Value of electrocardiogram in predicting and estimating infarct size in man

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SUMMARY The value of the electrocardiogram in assessing infarct size was studied using serial estimates of the MB isomer of creatine kinase (CK MB) in plasma, serial 35 praecordial maps in 28 patients with anterior myocardial infarction, and serial 12 lead electrocardiograms in 17 patients with inferior myocardial infarction. In patients with anterior infarcts, $\Sigma ST$, $\Sigma R$, $\Sigma Q$, $\Sigma R/(Q+S)$, and the number of sites with ST elevation more than 2 mm or with QS waves, were obtained from each map. Correlation between both maximum $\Sigma Q$ and maximum $\Sigma ST$ with cumulative CK MB was highly significant. There was also a significant correlation between $\Sigma R$ and $\Sigma R/(Q+S)$ with cumulative CK MB. There was no significant correlation between maximum number of sites with ST elevation or with Q or QS waves and cumulative CK MB. Maximum $\Sigma ST$ and number of sites with ST elevation predicted maximum $\Sigma Q$ and number of sites with QS or Q waves at a time when infarction was not complete. In patients with inferior infarcts, there was a significant correlation between maximum $\Sigma Q$ and maximum $\Sigma ST$ in leads II, III, and aVF, and cumulative CK MB.

This study shows that all the waves in the electrocardiogram are useful in assessing infarct size. The fact that maximum $\Sigma ST$ predicts final $\Sigma Q$ may be used to assess the efficacy of interventions designed to salvage ischaemic myocardium.

It has been shown that the immediate and long-term prognosis after myocardial infarction is related to the quantity of necrotic myocardium (Sobel et al., 1972; Braunwald, 1976). Experiments in animals now indicate that the size of an infarct may be reduced by appropriate interventions (Maroko and Braunwald, 1973). However, the clinical assessment of interventions designed to protect ischaemic myocardium has posed considerable difficulty. Various techniques (Shell and Sobel, 1976; Bleifeld et al., 1977; Poliner et al., 1977; Muller et al., 1978) have been proposed for measuring and following trends in infarct size in patients.

Electrocardiographic mapping of the infarct from multiple praecordial sites has been proposed for this purpose (Muller et al., 1978). Considerable evidence has accumulated regarding its validity in the experimental situation (Węgria et al., 1949; Kjekshus et al., 1972; Maroko et al., 1972a, b; Hartman et al., 1975; Ross, 1976). However, it has been suggested on the basis of both theoretical evidence (Holland and Brooks, 1975, 1976; Fozzard and Das Gupta, 1976; Holland and Arnsdorf, 1977) and some clinical reports (Norris et al., 1976; Thompson and Katavatis, 1976) that the use of praecordial mapping to measure human infarct size has limited value. Most workers have assessed the value of individual waves of the electrocardiographic complex (Norris et al., 1976; Selwyn et al., 1977a, b) and there are few data on the QRS complex as a whole and its relation to ST segment changes in the same patient.

The present study was undertaken to investigate further the value of changes in the QRS complex and the ST segment elevation as a guide to infarct size in the coronary care unit. The main aims were to study the relation of the magnitude and extent of Q wave development, R wave loss, and ST segment elevation to each other and to infarct size estimated by calculating the total release of the myocardial isoenzyme of creatine kinase (CK MB) into the plasma.

Patients

Forty-five patients, aged between 46 and 75 years (mean 62.5 years), admitted to the coronary care unit (CCU) of the Radcliffe Infirmary with definite
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evidence of a recent myocardial infarction on a 12
lead electrocardiogram and significant increase in
cardiac enzymes, were studied. Patients with intra-
ventricular conduction defects (QRS duration
>100 ms) including hemiblocks and second and
third degree AV block were excluded. All patients
had normal frontal axes (0° to +90°).

