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# Natural history and evaluation of ST segment changes and MB CK release in acute myocardial infarction[1]

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*The experimental evidence relating ST segment elevation in the electrocardiogram to the progress and extent of ischaemic myocardial damage is discussed. There are difficulties in applying this to patients: the reproducibility of praecordial mapping was tested using a multiple analysis of variance. This showed that factors such as time after the onset of myocardial infarction and posture can affect measurements of $\Sigma ST$ elevation significantly. There was a pattern of changes in $\Sigma ST$ elevation and of changes in plasma MB CK activity in a group of patients with uncomplicated anterior infarction. A significant but weak correlation was found between $\Sigma ST$ elevation in the first hour and the total MB CK activity released into the plasma, but not at any other time. The use of $\Sigma ST$ elevation as a measure of the extent of ischaemic damage is unreliable. In 5 patients with a variety of complications of acute anterior infarction, changes in $\Sigma ST$ elevation were significantly different from the uncomplicated group, and MB CK release profiles suggested further necrosis. The pattern and time course of ST segment changes may be of use in assessing the progress of ischaemic myocardial damage.*

ST segment elevation associated with acute myocardial infarction was described by Pardee (1920) and remains a useful diagnostic sign. Ekmekci *et al.* (1961) have shown that ST segment elevation in ischaemic heart disease represents severe acute regional myocardial ischaemia. Maroko *et al.* (1971) reported a relation between total or summed ST segment elevation ($\Sigma ST$) and the extent of ischaemic myocardial damage in experimental myocardial infarction in dogs. However, this has not in practice enabled the clinician to assess the progress and extent of ischaemic damage in patients suffering from acute myocardial infarction (Norris *et al.*, 1976).

The purpose of this study was to assess the reproducibility of praecordial electrocardiographic mapping, the natural history of ST segment changes, and release of creatine kinase myocardial isoenzyme (MB CK) activity after uncomplicated anterior infarction. The relation between changes in $\Sigma ST$ elevation and total MB CK release has been investigated to find out whether the praecordial map can be used to assess the extent of ischaemic myocardial damage. An analysis of the pattern and time course of ST segment elevation and of release of MB CK activity is presented as a means for assessing the progress of ischaemic damage in acute myocardial infarction.

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## Patients and methods

Fifty-six patients admitted to the coronary care unit at the Hammersmith Hospital with a clinical diagnosis of acute anterior myocardial infarction were studied. There were 42 men and 14 women, aged between 42 and 76 years, mean 56 years. All these patients developed electrocardiographic evidence of acute myocardial infarction on the standard 12-lead electrocardiogram and all had a diagnostic rise in serum enzymes.

Forty-seven patients from this group had none of the following complications: (a) clinical evidence of pulmonary oedema or congestive heart failure; (b) chest *x*-ray evidence of cardiac enlargement or interstitial pulmonary oedema; (c) cardiac rhythm disturbances other than isolated unifocal ventricular ectopic beats; (d) sinus tachycardia of more than 110 beats per minute or systemic hypotension (systolic blood pressure less than 110 mmHg) for longer than 15 minutes. All these patients survived 14 days in hospital and on discharge had no clinical or chest *x*-ray evidence of congestive

heart failure, cardiac enlargement, or pulmonary oedema, and did not require diuretics, inotropic agents, nitroglycerin, or antiarrhythmic drugs.

Nine patients had a number of complications after admission to the coronary care unit. These were (a) recurrent chest pain 1 to 12 hours after the onset of the first episode in 6; (b) ventricular fibrillation followed by recovery in 1; and (c) sudden onset of pulmonary oedema after admission to the coronary care unit in 2.

Praecordial electrocardiographic maps were recorded in all patients on admission, after 1 hour, then 4 hourly for 12 hours, and daily thereafter; additional recordings were made if the clinical condition changed. Fifteen patients were mapped repeatedly between 2 and 6 hours after the onset of chest pain. This was done (a) at 5, 15, 30, and 60 minutes, the electrodes being removed between recordings, (b) at 5, 15, 30, and 60 minutes with the electrodes left in place; and (c) with the patient at rest and in turn lying at 45°, lying flat, again lying at 45°, and finally in the left oblique position.

