Factors influencing R wave amplitude in patients with ischaemic heart disease

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SUMMARY R wave amplitude changes during exercise have been ascribed to alteration in left ventricular volume and their measurement advocated for the improved diagnosis of coronary disease. The reproducibility of exercise QRS changes and their relation to ST segment depression, respiratory pattern, and left ventricular volume during ischaemia were studied in 10 patients with angina and coronary disease. QRS amplitude was measured in a 16 lead precordial map during three identical exercise tests in each patient and left ventricular volume assessed continuously using gated blood pool imaging with a single scintillation probe during manoeuvres to provoke ischaemia. During exercise, QRS amplitude increased or remained unchanged in four patients and fell in six patients in a consistent manner for each patient. R wave amplitude was not affected by changes in respiratory pattern. R wave amplitude did not alter in 33 of 39 episodes of left ventricular volume increase (mean 32%) or decrease (mean 36%) in end-diastolic counts. These findings suggest that precordial R wave changes during ischaemia are not determined primarily by alteration in left ventricular volume or the respiratory pattern. Though reproducible in each patient and following a definite relation to ST segment depression, the variable directional response during exercise suggests that R wave amplitude changes have little diagnostic value.

Analysis of R wave amplitude changes that occur after exercise has been proposed for the improved diagnosis of coronary disease and has been the subject of much interest in recent years.^{1,2} In spite of conflicting clinical studies reporting the value of exercise induced R wave amplitude changes in the diagnosis of ischaemic heart disease,^{3,4} there have been no detailed studies in man investigating the factors that influence the QRS changes both during and after exercise. This study was designed to determine the reproducibility of R wave changes that occur with exercise, the temporal relation between R wave and ST segment alterations, and, finally, the factors that may influence R wave amplitude in patients with ischaemic heart disease.

Patients and methods

Ten male patients (aged 41 to 69 years, mean 53) with proven three vessel coronary artery disease and normal left ventricular function at rest were studied. Patients were selected because they had a normal resting electrocardiogram, were known to have a positive exercise test in terms of ST segment response, and had a history of

stable angina pectoris for at least three months. None had had a previous myocardial infarction nor were any taking cardiac drugs apart from sublingual glyceryl trinitrate at the time of the study. Informed consent was obtained from each patient.

All patients underwent both exercise testing and gated blood pool studies using technetium-99m.

TECHNIQUES

Exercise testing

Exercise tests were performed using precordial electrocardiographic mapping before, during, and for 10 minutes after exercise.⁵ The 16 point precordial electrocardiogram was recorded using a direct writing ink-jet minograf (Elema-Schonander) recording on four channels simultaneously. The 16 points were distributed evenly over the left hemithorax and the boundaries were the angle of Louis, the right sternoclavicular joint, the posterior axillary line, and 6 cm below the xiphisternum. Disposable press stud electrodes were used and were secured using adhesive tape so as to keep the electrodes stable without interfering with respiration. Screened electrode cable was used

and the 16 electrodes were connected to the electrocardiograph using a four-way switching system.

Graded maximal exercise tests were performed on a bicycle ergometer. Patients cycled at a constant speed (50 revolutions per minute) and the work load was increased by 25 watts each minute. All 10 patients developed chest pain during the exercise tests. The work load procedure and conditions of subsequent exercise tests in the study were identical to those of the first test.

Sixteen lead electrocardiographic recordings were made before exercise, each minute during exercise, and after 10 minutes of recovery. During exercise, four leads were monitored continuously.

Interpretation of records

At each of the 16 positions ST segment depression was measured in three complexes and an average taken. The TP segment was used as the isoelectric line. ST segment depression was measured in millimetres (mm) to the nearest 0.5 mm. The ST segment was considered depressed if there was a fall of 1 mm or more lasting 0.08 s or longer.⁶

R wave amplitude was measured using the TP segment as the isoelectric line. The following standard criteria were used.^{2,7}

- (1) The sum of the R wave measured in mm.
- (2) The sum of the R wave plus the ST segment depression in mm (R wave index).
- (3) The sum of the R waves in the left precordial leads plus the sum of the S waves in the right precordial leads measured in mm (R+S).

