R wave amplitude during exercise

Relation to left ventricular function and coronary artery disease

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SUMMARY Change in R wave amplitude (mean ΔR) was measured sequentially during and after 12 lead maximal treadmill exercise tests in 14 subjects with normal coronary arteries and 62 patients with coronary artery disease. In normal subjects mean ΔR decreased maximally one minute after exercise and returned to control levels within three minutes. In contrast, mean ΔR increased in patients with coronary artery disease, the greatest change occurring in patients with either triple vessel or left main disease or those with an akinetic region on the left ventriculogram. R wave amplitude returned to resting levels in five minutes. Increase in R wave amplitude was not directly related to changes in the ST segment.

Changes in R wave amplitude during maximal treadmill exercise may improve the discrimination between patients with and without coronary artery disease and may help to identify those patients with abnormal left ventricular function.

Mathematical models of electrical activity of the heart predict that changes in intraventricular volume will be associated with changes in R wave amplitude measured by the surface electrocardiogram, an increase or a decrease of volume giving rise to a corresponding change of R wave amplitude.¹⁻³ Animal experiments when intraventricular volume was manipulated by acute haemorrhage and overtransfusion have confirmed this prediction.⁴ In man similar observations have been reported after acute surgical blood loss.⁵

More recently, changes in R wave amplitude have been studied during exercise.⁶⁻⁸ Measured in a single electrocardiographic lead, R wave amplitude decreased in normal subjects while an increase or no change was seen in patients with coronary artery disease. These investigators concluded that R wave amplitude criteria, in conjunction with ST segment depression, improved both the sensitivity and specificity of exercise testing.

The purpose of this study was to measure R wave

amplitude during and after maximal 12 lead treadmill exercise and to evaluate the relation of changes to the severity of coronary artery disease and to abnormalities of left ventricular contraction.

Patients and methods

Seventy-six patients, referred to the National Heart Hospital for chest pain, underwent both maximal treadmill exercise testing and coronary angiography. The following patients were excluded: those with valvular heart disease, primary myocardial disease, conduction defects, or those on digitalis; those with technically inadequate stress tests and those who failed to complete the exercise test.^{9 10}

Fourteen patients (nine men, five women, mean age 38 years) had normal coronary angiograms and normal resting electrocardiograms; 62 patients (50 men, 12 women, mean age 48 years) had coronary artery disease proven at angiography. Twenty-eight of these (45%) had a history of myocardial infarction and pathological Q waves in the resting electrocardiogram.

EXERCISE TEST

All patients underwent 12 lead maximal treadmill exercise testing¹¹ within one month of coronary

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angiography. The 12 leads recorded were the same as a standard 12 lead resting electrocardiogram except that the limb leads were sited on the trunk close to the limb in question. Recordings were made in the erect position, before, and at the end of each three minute stage of exercise, and at one minute intervals after exercise in the sitting position until the electrocardiogram returned to its resting state. The test was terminated when predicted maximum heart rate for age, sex, and weight (women) or height (men) had been achieved, or with the onset of chest pain associated with electrocardiographic changes. Patients who failed to reach either of these end points were excluded. The Bruce protocol was used with the addition of a warm-up stage at 1.0 mph and 5 per cent gradient to avoid the sudden increase in oxygen consumption during stage 1 of the unmodified Bruce protocol.¹² Horizontal or downsloping ST segment depression of 1 mm or more persisting for 80 ms beyond the J point in at least one lead was regarded as a positive test for ischaemia (calibration 10 mm=1 mV). Electrocardiographic recordings were made with a fully automated three channel Cambridge 3038 portable electrocardiographic recorder.* The frequency response was 0.05 to 100 Hz (-3dB), with the time constant (67% loss of amplitude) greater than 3.2 s. Recording equipment and procedures complied with American Heart Association standards.^{13 14} Blood pressure measurements were taken before each electrocardiographic recording before, during, and after exercise.

R wave amplitude was measured by two observers without prior knowledge of or reference to the results of angiography. The amplitude was measured in mm (10 mm=1 mV) from the PQ segment to the top of the R wave and averaged in each individual lead over four to 10 beats, depending on heart rate, to minimise the effect of respiration. Leads II, III, aVF, V4-6 were chosen for detailed analysis as they usually had dominant R waves. Results are expressed as the mean change in R wave amplitude (mean ΔR) which is calculated by subtracting the sum of R waves in the six leads from the pre-exercise value and then dividing by six. A mean ΔR of -2 mm would therefore reflect a total 1.2 mV decrease in the six leads. In a separate group of eight normal volunteers who underwent two exercise tests changes in mean ΔR were reproducible.