Electrocardiograms were recorded using a direct writing ink jet apparatus (Mingograph, Elema-Schonander) recording on 3 channels simultaneously. The gain employed was 10 mm for 1 mV and the paper speed was 25 mm per second. The electrodes were the Welsh suction type with a contact diameter of 1 cm. In order to avoid the spread of potentials the electrode jelly was applied only over a small area and the electrodes were carefully separated. Electrocardiograms were recorded from 72 points distributed evenly over the praecordium as described by Reid *et al.* (1971). At each point 3 complexes were analysed and the mean value for ST segment elevation used. In order to avoid the significant effects of respiration, electrocardiograms were recorded before and during a 5-second period with breathing stopped at end-expiration; in patients unable to cooperate the mean ST segment elevation throughout a respiratory cycle was calculated. The ST segment elevation was measured in mm to the nearest 0·5 mm at 0·06 s after the nadir of the S wave, using the TP segment as the isoelectric line, or the PQ segment when the TP segment was difficult to locate because of tachycardia. If the QRS complex was wider than 110 ms in any praecordial map, the patients' electrocardiograms were excluded from the study (Grant, 1970). Measurements were only made during sinus rhythm. ST segment elevation less than 2 mm was ignored, and the sum of all the ST segment elevations measured in the 72 praecordial leads was recorded as ΣST.

After the onset of chest pain, ΣST elevation was calculated from the praecordial maps at the beginning and end of each time period. The changes in ΣST elevation were calculated by treating the value for ΣST at the beginning of each time period as 100 per cent and using the value at the end of that time period to calculate the percentage change. The significance of changes in ST segment elevation was analysed by a multiple analysis of variance. This calculation takes into account the effects of the variables described above in estimating the significance of changes in ΣST observed in time. A two-tail test of significance was used to assess the difference between the complicated and uncomplicated groups.

Venous blood samples (taken at 3-hour intervals for up to 4 days after the onset of chest pain) were drawn from (a) 13 of the 47 patients who had no complications and (b) 6 patients with recurrent chest pain and 1 patient after ventricular fibrillation. The blood samples were placed in lithium heparin tubes and centrifuged at 2000 *g* for 10 minutes. Total plasma CK activity was measured spectrophotometrically (using a Cecil 272 system spectrophotometer, Cecil Instruments, Cambridge) by the method of Oliver (1955) as modified by Hearse *et al.* (1973). Using this method the upper limit of plasma CK activity in healthy subjects is 50 mU/ml (Ogunro *et al.*, 1976). Samples with activity more than 250 mU/ml were diluted before determination of total CK; in order to minimise the dilution-activation effect observed with plasma CK, heat inactivated plasma was used as the diluent (Graig *et al.*, 1967). Isoenzymes were separated by electrophoresis on agarose gel and quantified in aqueous solution by fluorimetry (Ogunro *et al.*, 1977). MB CK isoenzyme release curves were constructed by measuring the plasma MB CK activity (mU/ml) at the stated time intervals after the onset of chest pain. The area under each curve was used as an index of the total activity of MB CK released into the plasma.

## Results

### REPRODUCIBILITY

The analysis of variance in the 15 patients studied showed that a change in posture from lying at 45° to the upright, oblique, or flat position in bed produces a highly significant change in ΣST measured within 5 minutes ($P < 0·001$). The analysis showed that if posture was not changed and mapping was repeated at intervals significant changes could only be seen at 15 minutes ($P < 0·01$), 30 minutes ($P < 0·001$), and 60 minutes ($P < 0·001$). This can be shown whether the electrodes are removed between recordings or left in place.

RELATION BETWEEN ΣST SEGMENT ELEVATION AND TOTAL MB CK ACTIVITY RELEASED

The relation between the maximum ΣST segment elevation measured (in 8 patients) within 1 hour from the onset of chest pain and total MB CK activity released into the plasma is significant but weak (Fig. 1A). There was no relation between ΣST segment elevation measured at any other time and total MB CK activity released; for example, Fig. 1B shows ΣST at 6 hours after the onset of chest pain (in 13 patients).

