Spatial R Wave Amplitude Changes During Exercise: Relation With Left Ventricular Ischemia and Function

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Thirty patients who exhibited increased and 65 patients decreased spatial R wave amplitude during exercise testing were compared for left ventricular function and ischemic variables. Spatial R wave amplitude was derived from the three-dimensional Frank X,Y,Z leads using computerized methods. All patients had stable coronary artery disease and they were classified into two groups: one that attained a higher (n = 48) and one a lower (n = 47) median value of maximal heart rate during exercise (161 beats/min). Within these two groups, patients with increasing or decreasing spatial R wave amplitude during exercise were analyzed for differences in oxygen consumption, exercise-induced changes in spatial R wave amplitude, ST segment depression laterally (ST60, lead X), ST displacement spatially, left ventricular ejection

Increases in the R wave amplitude of the electrocardiogram during exercise have been reported to indicate left ventricular dysfunction or coronary artery obstruction, or both (1-3), while decreases have been found consistent with normal left ventricular function (4,5). The physiologic mechanism for these changes, once thought to be related to changes in heart volume and the Brody effect (6), has more recently been suggested to be increased intramyocardial conduction secondary to ischemia (7,8), change in contractility (3) or simply changes in heart rate and axis (9). In some cases, R wave responses to exercise have yielded diagnostic results comparable with those of ST segment changes (2) and, in combination with ST segment changes, have yielded higher sensitivity than ST segment changes alone (10). Directional variability in the R wave amplitude induced by exercise has been significantly correlated with the ability to increase physical working capacity among patients with coronary artery disease (11). Some studies (12,13) demonstrated left ventricular function to be related to R wave amplitude at rest and to its change during exercise. Others (14,15) did not find R wave changes during exercise to have a definite physiologic explanation or clinical value.

The purpose of this investigation was to evaluate the relation between spatial R wave amplitude response to exercise and left ventricular function, using left ventricular ejection fraction at rest, change in left ventricular ejection fraction with exercise and thallium-201 ischemia during exercise. Significant differences were demonstrated only in exercise-induced spatial R wave amplitude changes (p < 0.0001). There was no significant correlation between exercise-induced change in heart rate and change in spatial R wave amplitude in either the group with increasing or the group with decreasing spatial R wave amplitude.

It is concluded that changes in spatial R wave amplitude during exercise are not related to ischemic electrocardiographic or thallium-201 imaging changes or to left ventricular ejection fraction determined at rest or during exercise.

(J Am Coll Cardiol 1985;6:603-8)

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Methods

Study patients. Ninety-five men with stable coronary artery disease were studied. Coronary artery disease was documented by one or more of the following: 1) history of myocardial infarction from chart review; 2) stable exertional angina pectoris confirmed by angiography or an abnormal exercise test, or both; or 3) coronary artery bypass surgery. Patients were excluded if they had congestive heart failure,
unstable arrhythmias, diabetes mellitus, significant symptomatic pulmonary disease, systemic hypertension (>150 mm Hg systolic or >100 mm H g diastolic, or both), severe claudication, orthopedic problems or left bundle branch block on the electrocardiogram at rest. Disease stability was assured by history and by not allowing any patients to participate within 4 months after a cardiac event, a change in symptoms or cardiac surgery.

On entry into the study, patients were scheduled for three exercise tests performed on separate days, usually within a 2 week period. Included were a thallium-201 treadmill test, separate treadmill tests for electrocardiography and maximal oxygen uptake and a supine bicycle radionuclide study. Cardiac medications were stopped before testing began (digoxin 2 weeks before and beta-receptor blockers 3 days before).

Exercise testing. For the acquisition of maximal oxygen uptake, and electrocardiographic and thallium-201 scintigraphy data, subjects underwent maximal exercise tests on a motor-driven treadmill using the USAFSAM protocol (16). The test consisted of 2 minute exercise stages that progressed by increasing the grade (5%) with each stage. Treadmill speed began at 2 mph and increased to 3.3 mph after the first stage. For radionuclide angiographic data, a supine bicycle test was utilized.

