Evaluation of Precordial Electrocardiographic Mapping as a Means of Assessing Changes in Myocardial Ischemic Injury

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SUMMARY

Precordial electrocardiographic mapping has been proposed as a method for evaluating the extent of myocardial injury in patients with acute myocardial infarction. To assess the relationship between direct measures of myocardial cell damage and findings obtained by precordial mapping, the left anterior descending coronary artery (LAD) was occluded in dogs instrumented for simultaneous recording of epicardial and precordial electrocardiograms. The sum in millivolts of ST-segment elevation recorded from 30 electrodes placed in a Silastic grid sutured to the epicardium (EpiST) was compared to that recorded from 30 precordial electrodes (PreST). While ischemic injury was: 1) maintained constant with a fixed occlusion; 2) reduced by partial reperfusion; 3) increased by addition of a second occlusion; or 4) increased repeatedly by intermittent infusions of isoproterenol, EpiST and PreST were always closely correlated in each of the 16 dogs studied: \( r = 0.92 \pm 0.01 \) (SEM). In seven control dogs, 30 minutes after coronary occlusion, PreST had fallen to 77.4 ± 6.6% of its value 15 minutes postocclusion. In seven experimental dogs, two branches of the LAD were occluded. Fifteen minutes after double occlusion, one occlusion was released; 30 min after the initial occlusion PreST had fallen significantly more than control, to 43.1 ± 13.1% of its value 15 minutes postocclusion. Simultaneously, epicardial sites in the reperfused area also showed normalization of ST segments and 24 hours later exhibited normal myocardial creatine phosphokinase activity and normal histologic appearance. During the same experiment, the mean precordial R wave voltage of sites with ST-segment elevations exceeding 0.15 mV 15 minutes following occlusion fell significantly (\( P < 0.05 \)) more in the control group (from 1.14 ± 0.15 to 0.75 ± 0.06 mV) than in the reperfused group (from 1.06 ± 0.09 to 0.96 ± 0.17 mV) during the ensuing 45 minutes. Thus, more rapid normalization of PreST or preservation of precordial R wave voltage reflected the actual prevention of myocardial necrosis by reperfusion. These findings demonstrate the usefulness of precordial electrocardiographic mapping for evaluating changes in myocardial ischemic injury. Sites at which appearance of epicardial ST segment is not a reliable index of ischemic injury were associated with the development of intraventricular conduction blocks with Q to intrinsic deflection intervals exceeding 40 msec or QRS durations exceeding 65 msec; these changes were associated with precordial RSR' configurations. Such sites, whether recorded from precordial or epicardial leads, should be excluded from ST-segment measurements used in the assessment of myocardial ischemia.

Additional Indexing Words:
- Acute myocardial infarction
- Myocardial necrosis
- Epicardial electrograms
- ST segments
- Creatine phosphokinase
- Focal block

Recent studies in experimental animals indicate that the extent and severity of myocardial ischemic injury following coronary occlusion can be modified by a variety of pharmacologic and physiologic interventions.\(^1,2\) In these experiments, the sum of ST-segment elevations from multiple epicardial electrograms (EpiST) was used as an index of the extent and severity of myocardial ischemic injury. It was also demonstrated that epicardial ST-segment elevations following acute coronary artery occlusion can be useful in predicting the amount of necrosis as reflected in histologic appearance and creatine phosphokinase (CPK) activity of myocardial biopsy specimens obtained 24 hours following occlusion.\(^1,5\)

Since the methods employed in the animal experiments require thoracotomy and therefore cannot be used in intact patients, the effects of these various interventions on the extent and severity of cardiac damage in patients with acute myocardial infarction remain speculative. For many years precordial electrocardiographic leads have been used as substitutes...
for direct epicardial leads to make qualitative judgments about myocardial ischemic damage. More recently it has been proposed that changes in the sum of ST-segment elevations from multiple precordial leads (Pre\textsuperscript{2}ST) in patients with anterior myocardial infarctions reflect alterations in the extent of myocardial ischemic injury.