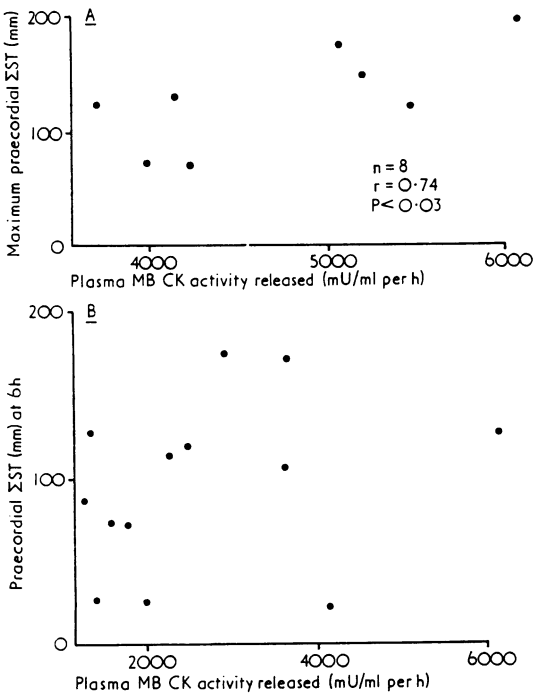


Fig. 1 *(A) The relation between maximum ΣST elevation measured within 1 hour of onset of chest pain and total MB CK release (area under plasma MB CK activity curve) after uncomplicated myocardial infarction in 8 patients. (B) The same relation is shown but ΣST is at 6 hours from the onset of chest pain.*

Table 1 *Changes in ΣST elevation in 47 patients after uncomplicated myocardial infarction*

| *Percentage increase in ΣST ±2 SD* | | | | | | |
|---|---|---|---|---|---|---|
| *Hours from the onset of chest pain* | | | | | *Days from onset* | |
| *0–1* | *1–4* | *4–8* | *8–12* | *12–24* | *1–4* | *4–7* |
| +441·5 | −34·2 | −17·1 | −11·6 | −14·7 | −18·3 | −13·0 |
| Range | | | | | | |
| +62 to +1980 | ±31 | ±33·8 | ±51·0 | ±52 | ±51 | ±54 |
| N=8 | N=26 | N=41 | N=47 | N=47 | N=40 | N=31 |

N=The number of individuals available for study in each time interval.

UNCOMPLICATED GROUP

The mean ΣST segment changes over 7 days in 47 patients suffering from uncomplicated anterior infarction are shown in Fig. 2. The percentage changes in ΣST elevation ±2 standard deviations (SD) during 7 time intervals over the first 7 days after the onset of chest pain are shown in Table 1. There were large increases in ΣST in 8 patients within 20 minutes from the onset of chest pain (mean + 441·5%) while there was a decrease in ΣST with considerable individual variations during the other time intervals.

Fig. 3 shows the mean MB CK activity release profile (plotted as a percentage of the peak MB CK activity) for 14 of the patients following uncomplicated anterior infarction. The mean time (±2 SD) taken for MB CK to reach peak activity was 19·4 ±5·8 hours. The time taken (expressed as a mean ± 2 SD) for this enzyme to reach specific percentages of the peak value for the uncomplicated group is shown. This curve describes the pattern of MB CK release for the uncomplicated group.

COMPLICATED GROUP

Table 2 shows the percentage changes in ΣST during the same time intervals in 6 patients who had recurrent episodes of chest pain at different times after the onset of the first episode. There were 4 patients who suffered recurrent chest pain between 1 and 12 hours after the initial episode of pain; the changes in ΣST elevation during this time are shown in Table 3. The ΣST segment changes for 26 patients from the uncomplicated group studied over the same time period are also shown in Table 3. An unpaired t test shows a significant difference between the changes in the two groups (mean difference 79·70; T=6·83, P<0·01). These 4 patients showed an alteration in the pattern of release of MB CK activity suggesting a second episode of necrosis (Fig. 4). In caxes 5 and 6 ΣST changes were within the range of mean ±2 SD for the uncomplicated group and the MB CK activity release curve also showed a pattern within the range found for the uncomplicated patients. The changes in ΣST in patients with two other complications are also shown in Table 2. In the case of ventricular fibrillation with recovery, the changes in ΣST were outside the mean ±2 SD for the uncomplicated group and the MB CK activity release profile suggested further necrosis. In 2 patients developing heart failure after admission, the ΣST changes were within the range

