients with normal coronary anatomy. The high incidence of false positives was due to patient selection as noted previously. The R wave increased in 14 (17%) by 3.6 mm ± 0.9 SEM. Three (4%) showed no change and 64 (79%) showed a decrease of 3.45 ± 0.25 mm (fig. 2). These differences in the R wave amplitude were significant.
(P < 0.01). The index (ΔRST) was negative in 57 (70%) and in 24 (30%) of the patients was 0 or positive. Thus, of the 81 patients with normal coronary anatomy, 59% had a negative test and 41% were false positives by ST criteria. Evaluation by changes in R wave amplitude revealed 64 (79%) had a true negative test and 17 (21%) had a false positive one. By using ΔRST as a criterion, 57 (70%) had a negative index (true negative test) and 24 (30%) had an index of 0 or a positive value (false positive test) (fig. 3 and 4).

The R wave was more specific than the ST segment (P < 0.01) or index (P < 0.05) in detecting normal subjects. The index, although not significantly different from the ST, still gave better results.

Ventricular Function

Although all patients had normal coronary arteries, it is very interesting that eleven (65%) of the seventeen with increased or no change in R wave amplitude had segmental abnormalities in the left ventriculogram and five of them had significant ST-segment depression.

CAD Group

Treadmill Stress Test

There were 78 patients in this group. Of these, 44 (57%) were true positives by ST criteria and the remaining 34 (43%) were negatives. The R wave increased in 46 (59%) by +2.98 ± 0.41 mm, remained the same in 7 (9%), and decreased in 25 (32%) by −2.83 ± 0.33 mm (fig. 2). All these differences were significant (P < 0.01).

The index was 0 or positive in 59 (76%) patients and negative in 19 (24%). Thus, the sensitivity by ST was 57%, by R 68%, and by ΔRST 76% (fig. 3).

Severity of Disease

Of the 46 patients with an increase in R wave amplitude, 10 (22%) had single vessel disease, 17 (37%) had two vessel disease and 19 (41%) had three vessel disease. Of the 25 patients with a decrease in R wave amplitude, 10 (40%) had single vessel disease, 10 (40%) had two vessel disease and five (20%) had three vessel disease. Out of seven patients with no change in the R wave, five (71%) had two vessel disease, and two (29%) had three vessels with significant cross-sectional narrowing (table 1).

Diaphragmatic Myocardial Infarction Group

Treadmill Stress Test

Of the 61 patients with previous diaphragmatic infarction, 29 (48%) were classified as having a positive exercise ECG and 32 (52%) as having a negative test using ST-segment depression as the criterion. The R wave increased in 32 (53%) patients by +4.58 ± 0.65 mm and decreased in 22
(36%) by $-2.28 \pm 0.31$ mm ($P < 0.01$). In seven patients (11%) the R wave did not change (fig. 2). The index ($\Delta$RST) was 0 or positive in 41 (67%) patients and negative in the remaining 20 (33%) of the 61 patients. Thus, the sensitivity in patients with diaphragmatic infarction was 48% by ST criteria, 64% by R, and 67% by $\Delta$RST. The false negative responders were 52% using the ST, and 36% using the R wave amplitude. The index in this group was again more sensitive with a false negative incidence of 33% (fig. 3).

Severity of Disease

Of the 32 patients with an increase in R wave amplitude, three (9%) had single vessel disease, 13 (40%) had two diseased vessels, and 16 (50%) had three vessel disease. Of the 22 with a decrease in R wave amplitude, seven (32%) had single vessel disease, 10 (45%) had two vessel disease and five (23%) had three diseased vessels. Out of seven with no change in R wave, three (43%) had two and four (57%) had three vessel disease (table 1).

Anterior Myocardial Infarction Group

Treadmill Stress Test

In this group, 46 patients with a previous anterior myocardial infarction were studied. Of these, 16 (35%) were found to have a positive exercise ECG, and 30 (65%) were false negative using ST criteria. The R wave increased in 15 (33%) by $+2.73 \pm 0.49$ mm, showed no change in nine (19%), and decreased by $-2.59 \pm 0.31$ mm in 22 (48%) ($P < 0.01$), (fig. 2). Thus, with R wave changes as the criteria, 24 patients (52%) were found to have a positive exercise ECG and 22 (48%) were false negative. The index was 0 or positive in 27 (59%) and negative in 19 (41%) of the 46 patients (fig. 3).

Severity of Disease

The distribution of the diseased vessels in this group was as follows: Of the 15 with increase in R wave, two (13%) had single vessel disease, six (40%) had two and seven (47%) had three vessels with significant disease. Of the 22 with decrease in R wave, seven (32%) had single vessel disease, seven (32%) had two, and eight (36%) had three vessel disease. Finally, of the nine patients with no changes in the R wave, two (22%) had single, five (56%) had two, and two (22%) had three vessels with significant obstruction (table 1).