Five of the 16 precordial leads covered the positions usually occupied by the chest leads of the standard 12 lead electrocardiogram; one position corresponded exactly to V5. Thus, it was possible to measure R wave, R wave index, and R+S in all 16 leads and the standard precordial leads; R wave and R wave index were calculated in V5.

All calculations were made before exercise, each minute during exercise, at peak exercise, and immediately and each minute after exercise for 10 minutes.

Gated blood pool imaging

Each patient was given sodium stannous pyrophosphate (0.2 mg/kg intravenously), followed after 30 minutes by a separate injection of 10 mCi technetium-99m, to label the red blood cells.⁸ The equilibrium of activity in the left ventricle was measured continuously using a single scintillation probe (Nuclear stethoscope Bros. Inc.).⁹ With patients lying supine, the scintillation probe was positioned in the 40° left anterior oblique projection, with 15° caudal angulation, and the optimal position for the left ventricle was determined with the aid of the microprocessor-based positioning programme. Background activity was assessed by

moving the probe in a posterolateral direction with respect to the left ventricle. The analogue signal from the probe, modified to give a wide band width, was recorded continuously on analogue tape (Racal Store-14) and synchronously with the 12 lead electrocardiogram. The recordings were replayed at 60 times the recording speed on to paper running at 15 mm/s using a Minograf 14 channel ink-jet recorder. The analogue signal was calibrated in terms of counts using two point sources of known activity. The activity above background over the left ventricle was taken as an index of left ventricular volume as the output voltage of the probe was shown to be linearly related to count rate.

A bipolar size 6 French pacing wire was passed via the right femoral vein to the right atrium. A size 21 gauge butterfly was inserted into a vein in the dorsum of the right hand to provide venous access for drugs.

Procedure

In order to determine reproducibility, the effects of respiration, and the relation between ST segment depression and R wave amplitude each patient underwent three exercise tests on separate days using the procedure already described.

The effect of different respiration patterns on R wave amplitude was studied by recording a 16 lead precordial electrocardiographic map immediately after the end of each exercise test, during tidal breathing of both high and low functional residual capacity.

In order to determine the relation between R wave amplitude and left ventricular volume, directional changes in left ventricular volume were continuously followed using the single scintillation probe and gated blood pool imaging, together with a simultaneous recording of the 12 lead electrocardiogram. Ventricular volume was increased transiently by inducing myocardial ischaemia with either ergonovine maleate (dose 0.025 to 0.375 mg iv) or a cold pressor test. The cold pressor test was performed by placing the left hand in ice-cold water for two minutes. Left ventricular volume was decreased with right atrial pacing (heart rate 100 to 160 beats a minute) or by terminating an ischaemic event with amyl nitrate.

Statistical analysis was performed using Student's test and analysis of variance.

Results

The results have been expressed using the R wave amplitude for the 16 leads of the exercise tests and for the standard chest leads during the gated blood pool imaging. Calculations of R wave index and R+S using the 16 precordial leads, standard chest leads, or V5, did not affect the results obtained.

During exercise the maximum heart rate reached

was 120 to 170 (mean 139) beats per minute: the work load achieved was 12 000 to 31 500 (mean 20 250) Watt seconds. Exercise duration was 4.1 ± 1.29 minutes (mean $\pm$ standard deviation).

(a) REPRODUCIBILITY

R wave amplitude fell in six patients and was unchanged or increased in four patients. In all patients R wave amplitude returned to the control level within 10 minutes after the end of exercise. In each case, the exercise induced R wave response for the second and third exercise tests followed a similar pattern to that recorded in the first test. Fig. 1 and 2 show two typical examples. Fig. 3 shows the mean R wave amplitude recorded before, at peak exercise, and after exercise in the three exercise tests, for the 10 patients. There was no significant difference between the R wave amplitude in the three tests at any time before, during, or after exercise ($p > 0.05$).

(b) RESPIRATION

No significant difference was seen between R wave amplitude measured at high and low functional residual capacity (Fig. 4) ($p > 0.05$).