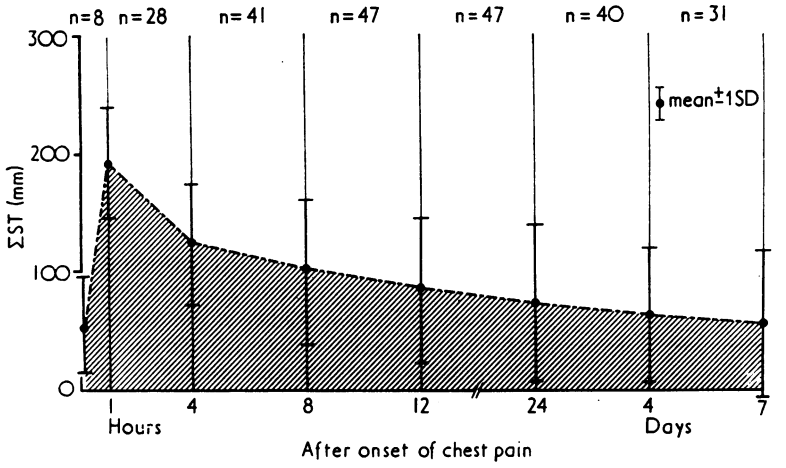


Fig. 2 *Mean ΣST elevation in mm at 7 points in time from onset of chest pain in uncomplicated anterior myocardial infarction (47 patients).*
*n=number of observations.*

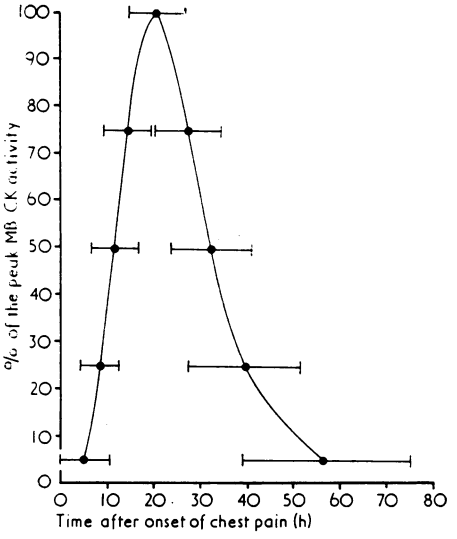


Fig. 3 *Plasma MB CK activity (expressed as percentage of peak MB CK value) in 14 of the 47 patients suffering from uncomplicated anterior infarction. Time taken for plasma MB CK activity to reach 5, 25, 50, 75, and 100 per cent of peak MB CK value is plotted for release and clearance phases of curve.*

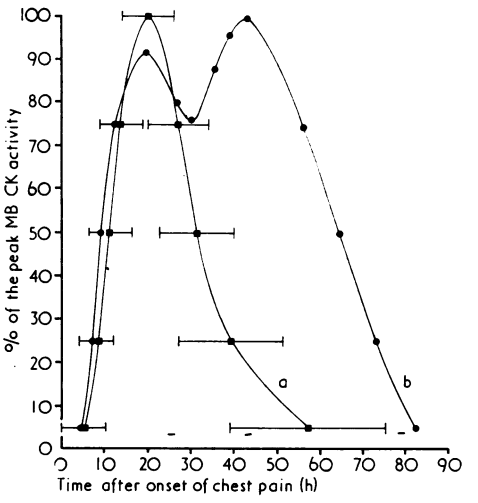


Fig. 4 *Plasma MB CK activity (expressed as percentage of peak MB CK value) in (a) uncomplicated patients, and (b) typical patient suffering from recurrent chest pain. Time taken for plasma MB CK activity to reach 5, 25, 50, 75, and 100 per cent of peak MB CK values is plotted for release and clearance phase of curve.*