It has been demonstrated in animal studies that interventions which had previously been shown to augment or reduce epicardial ST-segment elevations and myocardial necrosis produce similar directional changes in Pre\textsuperscript{2}ST; thus, while propranolol and norepinephrine decrease, isoproterenol and systemic arterial hypotension increase precordial ST-segment elevations following experimental coronary artery occlusion. However, more direct evidence of correlation of findings between epicardial and precordial leads is lacking since simultaneous epicardial and precordial leads have not been recorded. Accordingly, one purpose of the present investigation was to study the relationship between changes in EpicST, known to correlate with the extent and magnitude of myocardial necrosis, and changes in Pre\textsuperscript{2}ST, a measurement easily and safely made in patients. A second objective was to provide a more direct assessment of the potential value of precordial mapping, by comparing alterations in precordial ST-segment elevations following an intervention, with the extent of myocardial damage 24 hours later, the latter reflected in histologic appearance and myocardial creatine phosphokinase (CPK) activity.

Recently it has been demonstrated that epicardial ST-segment elevations may decline with increasing ischemia in the center of large ischemic areas. Since this could impair the value of the ST segment as an index of ischemia, the third objective of this investigation was to study the changes in QRS duration and configuration accompanying these reductions in ST-segment elevation, in order to determine whether such "paradoxical" changes in the ST segments could be recognized as secondary ST-T wave changes accompanying QRS alterations in epicardial and precordial leads.

Since the loss of R wave voltage in the precordial leads in patients with acute anterior or lateral myocardial infarctions is thought to reflect loss of viable myocardium, analysis of changes of R wave height following coronary occlusion could represent a method complementary to ST-segment mapping in the detection of changes in myocardial ischemic injury. Accordingly, the fourth purpose of this study was to compare changes in precordial R wave height of sites with ST-segment elevations in dogs with a sustained coronary occlusion and in dogs in which a portion of the ischemic zone was reperfused.

**Methods**

Experiments were carried out in dogs weighing between 18 and 45 kg anesthetized, with sodium thiamylal. Respiration was maintained with a Harvard respirator; the heart was exposed through a left thoracotomy and suspended in a pericardial cradle. The left anterior descending coronary artery (LAD) or one of its major branches was intermittently occluded with a Schwartz intracranial arterial clamp in open-chest preparations or a snare occluder in closed-chest preparations. In seven dogs two snare occluders were placed around the LAD. These occluders were arranged in one of the following patterns: 1) around two large branches of the LAD, 2) around one branch of the LAD and the LAD proximally, or 3) around the distal and proximal LAD. The areas of ischemia were confined to the anterolateral surfaces of the left ventricle since these are the areas from which the body surface proximity effect is maximal. Fifteen minutes following occlusion of both branches, one occlusion was released, permitting reperfusion of a portion of the ischemic area. In 24 hour experiments a permanent ligature was placed on the coronary artery after acute measurements were completed. Arterial pressure was monitored with a Statham P23Db pressure transducer. All variables, including epicardial and precordial electrocardiograms, were recorded on an oscillographic recorder.

Epicardial electrograms were recorded with the use of an electrode grid sutured by its corners to the surface of the left ventricle. The grip was composed of 30 multistrand 34 gauge stainless steel wires sutured 0.5 cm apart in a 2-by-4 cm sheet of silastic (fig. 1). For the groups in which epicardial and precordial measurements were correlated, the pericardial cradle was released and the heart with the grid

![Figure 1](http://circ.ahajournals.org/)

*Figure 1*  
Instrumentation for recording both epicardial and precordial electrocardiograms. Thirty epicardial leads are attached to a fenestrated sheet of silastic which is sutured to the surface of the left ventricle. Thirty needle electrodes are positioned on the precordium from the midaxillary line to the left sternal border. All 60 leads are connected to a switch box and recorded four at a time.
attached was returned to its previous position in the thorax. The chest was then closed and the epicardial leads were connected to a selector switch for simultaneous recording in groups of four. Special care was taken to maintain the volume conductor properties of the chest. The chest was closed in layers. Following the approximation of the ribs with four stitches with a double thread of number 2 silk, the intercostal muscles, the pectoral muscle, and the subcutaneous layers were closed separately with continuous catgut sutures. The skin was closed with a continuous silk suture. A number 24 Bardic chest tube was inserted in the sixth intercostal space in the left midaxillary line. The distal end of the tube was connected to a water seal to permit removal of air from the thorax.