All Patients with Coronary Artery Disease

This group included all 185 patients with coronary artery disease with or without a previous infarction. Of these, 89 (48%) had a true positive and 96 (52%) a false negative exercise ECG according to the ST pattern. Using the R wave amplitude changes, 116 (63%) were true positives ($P < 0.01$) and 69 (37%) were false negatives. The sensitivity increased when the index ($\Delta$RST) was used for the interpretation. Thus, 127 (69%) of the 185 patients were classified correctly ($P < 0.01$) and only 58 (31%) patients were found to have a false negative exercise ECG (fig. 4). The index was more sensitive than ST and R ($P < 0.01$).

Severity of Disease

Of the 93 patients with increase in R wave, 15 (16%) had single vessel disease, 32 (34%) had two, and 42 (45%) had three diseased vessels. Of the 69 with a decrease in R wave, 24 (35%) had single vessel disease, 27 (39%) had two, and 18 (26%) had three significantly occluded vessels. Out of 23 with no change in R wave, two (9%) had one, 13 (56%) had two, and eight (35%) had three vessel disease (table 1).

False Positive and False Negative Group

In order to test our data, the 33 false positives and the 96 false negative patients by ST-segment criteria were analyzed separately. All of these patients had been interpreted 100% incorrectly by ST alone. Using the R wave amplitude changes, there were a total of 17 false positive responses. Of the 33 false positive ST responses, 23 (70%) were correctly identified by the R wave. The R wave reduced the 96 false negative ST responses by 47 (51%). The index ($\Delta$RST) was more sensitive but somewhat less specific. There were 24 false positive responses and 58 false negative responses by using the index (fig. 5).

The breakdown in males and females, and the sensitivity

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**Table 1. Correlation Between R Wave Amplitude Changes and Diseased Vessels**

<table>
<thead>
<tr>
<th>R wave changes</th>
<th>Vessels</th>
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</thead>
<tbody>
<tr>
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<tr>
<td></td>
<td>25 (32)</td>
<td>10 (40)</td>
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<tr>
<td></td>
<td>7 (9)</td>
<td>5 (71)</td>
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<tr>
<td>DMI N = 61</td>
<td>32 (53)</td>
<td>3 (9)</td>
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<tr>
<td></td>
<td>22 (36)</td>
<td>7 (32)</td>
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<td>7 (32)</td>
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<tr>
<td></td>
<td>9 (19)</td>
<td>6 (56)</td>
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<td>93 (50)</td>
<td>15 (16)</td>
</tr>
<tr>
<td>Disease</td>
<td>69 (37)</td>
<td>24 (35)</td>
</tr>
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<td>N = 185</td>
<td>23 (13)</td>
<td>2 (8)</td>
</tr>
</tbody>
</table>

Numbers in parentheses represent percentages.
and specificity for all groups and all three criteria, are shown in Table 2.

Statistical Analysis

The three criteria were analyzed in patients with and without coronary artery disease, using the McNemar test. The results are as follows:

Normal patients:
- R versus ST $\chi^2 = 9.4$ ($P < 0.01$)
- R versus RST $\chi^2 = 5.1$ ($P < 0.05$)
- RST versus ST $\chi^2 = 2.1$ N.S.

Overall diseased group:
- R versus ST $\chi^2 = 11.3$ ($P < 0.01$)

Discussion

The most extensively studied parameter of exercise ECG is ST depression, which has been found to be fairly well correlated with the presence of coronary artery disease on angiography as well as with coronary events in a long term follow-up study. McConahay, Mason, Kassebaum, Bailey, and Lewis et al. report sensitivities from 70 to 50% and specificities in the range of 80 to 90%, all higher than in our series. Our reported sensitivity of 48% and specificity of 59% were low because of the large numbers of false positive and negative responses which we purposely included to determine if the R wave changes or index could reduce these false responses by ST criteria and therefore enhance the sensitivity and specificity of the treadmill stress test.

The fact that CMR may explore primarily the anterior wall can be a cause for a false negative exercise ECG in patients with previous anterior infarction and disease in the vessels nourishing the anterior wall only. Had we used ischemic changes in the other leads recorded, we would expect a 5 to 10% increase in sensitivity.

The sensitivity, measured by ST-segment depression and the presence of false negative responders, depends on the severity of the disease so patients with single vessel disease are commonly false negatives. Our data support this

| Table 2. Specificity and Sensitivity in Males and Females by ST, R, and $\Delta$RST |
|---------------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
|                                | Normal (N = 81)   | CAD (N = 78)      | DM1 (N = 61)      | AMI (N = 49)      | Overall disease (N = 185) |
| ST                              | FP  | FN  | TP  | FP  | FN  | TP  | FP  | FN  | TP  | FP  | FN  | TP  |
| (45)                            | (55) | (33) | (67) | (41) | (59) | (47) | (45) | (55) | (88) | (12) | (67) | (33) | (57) | (43) | (50) | (50) | (63) | (37) |
| 23                              | 28  | 10  | 20  | 26  | 37  | 8   | 25  | 28  | 7   | 1   | 26  | 13  | 4   | 3   | 77  | 78  | 19  | 11  |