(c) RELATION BETWEEN R WAVE AND ST SEGMENT DEPRESSION

In the six patients in whom R wave amplitude fell with exercise, it was found that this occurred gradually during exercise and in parallel with the fall in the ST

segment. Similarly in the four patients in whom there was an increase in R wave amplitude, the rise occurred gradually during exercise and in conjunction with the fall in the ST segment. Return of the R wave amplitude to control value after exercise occurred gradually in all 10 patients during recovery of the ST segment depression. Fig. 1 and 2 show two typical examples. The six patients with an exercise induced fall in R wave amplitude could not be distinguished from the four patients in whom the R wave amplitude increased, on the basis of clinical status, angiographic anatomy, or exercise performance.

(d) LEFT VENTRICULAR VOLUME

Changes in both left ventricular end-systolic and end-diastolic volumes were recorded 39 times in the 10 patients. Left ventricular volume was increased by inducing ischaemia using ergonovine and the cold pressor test (24 to 100, mean 60% increase in end-systolic counts and 17 to 65, mean 32% increase in end-diastolic counts, respectively), and reduced by right atrial pacing or terminating ischaemia with amyl nitrite (21 to 50, mean 29% decrease in end-systolic counts and 21 to 69, mean 36% decrease in end-diastolic counts, respectively). The Table shows the relation between increases and decreases of left ventricular volume and alterations in R wave amplitude. In 33 of the 39 episodes increasing (13 episodes) or decreasing (20 episodes) ventricular volume was not associated with alterations in R wave amplitude. Fig. 5

Fig. 1 The temporal relation is shown between R wave amplitude (measured in all 16 leads) and ST segment depression (measured in all 16 leads) in three exercise tests in a single patient. In this example there was a consistent fall in R wave amplitude during exercise occurring in parallel with the fall in the ST segment; both returned to resting values on recovery. (IP, immediately after exercise.)

Fig. 2 The temporal relation is shown between R wave amplitude (measured in all 16 leads) and ST segment depression (measured in all 16 leads) in three exercise tests in a single patient. In this example there was a consistent increase in R wave amplitude during exercise occurring in parallel with the fall in the ST segment; both returned to resting values on recovery. (IP, immediately after exercise.)

Fig. 3 The mean R wave amplitude ($\pm$ standard error of the mean) measured in all 16 leads is shown for the group of 10 patients. There was no significant difference between R wave amplitude in the three exercise tests at any time before, during, or after exercise.

Table *Relation between left ventricular volume changes and R wave amplitude after ergometrine, cold pressor, atrial pacing, and amyl nitrite*

Intervention	Number of episodes	Left ventricular volume change	R wave change
Ergometrine	10	}	Unchanged 13 (93%)
Cold pressor	4		Increased 1 (7%)
Atrial pacing	9	}	Unchanged 20 (80%)
Amyl nitrite	16		Decreased 5 (20%)

Fig. 4 The relation between respiratory pattern and R wave amplitude measured in all 16 leads is shown for the three exercise tests (mean $\pm$ standard error of mean). No significant difference was seen between R wave amplitude measured at high and low functional residual capacity.

Fig. 5 The effect of amyl nitrite on R wave (measured in the standard chest leads) and left ventricular volume (assessed using a single scintillation probe) is shown on three occasions in the same patient. A fall in left ventricular volume after the administration of amyl nitrite (A) was seen as a fall in equilibrium counts and accompanied by small variable changes in R wave amplitude.

Fig. 6 The effect of ergometrine on R wave (measured in the standard chest leads) and left ventricular volume (assessed using a single scintillation probe) is shown. An increase in left ventricular volume seen as an increase in equilibrium counts was accompanied by no change in R wave amplitude.

shows the effect of decreasing left ventricular volume using amyl nitrite on three occasions in the same patient. The changes in R wave amplitude were small at all times in spite of large falls in left ventricular volumes (27% decrease in end-diastolic counts); one episode was associated with no change in R wave amplitude, one with a small fall, and the third with slight increase. Fig. 6 shows an increase in left ventricular volume (increase in end-diastolic counts of 35%) during ischaemia induced by ergonovine, during which there were no detectable changes in R wave amplitude.