Precordial electrocardiograms were obtained from 30 needle electrodes positioned 2 cm apart in a 6-by-14 cm grid extending from the left parasternal line to the midaxillary line. ST-segment elevation was measured above the T-P segment 20 msec after the end of the QRS complex. Sites at which the Q to intrinsic deflection interval exceeded 40 msec or at which the QRS duration exceeded 65 msec were excluded from analysis of ST-segment elevation. The sum of ST-segment elevation in millivolts (1 mm = 1 mV) in the 30 epicardial leads (EpiST) and in the 90 precordial leads (1 mm = 0.1 mV) (PreST) were used as indices of the magnitude of ischemic injury.

All measurements of epicardial and precordial ∆ST were initiated within one hour and completed within seven hours of the end of the surgical procedure. Thus, all of the measurements were made during prolonged acute experiments. Control tracings taken prior to all occlusions demonstrated the classical T wave changes resulting from thoracotomy, and almost complete absence of ST-segment elevation. The epicardial ∆ST prior to occlusion averaged 2.8 ± 1.2 mV and the precordial ∆ST prior to occlusion was 0.19 ± 0.01 mV. Fluid was noted in the thorax following the acute experiments. Twenty-four hours following implantation of the grid an early inflammatory reaction was present which precluded measurement of ST-segment elevation.

To minimize any effect of the silastic sheet on epicardial and precordial potentials, 0.25 cm2 holes were placed in the sheet between adjacent electrodes. In a control experiment there was no difference between electrograms recorded first with the electrode grid and then with a hand-held cotton wick electrode with the heart suspended in a pericardial cradle. To evaluate the effects of the silastic sheet on precordial potentials, fifteen minute occlusions were performed with and without the grid attached to the heart. Precordial ∆ST 15 minutes following occlusion was lower when the grid was present (∆ST = 4.7 mV) than when the grid was absent (∆ST = 7.3 mV). This tendency of the grid to attenuate precordial potentials would be expected, if anything, to impair rather than improve any correlation between epicardial and precordial potentials. Multiple rather than single electrocardiographic leads were used to maximize the sensitivity of the method and to permit assessment of the extent as well as severity of myocardial injury.

In group I (16 dogs), the relationship between Epi∆ST and Pre∆ST was studied by recording epicardial and precordial ST-segment maps simultaneously prior to and every 5 minutes up to three hours following coronary occlusion. This group was divided into three subgroups: subgroup IA (six dogs): sustained occlusion of a single vessel with no interventions; subgroup IB (five dogs): alteration of ischemic injury 15 minutes following the initial occlusion either by release of one of the two occlusions or addition of a second occlusion; subgroup IC (five dogs): alteration of ischemic injury by repeated infusions of isoproterenol (0.15 to 0.50 μg/kg/min) in animals prior to beta-adrenergic blockade. In the same dogs, following administration of propranolol (1 mg/kg i.v. in a bolus), a much larger dose of isoproterenol was infused (4.0 to 40.0 μg/kg/min).

In group II (14 dogs), the use of precordial mapping to detect an intervention, designed to reduce myocardial necrosis was tested. In seven control dogs (group IIA), epicardial and precordial ∆ST were measured at 5 min intervals for 30 min following a sustained occlusion of the LAD. In the remaining seven dogs (group IIB), the LAD was occluded simultaneously at two different sites. Fifteen minutes following occlusion (i.e., immediately after the 15 minute postocclusion epicardial and precordial electrocardiographic measurements), a zone of myocardium was reperfused by release of one of the occlusions. Epicardial and precordial ∆ST were measured at 5 min intervals for 30 min following the initial double occlusions. The precordial R wave voltage of sites with ST-segment elevations exceeding 0.15 mV was calculated 15 and 60 min following the initial occlusion in the control and reperfused groups. Surviving dogs were sacrificed 24 hours later and the hearts were quickly removed. Full wall thickness myocardial specimens (500 mg) were obtained as previously described from the same sites at which epicardial recordings had been made 24 hours previously. The specimens were analyzed for CPK activity according to the method described by Rosalki. Specimens for histologic analysis were fixed in Bouin’s solution and stained with hematoxylin and eosin. These specimens were coded and classified as normal or as showing signs of an early myocardial infarction by an independent observer.