Of the 45 patients, 41 gave no history of a previous
infarct, and a previous electrocardiogram was
available in 14 of these. Twenty-eight patients had
anterior infarcts and 17 inferior infarcts; none of
the 4 with a history of previous infarction had
pathological Q waves on their initial electrocardio-
gram. Four patients later reinfarcted as shown by
new electrocardiographic and enzyme changes.
Routine management of the patient was not altered
by the study procedure; diuretics and antiarrhyth-
mic drugs were administered as clinically indi-
cated. Lignocaine was given to 8 patients, 11 patients
received oral beta-blockers, and disopyramide was
used in only 1 patient. No patient had a systolic
blood pressure less than 90 mmHg. Three patients
required cardioversion for ventricular fibrillation,
one of whom showed a further rise in CK MB.

Methods

PRAECORDIAL ELECTROCARDIOGRAPHIC
MAPPING
Praecordial electrocardiographic mapping was done
in all patients with anterior myocardial infarction.
Thirty-five praecordial sites were selected by
focusing an ordinary projector beam through a
35 mm slide with 35 holes arranged in 5 horizontal
rows and 7 vertical rows. The horizontal rows were
designated from top to bottom A to E and the
vertical rows from right to left 1 to 7. The distance
between the first and second vertical rows was
twice the distance between the others to avoid
electrode placement on the sternum. With the
patient sitting up at 45 degrees, A1 was focused on
a point 2.5 cm to the right of the sternum in the
second intercostal space. E1 was focused 2 cm
below the level of the xiphisternum in the same
line as A1. The position of the projector was
adjusted so that A7 fell on a spot high in the left mid-
axillary line in such a way that rows A to E were
horizontally placed. All the spots were then marked
using indelible ink to allow accurate repositioning
of the electrodes each time a recording was obtained.

The electrocardiograms were recorded using a
four-channel ink-jet Elema-Schönander Mingograf
34 recorder. Suction cup electrodes with a contact
diameter of 15 mm were used. The electrocardio-
gram was recorded from each praecordial site at 2
different gains simultaneously (1 mV=10 mm and
1 mV=40 mm) so that an accuracy of 0.025 mV
could be obtained. Paper speed was 25 mm/s.

Each recording was made during quiet breathing
and great care was taken to reposition the patient
at the same angle on each occasion. The first
recording was obtained at a mean time of 6 hours
after the onset of pain (at less than 4 hours in 19
patients, at 4 to 6 hours in 12 patients, at 6 to 12
hours in 10 patients, and at more than 12 hours in
4 patients). Subsequently, recordings were obtained
at 8-hour intervals during the first 24 hours, at
12-hour intervals on the second day, and thereafter
daily.

Initial studies showed that praecordial electro-
cardiographic mapping was of limited value in
inferior infarction. Therefore, in order to record
changes from the inferior surface of the heart, the
standard 12 lead electrocardiogram was recorded
serially, the V lead positions being marked on the
chest wall to obtain reproducible recordings.

ELECTROCARDIOGRAPHIC MEASUREMENTS
Anterior infarct patients
The amplitude of the Q, R, and S waves, and of ST
segment elevation (at 60 ms after the J point) was
measured in 5 beats from each site, using the TP
segment as a baseline. Measurements were made on
both the amplified (1mV=40 mm) and regular
recordings (1 mV=10 mm). These were then
summed from 35 leads to obtain \( \Sigma R, \Sigma Q, \Sigma S, \)
and \( \Sigma ST. \) In addition, \( \Sigma(Q+S) \) and \( \Sigma R/\Sigma(Q+S) \) were
calculated for each map.

Inferior infarct patients
In patients with inferior infarction, QII + III + aVF
and ST segment elevations in II + III + aVF were
calculated.

SERIAL CK AND CK MB ANALYSES
Blood samples were obtained from a peripheral
vein through an indwelling cannula at 4-hourly
intervals for 72 hours after the onset of pain.
Samples were immediately centrifuged for 15
minutes. Plasma was pipetted into plain sterile glass
tubes and stored at –20°C. CK was estimated
using the method of Oliver (1955) with dithio-
theiral as activator as utilised by the Searle CPK-
UVI kit. The method described by Mercer and
Varat (1975) was used to separate the CK iso-
enzymes.