Table 2 *Changes in ΣST in 9 patients after complicated anterior infarction*

| | | *Percentage increase in ΣST elevation* | | | | | |
|---|---|---|---|---|---|---|---|
| | | *Hours from the onset of chest pain* | | | | *Days from onset* | |
| | | *1–4* | *4–8* | *8–12* | *12–24* | *1–4* | *4–7* |
| Recurrent chest pain | 1 | − 4 | +130* | −20 | + 1 | −11 | − 5 |
| | 2 | | − 31 | +57* | −25 | − 2 | −16 |
| | 3 | +42* | − 28 | −24 | + 5 | −12 | + 5 |
| | 4 | −14 | +123* | −35 | +11 | −11 | − 3 |
| | 5 | −48 | + 9 | −35 | +16 | + 2* | + 3 |
| | 6 | | − 23 | + 9 | −18* | +10 | −25 |
| Ventricular fibrillation with recovery | 1 | + 8 | −223 | + 4 | −19 | + 5 | −46 |
| Onset of heart failure after admission | 1 | | − 10 | + 7 | +30* | −14 | −52 |
| | 2 | −34 | + 3 | −15 | + 2 | + 6 | + 4 |

*Time interval when complication occurred.

Table 3 *Changes in ΣST elevation in 4 patients with recurrent chest pain between 1 and 12 hours*

| | | ΣST elevation (mV) Hours from the onset of chest pain 1 | 12 | % change ΣST between 1–12 hr |
|---|---|---|---|---|
| Recurrent chest pain | 1 | 94 | 165 | +75·5 |
| | 2 | 210 | 229 | + 9·1 |
| | 3 | 173 | 160 | - 7·5 |
| | 4 | 81 | 101 | +25·7 |
| No complication (26 patients) (mean ±SD) | | 173·8 ±68·4 | 85·9 ±59·1 | -54 ±19·3 |

of mean ± 2 SD calculated for the uncomplicated group, as was the pattern of MB CK activity release, suggesting that there had been no additional necrosis. Fig. 5 shows two examples of ST segment mapping over 8 hours (a) in uncomplicated anterior infarction and (b) in a patient who had recurrent chest pain. This patient also had an extended and altered pattern of MB CK activity release outside the range of mean ± 2 SD for the uncomplicated group, suggesting a second episode of necrosis.

## Discussion

The technique of praecordial mapping of ST segment changes has been clearly described by Reid *et al.* (1971), but studies of the reproducibility of this technique have not included factors, other than ischaemic injury, that may also affect ST segment elevation. Important factors such as time, posture, and respiration must be considered when evaluating the significance of ST changes resulting from cardiac events. Experimental studies have