In group III (17 dogs), the behavior of ST segments from epicardial sites in the center of extremely large areas of ischemia was studied with special attention to ”paradoxical” reductions in ST segment elevations, i.e., lowering of the ST segment, in sites of augmented ischemia. Ischemia was created initially by occlusion of a branch of the LAD; 40 minutes later the area of ischemia was enlarged by occlusion of the LAD near its origin. The area of ischemia was then reduced by release of the high LAD occlusion with maintenance of the branch occlusion. Measurements of the QRS duration and the time interval from the onset of the QRS complex to the beginning of the intrinsic deflection were made at a paper speed of 200 mm/sec at all sites at which ”paradoxical” reduction of ST segment elevation occurred.

Results

Group I: Correlation of Epicardial and Precordial ST-Segment Maps

In the 16 dogs with coronary occlusion without any subsequent intervention (subgroup IA), with partial coronary artery reperfusion or with an extension of injury by occlusion of an additional branch (subgroup IB), or with changes in the severity and extent of ischemic injury by repeated infusions of isoproterenol (subgroup IC), the average relationship between epicardial and precordial ∆ST was: Epi∆ST (in mV) = 8.4 Pre∆ST (in mV) + 4.5. Epicardial and precordial ∆ST following coronary occlusion correlated closely in all cases: r = 0.92 ± 0.01 (N = 220 observations in 16 dogs).
In subgroup IA (fig. 2, panel A), in which a single coronary occlusion was simply maintained, EpiΣST averaged 2.8 ± 2.3 mV (± SEM) and PreΣST averaged 0.05 ± 0.05 mV prior to occlusion. Fifteen minutes following occlusion EpiΣST had risen to 57.0 ± 15.4 mV and PreΣST to 10.5 ± 1.9 mV. Thirty minutes following occlusion EpiΣST had declined to an average of 87.4% and PreΣST fell to 71.4% of the 15 min value. One hour following occlusion EpiΣST averaged 98.6% and PreΣST 89.5% of the value 15 minutes post occlusion.

In subgroup IB (fig. 2, panel B), prior to occlusion, EpiΣST averaged 1.25 ± 1.2 mV and PreΣST was 0.35 ± 0.35 mV. Fifteen minutes following occlusion of two branches of the LAD, EpiΣST averaged 99.2 ± 27.9 mV and PreΣST 12.9 ± 3.8 mV. One of the two occlusions was released after 15 minutes. Thirty minutes following the initial occlusion EpiΣST had decreased to an average of 38.9% (P < 0.01) and PreΣST also had fallen significantly to 54.3% (P < 0.05) of the 15 minute postocclusion value, while one hour following occlusion EpiΣST averaged 50.7% and PreΣST 69.8% of the 15 minute postocclusion value.

In the dog in which a second occlusion was added at 21 minutes (fig. 2, panel C), EpiΣST was 51 mV and PreΣST was 0.9 mV prior to the second occlusion. Thirty minutes following the first occlusion (i.e., 9 min following the added occlusion) EpiΣST had risen by 253% and PreΣST by a similar value, 255%.

In subgroup IC, 15 minutes following occlusion, total EpiΣST in the five dogs had risen to 88.0 mV and total PreΣST to 26.4 mV. Then isoproterenol (0.15 - 0.30 μg/kg/min) was infused, increasing heart rate from 144 ± 9.9 to 179 ± 10.8 beats/min and decreasing mean arterial pressure from 112.0 ± 10.0 to 98.0 ± 11.2 mmHg. Total EpiΣST increased to an average of 276 mV and preΣST rose similarly, to an average of 62 mV. Isoproterenol was discontinued, and reinfused, first in the same dose indicated above and then following beta-adrenergic blockade with propranolol (1 mg/kg) in a much larger dose, (4.0 μg/kg/min or more) to overcome the blockade and achieve similar hemodynamic results. In all instances EpiΣST and PreΣST followed one another in a parallel manner despite changes in ST segment contour produced by the isoproterenol infusion and the attendant tachycardia (fig. 3A). With the isoproterenol infusion there was an increase in the maximal degree of ST-segment elevation from leads in the center of the ischemic area as well as a symmetrical extension of the borders of the area of ST-segment elevation (fig. 3B).

Heart rate did not change significantly with the placement or release of coronary occlusions.