CK MB and mathematical calculations
The appearance function of CK MB released from
the infarcted myocardium was calculated (cumu-
lateive CK MB) by the method described by Sobel
et al. (1972) and modified by Norris et al. (1975).
**Reproducibility Studies in Control Subjects**

Twenty normal subjects between the ages of 30 and 70 years, and 5 patients 2 to 4 weeks after infarction, likely to have a stable electrocardiographic pattern, were studied to confirm the reproducibility of praecordial mapping and the standard 12 lead electrocardiogram. Recordings were examined for beat-to-beat variations during sinus rhythm and atrial fibrillation, variations during quiet and deep breathing, variations caused by electrode repositioning, and those resulting from changes in patient position.

The beat-to-beat variation of measurements of the QRS complex and of ST segment elevation in the same recording during sinus rhythm was small (mean 2.2%), compared with a mean of 15 per cent and 20 per cent in 2 patients who were in atrial fibrillation. The variations resulting from changes in posture and during deep breathing were considerable (mean 12.12% and 18.5%, respectively). In contrast, the variation caused by electrode repositioning, day-to-day variation, and variation during quiet breathing with the patient at 45 degrees and in sinus rhythm was less than 5.3 per cent. All patients were in sinus rhythm except 2 who were in atrial fibrillation in whom 10 consecutive beats were averaged.

**Results**

**Relation Between Cumulative CK MB and Praecordial Map in Patients with Anterior Infarction**

ST segment elevation (Fig. 1)

The maximum $\Sigma ST$ observed during the first 3 days was found to correlate significantly with cumulative CK MB ($r=0.733; P<0.001$). There was no significant correlation between $\Sigma ST$ at any other time and cumulative CK MB. The maximum number of recording sites with ST segment elevation more than 1 mm or more than 2 mm also did not correlate with cumulative CK MB.

**Q waves**

Correlation between the maximum $\Sigma Q$ and cumulative CK MB was highly significant ($r=0.827; P<0.001$; Fig. 2). No correlation was observed between the number of recording sites showing pathological Q waves ($r=0.265; P>0.1$), or QS waves ($r=0.363; P>0.1$) and cumulative CK MB.

**R wave and R/(Q+S) ratio**

The inverse relations between minimal $\Sigma R$ (Fig. 3) and minimal $\Sigma R/(Q+S)$, and cumulative CK MB were less significant ($r=-0.623; P<0.01$ and $r=-0.624; P<0.01$, respectively) than the relation between maximum $\Sigma Q$ and cumulative CK MB.

**Inferior Infarction**

Preliminary studies not surprisingly failed to show any significant relation between infarct size estimated from CK MB and the praecordial electro-
Electrocardiogram and myocardial infarct size

Fig. 3 Minimum $\Sigma R$ is plotted against cumulative release of CK MB in patients with anterior infarction. A fair correlation is seen.

Cardiogram in patients with inferior myocardial infarction. However, the sum of the ST segment elevations and of Q wave amplitudes in leads II + III + aVF correlated with cumulative CK MB ($r = 0.505; P < 0.05$ and $r = 0.745; P < 0.01$, respectively; Fig. 4). There was no significant relation between the sum of R wave amplitudes in leads II + III + aVF and cumulative CK MB.

Fig. 4 Maximum $QII+III+aVF$ is plotted against cumulative release of CK MB in patients with inferior infarction. A fair correlation is seen.

**Interrelation of waves in electrocardiogram**

In patients with anterior infarcts, the maximum $\Sigma ST$ was found to predict maximum $\Sigma Q$ at a time when electrocardiographic evolution of infarction was not complete ($r = 0.820; P < 0.001$; Fig. 5). The number of sites with ST segment elevation more than 1 mm and sites with ST segment elevation more than 2 mm predicted the number of sites developing QS waves ($r = 0.602; P < 0.01$, and $r = 0.635; P < 0.01$, respectively; Fig. 6). In addition, in individual patients the maximum ST segment elevation recorded at each of the 35 sites correlated well with final Q wave and final R wave amplitude at the same time.