All tests were performed to symptom- or sign-limited maximal effort. Cessation of the test was determined by any of the following: angina pectoris of moderate severity, serious arrhythmia, systolic blood pressure decrease of 20 mm Hg or more after the initial stages, 0.30 mV or more of horizontal or downsloping ST segment depression or exertional fatigue.

Blood pressure was measured at the end of each stage of exercise by the arm cuff auscultation method with a clinical sphygmomanometer using the first and fourth sounds of Korotkov. Heart rate was recorded at the end of each minute. Maximal oxygen consumption (VO₂ max) was determined by collecting expired gases through a Koegel low-resistance breathing valve, leading into a series of evacuated weather balloons. Expired concentrations of oxygen and carbon dioxide were determined using an Applied Electronics); signals were digitized at 250 samples/s and stored on 8 inch floppy disks. A Digital Equipment Corporation PDP 11/34 computer was used to process the digital electrocardiographic/vectorcardiographic data for waveform analysis and R wave vector computation off-line. This technique has been described in detail previously (17).

Thallium-201 scintigraphy. Thallium-201, 2 mCi, was introduced into an antecubital vein 1 minute before the maximal exercise end point. Images were performed immediately and 4 hours after exercise in three views: anterior, 45° and 70° left anterior oblique. All images were obtained for a preset information density (2,000 counts/cm²) in the area of highest activity within the myocardium and recorded unprocessed on transparent X-ray film. The same intensity density area was used for the immediate and 4 hour delay images. A general purpose, parallel-hole collimator was used with a gamma camera (Picker-Dynamo with a micro Z processor). The blinded grading and interpretation of the ischemia score have been validated in our laboratory and are described in detail elsewhere (22).

Radionuclide angiography. The gated equilibrium technique was utilized for radionuclide imaging with the subject in the supine position with the legs horizontal. A 15 mCi dose of technetium was labeled to red blood cells and administered intravenously. After equilibration, the activity within the blood pool was recorded in a modified anterior oblique projection (angled between 30 and 45°) with a caudal tilt of 10 to 20° that permitted optimal chamber separation. With the axis of the pedals at the same level as the body, the patient performed three stages of supine bicycle exercise, each 3 minutes in duration. The work loads were set to approximate 40, 80 and 100% of the patient’s maximal aerobic capacity as estimated by both a supine bicycle trial and the previously described treadmill test. The test end points were as described for the treadmill test.

Scintigraphic data were recorded using a single-crystal camera with a general purpose parallel-hole collimator (25% window) and recorded simultaneously on video tape and on-line to the MDS A² system. All acquisitions were 1.5 minutes in duration with a spatial resolution of 64 × 64 bytes. Left ventricular ejection fraction was derived from a computer-generated, background-corrected time-activity curve using a variable region of interest. Inter- and intraobserver variability using this program is very low and the correlations for three observers ranged from 0.95 to 0.98. These
techniques have been validated and described in detail previously (23,24).

**Statistics.** Unpaired *t* tests were utilized to assess the differences in oxygen consumption, ST segment changes and left ventricular ejection fraction between patients whose R wave amplitude increased or decreased from standing rest to maximal exercise. The analysis was performed within the two groups of patients who attained a heart rate greater than and less than the median maximal heart rate of 161 beats/min. Correlation coefficients were calculated to evaluate the relation between change in spatial R wave amplitude and change in heart rate during exercise.

**Results**

The median maximal heart rate attained during exercise testing was 161 beats/min. Of the 48 patients attaining a maximal heart rate above this value, 16 (33%) demonstrated an increase in spatial R wave amplitude from rest to maximal exercise and 32 (67%) a decrease. Of the 47 patients with a maximal heart rate below 161 beats/min, 14 (30%) demonstrated an increase and 33 (70%) a decrease in spatial R wave amplitude from rest to maximal exercise (Table I).

Within the groups with a heart rate above or below the median rate of 161 beats/min, patients with increased and decreased spatial R wave amplitude during exercise manifested a significant difference in spatial R wave amplitude from rest to maximal exercise (*p* < 0.001), but no differences in maximal oxygen consumption, ST segment depression in lead X, ST displacement spatially, left ventricular ejection fraction at rest or change in left ventricular ejection fraction with exercise or thallium-201 ischemia scores were obtained.