Group II: The Use of Precordial Mapping to Detect a Reduction of Myocardial Necrosis

In seven control dogs with a single sustained LAD occlusion, EpiΣST decreased by only 15.2 ± 7.0% between 15 and 30 minutes postocclusion. In contrast, in seven dogs reperfused at 15 minutes by release of one of the two occluded vessels, the average epicardial ST segment elevation from 23 sites which were in the reperfused areas fell by 78.1 ± 3.8% in 15 minutes. In addition, the 15 myocardial biopsies obtained from reperfused sites 24 hours later showed an average CKP value of 30.8 ± 1.2 I.U./mg protein, a value similar to that found in specimens from areas where flow was never altered by occlusion (33.9 ± 1.5 I.U./mg protein, N = 14, P = NS) but significantly higher than the tissue CKP activity of nonreperfused areas (12.8 ± 0.7 I.U./mg protein, N = 26, P < 0.005, fig. 4). Also, biopsies taken 24 hours later from these 15 sites which had shown ST-segment elevations of 9.4 ± 1.0 mV before reperfusion and
As areas been had of myocardial specimens reperfused column) (P occlusion which permanent significantly higher no epicardial was given at the rate of 4.0 μg/kg/min following an i.e. bolus of 1 mg/kg of propranolol. Time, in minutes following coronary occlusion. Panel B) Precordial ST-segment elevations in mV in 30 precordial leads 20 minutes following coronary artery occlusion prior to and during an infusion of isoproterenol. A progressive decrease in ST-segment elevation from the center of the ischemic area to its periphery was noted in all precordial maps.

Figure 3

Panel A) An example of the correspondence between the EpiΣST and PreΣST as ischemic injury following coronary artery occlusion varied during intermittent intravenous infusions of isoproterenol (shaded rectangle). During the first and second infusions isoproterenol was administered at the rate of 0.17 μg/kg/min; during the third infusion isoproterenol was given at the rate of 4.0 μg/kg/min following an i.e. bolus of 1 mg/kg of propranolol. Time, in minutes following coronary occlusion. Panel B) Precordial ST-segment elevations in mV in 30 precordial leads 20 minutes following coronary artery occlusion prior to and during an infusion of isoproterenol. A progressive decrease in ST-segment elevation from the center of the ischemic area to its periphery was noted in all precordial maps.

Figure 4

The creatine phosphokinase activity (CPK) in I.U./mg of protein of myocardial specimens taken 24 hours following coronary occlusion. The CPK activity of sites remote from the occlusion, which showed no epicardial ST-segment elevation (shaded column), was significantly higher than the CPK activity of sites in the area of a permanent occlusion which demonstrated ST elevation (dotted column) (P < 0.005). However, sites in an ischemic area that were reperfused 15 minutes following occlusion (blank column) showed no significant difference in tissue CPK activity from sites which were never ischemic, thereby indicating salvage of myocardium. Bars indicate ± SEM. The numbers in each column denote the number of specimens.

In summary, sites in the nonreperfused areas showed only a slight fall in epicardial ST elevation from 15 to 30 minutes postocclusion, a marked loss of R wave voltage by one hour and markedly decreased CPK activity and abnormal histologic appearance 24 hours later. Sites in the reperfused areas showed a marked fall in ST elevation from 15 to 30 minutes postocclusion, no loss of R wave voltage by one hour, and normal CPK activity and histologic appearance 24 hours later (fig. 5).

It was also possible by precordial electrocardiographic mapping to detect this decrease of ischemic injury in the partially reperfused group, which had been documented by epicardial mapping, myocardial CPK activity and histologic appearance. Thus, in the partially reperfused group, PreΣST 30 min after occlusion (i.e., 15 min after reperfusion) fell to 43.1 ± 13.1% of its value 15 min after occlusion while in the group with a sustained occlusion PreΣST fell only to 77.4 ± 6.6% (P < 0.05) during this time interval. In the partially reperfused group the mean precordial R wave voltage of sites with ST elevation of 0.15 mV or greater fell only slightly (from 1.06 ± 0.09 mV to 0.96 ± 0.17 mV) from 15 to 60 min postocclusion, while in the nonreperfused group the mean precordial R wave voltage fell significantly more (from
Changes in the epicardial electrogram and tissue CPK activity in areas with fixed occlusion (A) and areas reperfused 15 minutes postocclusion (B). One hour after the initial occlusions the ST segment remains elevated and R wave height diminishes in "A" while in "B" ST segment elevation is absent and R wave height is maintained. Twenty-four hours later tissue CPK activity is markedly decreased in "A" and normal in "B".