Fig. 5 Maximum $\Sigma ST$ is plotted against maximum $\Sigma Q$ in patients with anterior infarction. A good correlation is seen.

Fig. 6 The number of sites with ST segment elevation more than 2 mm is plotted against the number of sites with QS waves in patients with anterior infarction. A fair correlation is seen.
Discussion

Since Maroko and Braunwald (1973) first described ST segment mapping, considerable interest has been focused on the electrocardiographic method for estimating infarct size. Experimental work in dogs with coronary artery occlusion (Maroko et al., 1972a, b) established the validity of the method. In their animal experiments, the site and, to a certain extent, the size of the infarction was determined by the site of occlusion of a particular coronary artery. However, in the clinical situation, varying sizes of infarct are encountered, more than one wall of the heart may be involved, and evolution of the infarct may be more variable in time (Yusuf et al., 1978).

The development of the enzyme method of estimation of infarct size has provided the clinician with another index of the extent of infarction. Electrocardiographic assessment may be influenced by factors other than infarct size, such as site of infarct, presence of arrhythmias or conduction defects, or changes in local ion concentration; the enzyme method does not have these drawbacks. The amount of CK released has been shown to bear a close relation to total CK depletion in rabbits (Kjekshus and Sobel, 1970), and to infarct size measured morphologically at necropsy in patients who died of acute myocardial infarction (Bleifeld et al., 1977). Though the model for the basis for calculation of infarct size from enzymes has been criticised (Roe et al., 1977), the enzyme method nevertheless provides an empirical estimate of infarct size by a totally independent method, with which electrocardiographic assessment of infarct size can be usefully compared.

ST segment elevation

The relation of praecordial ST segment elevation to histological and biochemical estimates of the extent of myocardial necrosis is well documented in experimental investigations on animals (Kjekshus et al., 1972; Maroko et al., 1972a, b). However, the relation of ST segment elevation to other estimates of infarct size in man is controversial. Morris et al. (1974) showed that ST segment elevation 48 hours after the onset of pain correlated with maximal AST (SGOT) in patients with anterior or inferior infarcts.

Blomqvist et al. (1975) showed that there was a significant correlation between $\Sigma$ST and the area of an infarct as determined by pyrophosphate scan. By contrast, Norris et al. (1976), Thompson and Katavatis (1976), and Selwyn et al. (1977a) showed no correlation or at best weak correlation between ST segment elevation and peak or total plasma enzyme.

In our study we have observed a strong positive correlation between maximum $\Sigma$ST and cumulative CK MB ($r=0.733; P<0.001$) in patients with anterior infarcts, and a weaker but significant correlation in inferior infarcts using the sum of ST segment elevation in leads II, III, and aVF ($r=0.505; P<0.05$). Several factors may be responsible for the different results obtained by different workers. Firstly, praecordial mapping reflects only changes affecting the anterior and anterolateral wall of the left ventricle and it is possible that in some studies the patients may have had involvement of other walls of the heart. In our study, none of the patients with anterior infarction had any fresh electrocardiographic changes in the inferior leads, though a small true posterior infarct may have been undetected. Secondly, variations in chest shape and size and localisation of infarction may lead to differences between patients. Thirdly, ST segment elevation is known to increase or decrease rapidly in some patients (Selwyn et al., 1977a) and variable intervals between onset of pain and time of electrocardiographic recording will introduce further error. To minimise this source of error we have taken recordings at regular intervals in all our patients.

R wave

A decrease in the amplitude of R waves during experimental myocardial infarction was reported by Wilson et al. (1935). Muller et al. (1978) showed a good correlation between loss of R wave amplitude and infarct size in experimental infarction. Recently, Selwyn et al. (1977b) have demonstrated a good correlation with estimates of infarct size from CK release.