CORONARY ANGIOGRAPHY

Left ventriculography was performed in the 30° right anterior oblique projection. Left ventricular wall motion was assessed subjectively by two

* Cambridge Instrument Company.

independent observers and reported as normal, hypokinetic (defined as reduced inward systolic movement), or akinetic (defined as absent inward systolic movement). Coronary angiography was performed in the posteroanterior and oblique projections using the Sones technique. Seventy per cent reduction in the diameter of a major coronary artery was considered significant.

Results are expressed as mean $\pm$ the standard error of the mean. Statistical tests were performed using Student's t test for paired and non-paired samples and by linear regression.

Results

A typical example of a standard 12 lead electrocardiographic response to maximal treadmill exercise in a normal subject is shown in Fig. 1. The absence of pathological ST change and decrease in R wave voltage (most obvious in the inferolateral leads) may be seen.

For comparison, a positive test, from a patient with triple vessel disease, is shown in Fig. 2. ST depression occurred in most leads and R wave amplitude increased. However, ST depression in leads I, aVL, and V2-3 was not accompanied by R wave change, indicating that this can be independent of ST segment change in an individual lead.

Fig. 1 Paired 12 lead resting (left) and maximal exercise (right) electrocardiographic complexes from a normal subject. Decrease in R wave amplitude is most pronounced in leads II, III, aVF, and V4-6.

Of the 76 patients, 59 had positive and 17 negative exercise tests as judged by ST segment analysis. There were two false positives and five false negatives, giving a sensitivity of 92 per cent and specificity of 86 per cent (Table). All 14 patients with normal coronary arteries had normal left ventriculography, and R wave amplitude decreased during exercise (Fig. 3). The maximum fall of mean ΔR occurred one minute after exercise and returned to the pre-exercise value within three minutes. Maximum change in heart rate preceded maximum change in mean ΔR and recovered more slowly than R wave amplitude.

The 62 patients with coronary artery disease comprised 22 with single vessel, 12 with double vessel, and 28 with triple vessel or left main disease.

Fig. 2 Paired 12 lead resting (left) and maximal exercise (right) electrocardiographic complexes from a patient with severe triple vessel coronary artery disease and inferior wall hypokinesia. R wave voltage increase is most distinct in leads II, III, aVF, and V4-6, and occurs in the presence of both ST depression (V2-5) and elevation (II, III, aVF).

Table Sensitivity (true positive tests/no. of patients with coronary artery disease) and specificity (true negative/no. of patients with normal coronary angiography) of treadmill exercise testing

	ST analysis	R wave amplitude
Sensitivity	92% (57/62)	98% (61/62)
Specificity	86% (12/14)	100% (14/14)

In column 1 a positive test is defined as flat or downsloping ST depression of 1 mm or more 80 ms after the J point; in column 2 a positive test is defined by no change or an increase in R wave amplitude at maximal exercise compared with the resting value.

Left ventriculography was normal in 28. Eighteen patients had a region of hypokinesia and 16 akinesia. Sixty-one patients (98%) had an increase in mean ΔR . The one patient showing a decrease in mean ΔR had single vessel disease, a negative exercise test, and normal left ventriculography. The four other patients with false negative exercise tests also had single vessel disease. Fig. 4 shows the change in mean ΔR related to the severity of coronary artery disease. In contrast to normal

Fig. 3 Heart rate and mean change in R wave amplitude (ΔR) in 14 normal subjects during treadmill exercise. ΔR decreases most at one minute after exercise and returns to resting level three minutes after exercise.

Fig. 4 Exercise-induced change of R wave amplitude in patients with coronary artery disease. ΔR does not distinguish the number of vessels involved except between triple vessel disease (3) and double (2) or single (1) vessel disease at peak exercise ($p < 0.01$).

patients (Fig. 3) mean ΔR increased. The maximum increase occurred at peak exercise and mean ΔR returned to resting values five minutes after exercise. The change in mean ΔR was not influenced by the number of diseased coronary arteries except at peak exercise when mean ΔR was greater in patients with triple vessel or left main disease than with single vessel disease ($p < 0.01$).

Fig. 5 shows the change in mean ΔR related to abnormality of left ventricular contraction. The largest increase in mean ΔR occurred in those patients with akinetic regions of the left ventricle and remained statistically significant up to 5 minutes ($p < 0.001$).

There was no significant correlation between the mean ΔR and both the number of leads showing ST depression and the sum of ST depression seen in all 12 leads (Fig. 6). Patients with multiple vessel disease, however, had higher values of both mean ΔR and ΣST (Fig. 7).