| R                               | FP  | FN  | TP  | FP  | FN  | TP  | FP  | FN  | TP  | FP  | FN  | TP  |
| 16                              | 35  | 8   | 22  | 15  | 48  | 4   | 11  | 17  | 36  | 3   | 5   | 17  | 22  | 2   | 5   | 49  | 106 | 9   | 21  |

| $\Delta$RST                     | FP  | FN  | TP  | FP  | FN  | TP  | FP  | FN  | TP  | FP  | FN  | TP  |

Numbers in parentheses represent percentages.
Mechanism of R Wave Change

Brody\textsuperscript{14} postulated that the intracavitary blood mass influences the QRS complex. This has been documented by others in experiments with animals, by mathematical calculations, and by experimental models.\textsuperscript{17} It would appear that under the sympathetic drive of exercise both systolic and diastolic volume progressively decrease even though stroke volume is maintained. The failure of the ischemic ventricle to decrease its volume during strenuous exercise\textsuperscript{25, 26} seems to be responsible for the absence of the usual reduction of the R wave amplitude. In a previous study, an increase in R wave correlated with more severe disease and more severe segmental abnormalities in the left ventriculogram.\textsuperscript{7} Consequently, in this study an increase or no change in R wave was taken to indicate coronary disease while a decrease in R wave was taken as a normal response to exercise stress testing. This tends to be supported in our young normal subjects in whom 90% had the expected reduction in the R wave.

Although current evaluation of an exercise ECG is usually primarily based upon the ST-segment changes, other factors can affect the interpretation. These include angina during the test, presence of angina in the history, premature ventricular contractions or other arrhythmias during the test, duration of the test, hypotensive response to exercise, maximal systolic blood pressure, resting ECG, time of onset of the ST depression, heart rate response to exercise,\textsuperscript{26, 31} and others. Ellestad\textsuperscript{4} showed that using multivariate analysis, these findings and symptoms increase the percentage of correct interpretation. The addition of these two new criteria may also be useful in the above method. The ability to identify 79% of those with normal coronary arteries is especially encouraging in view of the large group of false positives included in this patient sample. By using R wave amplitude changes and the index (\Delta RST), the specificity increased by 20% and 11%, respectively. The sensitivity increased in the overall diseased group by 15% and 21%.

The preliminary studies are encouraging, but it remains to be demonstrated how much these criteria will improve the predictive power of the exercise stress test when they are applied to other patient cohorts.

Although statistically significantly better than ST-segment depression alone, the R wave and index criteria still leave a considerable number of false positive and false negative responders.

Acknowledgments

The authors thank Larry J. Leamy, Ph.D. for the statistical analysis, and Mrs. Fritzie Cohn for secretarial assistance.

References

Vectorcardiographic Quantification of Infarct Size in Baboons

SAMUEL A. WICKLINE, AND J. JUDSON McNAMARA, M.D.

SUMMARY A vectorcardiographic method has been developed for determining the absolute size of myocardial infarcts in baboons resulting from coronary artery ligation. Spatial area (mvolt · msec) and voltage (mvolt) difference-vectors were obtained for 8 animals by measuring the voltage loss and temporal deviation from pre-postligation McFee scalar leads. The difference vectors were then correlated with the absolute infarct volumes, which were derived by histological assessment 10 days after ligation. Absolute lesion sizes ranged from approximately 2 cc to 14 cc, involving 10–30% of ventricular muscle mass. The correlation coefficient, r, for the area deviation index was 0.98 (SEE = ± 0.24 cc); and for the voltage deviation index, r was 0.92 (SEE = ± 0.51 cc). These results demonstrate that the severity of infarction can be accurately determined if prepathological vectorcardiograms are available.

NONINVASIVE QUANTIFICATION of absolute infarct size using electrophysiological data would be of considerable benefit in the management of patients with acute infarctions and in the assessment of experimental therapeutic interventions. Although epicardial QRS and ST-complex changes during infarction have been correlated with subjacent myocardial necrosis,1–3 the invasiveness of the recording technique precludes its eventual clinical implementation. Recent investigations of infarcts using extensive body surface maps indicate that surface potential recordings also contain a substantial amount of potentially quantifiable information.4–7 These studies suggest that necrosis in specific ventricular wall segments will produce characteristic alterations in maps of body surface potential. By subtracting postinfarction and control thoracic potentials point-for-point, a voltage difference map that represents the original electrical contribution of the necrotic segment to the control map can be derived.8 This method of “difference mapping” appears promising, but body surface recording in general is too cumbersome and extenuating to be clinically practicable at present.

The simple vectorcardiogram offers an alternative source of noninvasive electrical data for examining acute and chronic infarctions. The vectorcardiographic representation of myocardial electrical activity as an equivalent dipole has proven its utility in diagnosis8–12 and theoretical...
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