When the analysis was repeated after excluding patients with anterior Q waves on the rest electrocardiogram (*n* = 20), there were no additional significant differences obtained in these variables.

Figure 1 presents the relation between percent change in heart rate and percent change in spatial R wave amplitude among patients with decreased (*n* = 65) and with increased (*n* = 30) spatial R wave amplitude during exercise testing. The correlation coefficients between these two variables were *r* = −0.01 and *r* = 0.01, respectively (NS).

**Discussion**

ST segment displacement is the most recognized manifestation of myocardial ischemia during exercise (25), and

### Table 1. Differences in Ischemic and Functional Variables Between Patients With Increasing and Decreasing Spatial R Wave Amplitude From Rest to Maximal Exercise

<table>
<thead>
<tr>
<th>Maximal Heart Rate</th>
<th>Spatial R Wave Amplitude</th>
<th>Maximal Heart Rate</th>
<th>Spatial R Wave Amplitude</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Increase (n = 16)</td>
<td>Decrease (n = 32)</td>
<td>Increase (n = 14)</td>
</tr>
<tr>
<td>R wave amplitude</td>
<td>4.72 ± 6</td>
<td>* −16.0 ± 9</td>
<td>9.43 ± 10</td>
</tr>
<tr>
<td>Functional capacity</td>
<td>2.48 ± 6</td>
<td>2.47 ± 5</td>
<td>1.72 ± 13</td>
</tr>
<tr>
<td>ST segment</td>
<td>−0.09 ± 0.09</td>
<td>−0.05 ± 0.15</td>
<td>−0.07 ± 0.13</td>
</tr>
<tr>
<td>displacement, lead X (mV)</td>
<td>0.19 ± 0.08</td>
<td>0.24 ± 0.14</td>
<td>0.19 ± 0.10</td>
</tr>
<tr>
<td>Angina during the test (%)</td>
<td>18.7</td>
<td>15.6</td>
<td>42.8</td>
</tr>
<tr>
<td>Thallium-201 ischemia score</td>
<td>2.3 ± 4.4</td>
<td>4.5 ± 3.7</td>
<td>3.9 ± 5.4</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>3.5 ± 17</td>
<td>2.7 ± 19</td>
<td>3.2 ± 18</td>
</tr>
<tr>
<td>Resting Ejection fraction</td>
<td>52 ± 13</td>
<td>54 ± 14</td>
<td>55 ± 14</td>
</tr>
</tbody>
</table>

*p* < 0.001. Values are mean ± SD.
thus is considered the most reliable and useful electrocardiographic index for the diagnosis of coronary artery disease. However, because of the sensitivity and specificity limitations of exercise-induced ST segment depression, there has been a recent interest in the diagnostic value of the R wave response to exercise. The reports by Bonoris and co-workers (1,5), suggesting that R wave changes during exercise are related to ventricular function and ischemia, initiated a considerable amount of interest in this phenomenon.

It has been suggested that the "diagnostic" increase in R wave amplitude with exercise in some patients with heart disease occurs because such patients actually perform submaximal tests and are subject to the normal variability in the R wave response (4,9); therefore, our patients were classified into groups whose heart rate was above and below the median rate of 161 beats/min attained during maximal exercise. Additionally, we used a spatial measurement of R wave amplitude in our study. The R wave amplitude measured spatially has the advantage of better representing global myocardial electrical forces, and is similar to the sum of the orthogonal lead R wave amplitude used by some investigators (26,27).

Because our recent data correlating ST segment changes and ischemia demonstrated by thallium-201 imaging showed that the standard ST segment criteria may not correlate as well with ischemia as previously thought in patients with anterior myocardial infarction (28), the analysis was repeated after patients with anterior myocardial infarction were excluded. This procedure did not change the results significantly.

Previous investigations. Earlier studies demonstrated R wave changes to be helpful in diagnosing coronary artery disease with exercise testing. R wave changes were shown to be sensitive independently (2) and, in combination with ST segment changes, to be superior to ST segment changes alone (9). The R wave was recognized as particularly useful in a group of patients whose ST segment changes specifically lacked in sensitivity and specificity (29), and in patients with left bundle branch block (30), among whom ST segment changes are of limited diagnostic value.