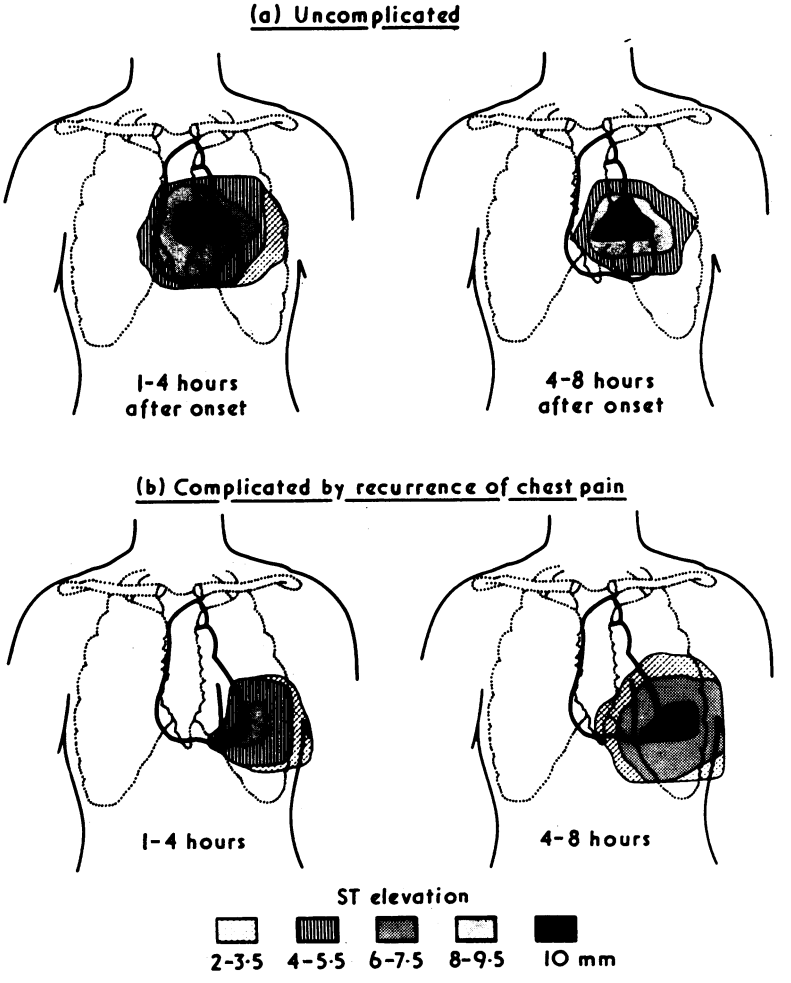


Fig. 5 *Praecordial mapping of ST segment elevation (a) over 8 hours in a patient with uncomplicated anterior infarction and (b) over the same 8 hours in a patient with recurrent chest pain with an altered pattern of MB CK release.*

shown a significant relation between ΣST elevation and the extent of ischaemic myocardial damage (Maroko *et al.*, 1971). It is important to realise that the epicardium was exposed in these experiments and the ST segment changes were recorded before and after production of regional ischaemia. The correlation reported was between ΣST elevation at 15 minutes after coronary occlusion and myocardial CK tissue depletion at 24 hours. It is uncommon to see patients within 15 minutes from the onset of chest pain, and in man mapping is performed on the praecordium. In addition, the position of the infarct in relation to the exploring electrodes, the resistance of chest wall tissues, and the effects of normal myocardium probably interfere with any quantitative relation between ΣST elevation and infarct size.

In a number of studies a qualitative relation has been shown between the total or peak serum enzyme activity changes and the severity of ischaemic damage in acute myocardial infarction (Sobel et al., 1972; Mathey *et al.*, 1974). MB CK is essentially cardiospecific and in this study the total activity released was used to assess the extent of cell necrosis.

Studies in animals have shown the pattern and time course of ΣST segment changes after the onset of acute uncomplicated regional myocardial ischaemia (Maroko *et al.*, 1971; Kjekshus *et al.*, 1972) and experiments have shown a good correlation between changes in ΣST elevation recorded simultaneously from the epicardium and from praecordium (Muller *et al.*, 1975). It has been shown that significant alterations in this pattern of behaviour of ΣST produced by a variety of factors can indicate improvement or deterioration in the progress of ischaemic myocardial damage (Maroko and Braunwald, 1973; Muller *et al.*, 1975). The pattern and time course of ΣST segment elevation over 7 days and MB CK activity released over 4 days after the onset of chest pain in patients suffering uncomplicated anterior infarction are described in this study.

In 5 patients suffering from a variety of complications the percentage change in ΣST elevation was outside the range of mean ± 2 SD observed in the uncomplicated group. In each case, this was accompanied by a pattern of MB CK release which was also outside the range of mean ± 2 SD calculated for the uncomplicated group, suggesting a second episode of necrosis. In those patients with complications who showed no significant alteration in the pattern of ΣST elevation, the pattern of MB CK release in the plasma resembled that of the uncomplicated group, with no evidence of further episodes of cell necrosis.

In conclusion, this study has shown that ST segment elevation in uncomplicated acute infarction is a rapidly changing electrocardiographic sign. Factors other than ischaemic injury must be considered in order to identify significant changes in ΣST elevation caused by cardiac events. There is only a rough correlation in anterior infarction between maximum ΣST elevation and total plasma MB CK activity at a time that is impractical for general clinical use. An assessment of the progress, rather than the extent, of ischaemic muscle damage may be obtained by comparing the pattern of changes in ΣST elevation in any patient with the pattern found in uncomplicated acute infarction.

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