1.14 ± 0.15 to 0.75 ± 0.06 mV, P < 0.05) during this time interval.

Group III: Changes in ST-Segment Elevation in Large Areas of Ischemic Injury (fig. 6)

Seventeen dogs in which ST-segment elevation was noted to diminish in the centers of large areas of ischemic injury were purposely selected for this portion of the study. Sites remote from the area of the occluded vessel, and thus without ST-segment elevation, showed a mean QRS duration of 39.3 ± 0.5 msec (N = 272) and remained unchanged with subsequent interventions. The mean QRS duration at ischemic sites at which the ST segment had risen was very slightly increased, 42.9 ± 0.6 msec (N = 133) (P < 0.005). However, the QRS duration of epicardial electrograms from sites at which the ST segment fell with increasing ischemia was greatly prolonged, to 119.4 ± 7.4 msec (N = 48) (P < 0.005).

Sites distant from the area supplied by the occluded vessel, and thus without ST elevation, showed a Q to intrinsic deflection interval of 23.9 ± 0.2 msec (N = 284) and remained unchanged with subsequent interventions. In sites at which the ST segment increased with ischemia this interval increased slightly to 26.5 ± 0.5 msec (N = 147) (P < 0.005). However, at sites at which the ST segment fell with increasing ischemia, the Q to intrinsic deflection interval was greatly prolonged to 53.1 ± 1.9 msec (N = 27) (P < 0.005) (fig. 6). Only three of 43 sites showing decreasing ST segments with increasing ischemia had a QRS duration of less than 65 msec and none had Q to intrinsic deflection intervals of less than 40 msec. Therefore, it would appear that sites at which ST segments may be unreliable indices of ischemic injury can be identified by Q to intrinsic deflection intervals exceeding 40 msec and/or QRS durations exceeding 65 msec.

When the extent and severity of ischemia caused by occlusion of a branch of the LAD are enlarged substantially by occlusion of the LAD near its origin, the QRS duration and ST-segment elevation may change rapidly and in opposite directions. In the typical experiment illustrated in figure 7, 40 minutes following the branch occlusion the QRS duration was normal and the ST segment was elevated 8 msec at an epicardial site in the center of the visibly cyanotic zone (fig. 7B). Following the addition of a high LAD occlusion, the area of ischemia was markedly enlarged, the QRS widened markedly and distinct ST segment elevation could no longer be easily recognized or measured (fig. 7D). Five seconds following release of the high LAD occlusion an extremely rapid and progressive decrease in QRS duration accompanied by an increase in ST-segment elevation to its previous level commenced (fig. 7E).

In most occlusions of a branch of the LAD significant QRS prolongation was not observed. When an epicardial electrode was swept from nonischemic myocardium across the ischemic area to the nonischemic myocardium on the opposite side, an increased ST elevation in the center of the ischemic zone was evident and no significant conduction delay was observed (fig. 8A). However, occlusion of the LAD near its origin often resulted in marked QRS prolongation in the center of the ischemic zone. An electrode swept from nonischemic myocardium to the center of the ischemic area demonstrated a lack of identifiable ST-segment elevation in the center of the deeply ischemic area, but this area was always characterized by QRS prolongation (fig. 8B).

The delay in conduction seen in the epicardial...
Figure 7

An example of changes in QRS duration and ST-segment elevation with changes in the degree of ischemia in one site in the center of an ischemic zone. Panel A) An epicardial electrogram prior to occlusion. Panel B) Forty minutes after occlusion of a branch of the left anterior descending coronary artery (LAD). Panel C) Three minutes after the addition of an occlusion of the LAD. Panel D) Ten minutes postaddition of an occlusion of the LAD. Note the elevation of ST segments from "A" to "B" and from "B" to "C". At "D" QRS duration has increased with concomitant disappearance of identifiable ST-segment elevation. Panel E) An extremely rapid decrease in QRS duration and increase in ST elevation immediately after release of the LAD occlusion. Bottom panel) Forty seconds after release of LAD. Paper speed is 25 mm/sec in panels A, B, C, D, and F and 100 mm/sec in panel E.