Discussion

The initial stimulus to study R wave amplitude changes during exercise arose from the work of Brody.¹⁰ He suggested, on theoretical grounds, that the R wave amplitude on the surface electrocardiogram was determined by the intracardiac blood volume. Several experimental¹¹⁻¹³ and some clinical studies¹² supported this "Brody effect" in patients with coronary artery disease. Bonoris *et al.*¹ evaluated exercise induced R wave amplitude changes and angiographic data in patients with coronary disease and postulated that R wave amplitude rose during exercise as a result of myocardial ischaemia inducing left ventricular dilatation. As normal patients were found to have a fall in QRS amplitude during exercise, attributed to a fall in left ventricular volume, analysis of R wave changes was recommended to improve the predictive accuracy of the exercise test in the diagnosis of coronary disease. In addition, the R wave amplitude rise has been pro-

posed as a means of identifying patients with ischaemic induced left ventricular dysfunction.² Recent work, however, has challenged both the diagnostic value of R wave measurement and its dependent relation to left ventricular volume. Simoons¹⁴ suggested that R wave changes during exercise were both less sensitive and less specific than ST segment changes, and this has been confirmed by others.^{3,7} The confusion has arisen, in part, from the use of different lead systems for electrocardiographic monitoring and of different criteria for calculating QRS amplitude. In addition, QRS amplitude has been shown to alter rapidly during experimental myocardial ischaemia and differing results may be obtained if measurements are made at different stages of exercise.¹⁵ Respiratory pattern changes after exercise have also been suggested to affect R wave measurement.

Our study was designed to clarify some of these issues. We used a 16 lead precordial electrocardiographic mapping system as this enabled us to measure the QRS amplitude over the whole precordium, as well as in the standard chest leads and in the single lead V5. We have also tested all the different previously reported criteria for calculating R wave amplitude. Our results show that the directional behaviour of the R wave during exercise was unaffected by choice of lead system or measurement criterion.

By making measurements before, during, and after exercise, we were able to study the temporal relation of the QRS amplitude with ST segment depression. Changes in QRS amplitude developed gradually, were maximal at peak exercise or shortly after the end of exercise, and, during recovery, gradually returned to control in conjunction with the ST segment in a consistent manner for each patient. Myocardial ischaemia, however, as represented by the development of ST segment depression, was associated with both an increase and a decrease in R wave amplitude. We were unable to identify any features that distinguished the patients with exercise induced fall in QRS from those in whom the QRS increased: all had three vessel coronary disease and achieved similar work loads and heart rate response during exercise: an alteration in breathing pattern was not responsible for the R wave changes seen.

Both experimental^{15,16} and clinical studies^{17,18} have challenged the relation of the surface QRS amplitude to left ventricular volume. Battler and colleagues¹⁶ were unable to show a relation in a study on dogs and David *et al.*¹⁵ found an inverse relation between cardiac volume and QRS amplitude after caval ligation. Ishikawa *et al.*¹⁷ found that an increase in R wave amplitude accompanied a decrease in heart size during treatment of heart failure resulting from different causes. There have been few studies in man during ischaemia because of the technical difficulties in

studying simultaneous left ventricular function and QRS amplitude during exercise. Battler *et al.*³ used gated blood pool mapping with gamma camera and found an increase in QRS amplitude in only one of nine patients in whom left ventricular end-diastolic volume increased at peak exercise. Our study differs as we chose to monitor left ventricular function with a single scintillation probe: this allows left ventricular dimensions to be related to the QRS amplitude changes on a beat to beat basis. We elected to use pharmacological and physical manoeuvres to both increase and decrease left ventricular volume, avoiding difficulties caused by body movement and respiration. In the event, R wave amplitude did not alter in the great majority of episodes of left ventricular volume increase and decrease associated with myocardial ischaemia.

These findings indicate that R wave changes during ischaemia in man are not determined primarily by changes in cardiac volume. Several other factors, individual to the patient, such as changes in wall motion and thickness, intramyocardial and trans-myocardial conduction abnormalities, and cancelling effects on electrical activity are presumably involved and may explain why ischaemia is associated with differing directional changes in R wave amplitude. Our findings in 10 patients cast doubt on the value of measurement of QRS amplitude in the prediction of coronary disease.

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