Discussion

The precise mechanism for the change in R wave amplitude on the surface electrocardiogram during exercise is unclear. R wave amplitude changes under a variety of conditions and is influenced by many factors such as blood conductivity, blood potassium, electrical axis, and movement of the chest wall and diaphragm. Several experimental

and theoretical studies^{1-5 15-19} indicate that a major determinant of R wave amplitude is the intraventricular volume. The end-diastolic volume of the left ventricle decreases during exercise in normal subjects²⁰⁻²⁵ while at the same time R wave amplitude decreases.^{7 26-32} These two phenomena may therefore be directly related.

Many studies using different techniques have shown that during acute ischaemia the end-diastolic left ventricular volume does not decrease but increases.^{23 24 33-37} Our results show that R wave

Fig. 5 Exercise-induced change in R wave amplitude in the 62 patients with coronary artery disease, subdivided according to the result of left ventriculography. Patients with akinesis demonstrated significantly greater increase which took longer to return to resting values than the others.

Fig. 6 Plot of the sum of ST segment depression on the 12 lead electrocardiogram (ΣST) and change in mean R wave amplitude (ΔR) at peak exercise in 62 patients with coronary artery disease. There is no significant correlation.

Fig. 7 Sum of ST segment depression on the 12 lead electrocardiogram (ΣST) at peak exercise and mean increase in R wave amplitude (ΔR) in 62 patients with coronary artery disease (CAD). ΣST shows better distinction between the groups than ΔR .

amplitude is also increased in those patients with coronary artery disease in contrast to normal subjects (Fig. 3 and 4). If R wave changes are attributable to volume change, a correlation between R wave amplitude and left ventricular contraction abnormalities should exist. Our results confirm this prediction and show that within the group of patients with coronary artery disease the size of the change in R wave amplitude relates to the findings of ventriculography (Fig. 5) rather than to the number of diseased vessels (Fig. 4). Yet even in the subgroup of patients with coronary artery disease and normal left ventriculography R wave amplitude increased; this is presumably because abnormalities of ventricular contraction, though not apparent at rest, occur on exercise with the onset of ischaemia. No distinct correlation was found between changes in R wave amplitude and ST segment depression (Fig. 6), though patients with three vessel disease or disease of the left main coronary artery had larger increases of R wave amplitude and greater ST depression than the others (Fig. 7). Thus ST segment changes may reflect the electrophysiological consequence of ischaemia while R wave amplitude is primarily affected by left ventricular volume.

Our results with regard to R wave amplitude during exercise are in accord with the findings of others.^{7 8 28 29} There are, however, three recent reports in which R wave amplitude did not distinguish between patients with and without coronary artery disease. Battler *et al.*³⁰ using a different lead system, supine bicycle exercise, and radionuclide angiography found QRS amplitude to be of no value in separating a normal from an abnormal exercise response.

Wagner *et al.*³² though showing a decreased R wave amplitude in their normal subjects concluded that it was unreliable in distinguishing the presence, absence, or severity of coronary artery disease. In contrast to our study, however, they used only two leads (II and V5) for analysis, employed sub-maximal exercise, and studied a group of patients having a preponderance of single vessel disease. In a group of patients with significant but unspecified coronary artery disease, Fox *et al.*³⁸ using erect bicycle exercise and precordial surface mapping found a consistent decrease in R wave amplitude in patients with or without electrocardiographic evidence of ischaemia. The reasons for these opposite or less clear-cut findings may be related to differences in the patients under study, the type of exercise, posture during exercise, and the recording leads selected.

In an attempt to improve the sensitivity and specificity of exercise testing we redefined all tests as positive or negative according to the results of

R wave analysis (Table). Thus, a positive (abnormal) test would be one in which R wave amplitude shows either no change or an increase at maximal exercise, and a negative (normal) response would be a demonstrable decrease in R wave amplitude. Four of the five false negatives and both false positives (by ST analysis) are correctly classified as abnormal and normal, respectively, in this way. Though our series is relatively small we agree with the conclusions of Bonoris *et al.*⁶ that, while in no way superseding the value of ST segment analysis, evaluation of R wave amplitude should not be ignored and may help separate patients with coronary artery disease from those without such disease. We are currently using both ST segment and R wave amplitude criteria prospectively to confirm these results.

Our results are impressively accurate but probably no more or less than expected for a selected group of patients referred with chest pain to a specialist hospital.³⁹ A larger group of patients needs to be studied before any definite claim can be made with regard to the clinical value of this observation or the possible advantages in studying a population with a low prevalence of coronary artery disease. In such a population the requirement that a normal exercise test be accompanied by a fall in R wave amplitude should improve the specificity of exercise testing.

Lastly, since R wave amplitude change with exercise appears to be related to an abnormality of left ventricular contraction, analysis of R wave change may provide a non-invasive indicator of left ventricular function, helping to identify those patients in whom it is more likely to be impaired.

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