In our study, we have observed only a fair inverse correlation between minimal $\Sigma R$ and cumulative CK MB release ($r=-0.623; P<0.01$). This may be partly the result of the large variation in $\Sigma R$ observed in our control group of normals ($\Sigma R$ varies from 150 to 300 mm). Though this may limit the value of $\Sigma R$ in comparing infarct size in different patients, it is still useful in following the course of infarction in an individual patient (Yusuf et al., 1978), and in comparing infarct size in 2 large groups.
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Q WAVE
Myers et al. (1948a, b; 1949) described an excellent correlation between the development of Q waves in specific praecordial leads and pathological evidence of infarction in the corresponding areas of the heart. Similarly, in patients undergoing cardiac surgery, it has been shown that praecordial Q waves generally overlie epicardial Q waves and that these indicate the presence of myocardial fibrosis (Bodenheimer et al., 1976). In addition, a close correlation between praecordial Q waves and ventricular performance in patients with coronary artery disease has been reported (Miller et al., 1972; Williams et al., 1973; Miller et al., 1974; Awan et al., 1977).

These observations are consistent with our finding that $\Sigma Q$ from praecordial maps correlates well with cumulative CK MB in patients with anterior infarcts ($r=0.827$; $P<0.001$). The range of variation of $\Sigma Q$ in our control group was between 0 and 12 mm in the 35 lead map. In contrast, $\Sigma Q$ in most patients with anterior infarcts was several times greater. Though the correlation between QII+III+aVF and cumulative CK MB in patients with inferior infarcts is less impressive ($r=0.745$; $P<0.01$), this is hardly surprising as these data were obtained from 3 electrocardiographic leads only. This may detract from its value in comparing infarct size in different patients but QII+III+aVF is useful in comparing groups of patients and in studying the evolution of an infarct (unpublished data).

RELATION OF NUMBER OF SITES WITH ELECTROCARDIOGRAPHIC ABNORMALITIES TO CUMULATIVE CK MB
Although several workers have used the number of sites (or area) with ST segment elevation or pathological Q wave development as an index of the extent of ischaemia or necrosis and to evaluate the efficacy of interventions (Maroko et al., 1972a, b; Muller et al., 1975; Selwyn et al., 1977a, b; 1978), we found no relation between the number of sites with ST segment elevation greater than 2 mm, ST segment elevation of any degree, or pathological Q or QS waves, and enzyme estimates of infarct size. A similar experience was reported by Nielsen (1973), who observed that the sum of ST segment elevations from an ordinary 12 lead electrocardiogram was a good prognostic indicator, whereas the number of leads with ST segment elevation was not related to prognosis. This is not surprising as the number of sites showing abnormalities does not provide information about the magnitude of change at a particular praecordial site. We believe, therefore, that $\Sigma ST$ or $\Sigma Q$ are better indices of infarct size than the number of sites with abnormalities.

PREDICTION OF INFARCT SIZE
In patients with anterior infarcts, maximum $\Sigma ST$ has been shown to be related to final $\Sigma Q$ and $\Sigma R$, and one could therefore use this measurement to predict infarct size. This relation could also be exploited in assessing interventions aimed at decreasing infarct size, as the slope of the line relating $\Sigma ST$ and $\Sigma Q$ would be difficult in control subjects and in subjects on beneficial treatment. Henning et al. (1978) have used a formula based on $\Sigma ST$ obtained from the first map and the rate of loss of R wave amplitude to predict cumulative CK MB. However, these authors stress that this observation was made in a highly selected group of patients. We have also shown a relation between number of sites with ST segment elevation and those with QS waves. This confirms the work of Askenazi et al. (1977) and supports the view that the number of sites with ST segment elevation can be used to predict Q wave extent.

We observed no significant relation between the sum of ST segment elevations in II, III, and aVF, and QII+III+aVF in patients with inferior infarcts.

In conclusion, measurements of ST segment elevation, Q wave development, and R wave loss from praecordial maps, can all be used to assess infarct size in patients with anterior infarcts. Measurements of Q waves and ST segment elevation in leads II, III, and aVF also provide useful but less accurate information about infarct size in patients with inferior infarcts.

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