However, several studies failed to confirm the value of R wave amplitude changes in the assessment of left ventricular function or electrocardiographic ischemia during exercise. Wagner et al. (14) compared R wave indexes of amplitude and ST segment criteria with angiographically determined coronary artery disease. Using R wave criteria, the sensitivity of exercise testing was 52% and specificity 63%, compared with 88 and 72%, respectively, using ST segment criteria. No significant correlation was found between the extent of angiographically determined coronary artery disease and R wave changes. Van Eenige et al. (15) similarly compared the diagnostic value of R wave amplitude changes with ST segment changes using angiography as the standard. Despite the use of different criteria for positivity, the use of different lead systems and the use of clinical subsets, no useful correlation could be established between R wave amplitude changes and the presence of coronary artery disease or left ventricular dysfunction. Deanfield et al. (31) demonstrated ST segment depression to be associated with both a decrease and an increase in R wave amplitude during exercise. Additionally, R wave amplitude was generally unaltered by changes in ventricular volume.

The relation between R wave amplitude changes during exercise and left ventricular ejection fraction was studied previously. The orthogonal Frank system was used to study this relation at rest (12,13). Using the sum of RX + RY + QZ, significant correlations with left ventricular ejection fraction at rest and R wave amplitude were demonstrated. Battler et al. (26), using a similar sum of the orthogonal R waves from 60 patients, found poor but significant correlations between left ventricular ejection fraction at rest and R wave amplitude at rest and during exercise (r = 0.50 and 0.51, respectively). In addition, they found no significant relation between changes in R wave amplitude and changes in left ventricular ejection fraction during exercise in these patients or in a group of 18 normal subjects. Luwaert et al. (27) demonstrated a significant although low correlation.
between the sum of orthogonal R waves and left ventricular ejection fraction at rest in 252 patients (r = 0.22).

Present findings. The purpose of the present study was to determine whether differences exist between patients who have increased and decreased spatial R wave amplitude during exercise, rather than to evaluate how the R wave amplitude, ST segment changes and left ventricular function relate to one another. The results of some previous investigations (24,29-31) are in general agreement with our study, in that no differences were demonstrated between patients with increased or decreased amplitude of the spatial R wave with exercise, using ischemia evidenced by spatial or lateral ST segment changes or thallium-201 scintigraphy, by left ventricular ejection fraction at rest and during exercise or by oxygen consumption. Eliminating patients with anterior infarction did not alter these findings. Although R wave changes were not associated with abnormal ST segment depression, 75% of our patients had significant (>1.0 mm) ST segment depression.

Because many normal subjects and patients with coronary artery disease normally manifest an increased R wave amplitude from rest to a submaximal work load it is not necessary to conduct similar studies using only patients achieving maximal or near maximal heart rates. The inclusion of patients limited by angina or other symptoms may have distorted the results of previous studies.

A definitive explanation for the mechanism causing R wave changes during exercise has yet to be described. It is often suggested that changes in intracardiac blood volume, the “Brody” effect, are a reflection of the electrical forces of the QRS amplitude (6,32). However, if these changes are due to changes in volume, one would expect R wave amplitude to increase when a patient changes from the standing to the supine position, because diastolic volume would increase. However, this change in R wave amplitude does not occur (4,33). The volume-R wave amplitude relation has been refuted by others (26,27). That cardiac enlargement secondary to congestive heart failure may cause a decrease in R wave amplitude also contradicts the Brody hypothesis (8). Correlations of the R wave to systolic volume and left ventricular ejection fraction suggest an association with contractility (2,3). Changes in axis shifts have also been shown to alter R wave amplitude; this shift of the QRS axis as well as that of the ST segment vector toward the right and posteriorly occurs normally during exercise (9,34-36). It is evident that this remains a fertile area for investigation.

Conclusions. This study indicates that changes in spatial R wave amplitude during exercise are not related to ST segment changes or thallium-201 ischemic changes induced by exercise, or to left ventricular ejection fraction measured at rest or during exercise. Our results generally refute the importance of changes in the R wave amplitude during exercise as a diagnostic index for coronary artery disease or ventricular function.

References


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