The tracings obtained from the center of large ischemic areas in the absence of ST-segment elevation was observed in four dogs instrumented for simultaneous epicardial and precordial mapping. The delayed onset of the intrinsic deflection on the epicardium was found to occur simultaneously with an R' in the overlying precordial lead (fig. 9).

Discussion

Cardiogenic shock has been reported to account for the majority of the in hospital deaths occurring in patients with acute myocardial infarction.24, 25 Efforts to reverse the shock state once it is established have not yielded promising results.26 The basic cause of this massive cardiac failure appears to be the extensive myocardial necrosis uniformly observed in these patients.27, 28 However, numerous interventions have been shown to reduce the amount of necrosis following coronary artery occlusion in experimental animals.1, 5, 8, 16, 17, 29, 30 In some instances these in-

Figure 8

The spatial characteristics of infarction block. Panel A) The epicardial electrogram as the electrode is swept continuously from a nonischemic area (1), to the center of an ischemic area (2), to a nonischemic area (3) in a dog without infarction block. Panel B) A sweep from a nonischemic area (1) to the margin of the ischemic area (2), to the center of the ischemic area (3), to the opposite margin of the ischemic area (4) to a nonischemic area (5) in a dog with a localized intraventricular conduction disturbance. Note the QRS prolongation and lack of ST segment elevation in the center of the area of ischemia.
Interventions have been shown to be effective when applied as late as six hours following occlusion. In addition, autopsy studies of patients dying with an acute myocardial infarction reveal marked heterogeneity of cell survival, with areas of necrotic cells interspersed with islands of viable myocardium. It is therefore possible that in some patients otherwise destined to suffer large infarcts, cardiogenic shock might be averted if an intervention capable of reducing myocardial damage, while still in its reversible stage, were appropriately applied. Also, if ischemic myocardium could be protected from undergoing necrosis, patients would be less likely to develop congestive heart failure following myocardial infarction and would possess a greater cardiac reserve should subsequent infarctions occur.

All of these considerations lend urgency to the search for a reliable method to assess changes in myocardial ischemic damage in patients. Regional myocardial blood flow in man can be measured by K+ analogues, inert gas washout, and radiolabeled microspheres. However, these methods do not distinguish areas of newly developed ischemia from poorly perfused, old scar tissue. In addition, even accurate identification of tissue whose perfusion has become impaired does not necessarily indicate the amount of cell injury, since myocardial oxygen demands vary. Analysis of serum CPK activity following occlusion permits estimation of infarct size but requires a period of approximately 11 hours of observation following the onset of the ischemic event before prediction of infarct size can be made. This obligatory delay in application of an intervention which could reduce infarct size might well impair the efficacy of any intervention. While myocardial scintigraphy with radiolabeled tetracycline can be used to identify areas of fresh necrosis, this technique cannot as yet be used to measure changes in the extent of myocardial damage.

Epicardial ST-segment mapping has been of value because it predicts, rather than measures, the final amount of myocardial necrosis following coronary occlusion. In addition, alterations in reversible myocardial injury are reflected almost instantaneously in changes in ST-segment elevations. Epicardial ST-segment elevation following experimental coronary occlusion has been shown to correlate with reduction of coronary blood flow, tissue PO2, and lactate production. Intramyocardial ST-segment elevation has been shown to correlate with decreases in tissue PO2 and increases in tissue PCO2. Epicardial or subepicardial ST-segment elevation 15 minutes following occlusion also predicts CPK activity and histologic appearance of myocardial biopsies taken 24 hours later. This useful empiric relationship permits identification of interventions which alter infarct size.

A potential limitation of epicardial mapping is the presence of sites in the center of large areas of severe ischemia in which conduction delay is present. Under these circumstances the extent of ST-segment elevation cannot be used to predict myocardial necrosis. The reduction of ST-segment elevation with the development of local conduction defects and the extremely rapid elevation of the ST-segments associated with the disappearance of these conduction defects following partial relief of ischemia (Fig. 7) suggest a causal relationship and may be explained by the gradient theory, as secondary changes in ST-T waves due to QRS prolongation. However, regardless of the basic mechanism responsible, these sites of severe ischemia in which abnormalities of intraventricular conduction interfere with the elevated ST segments can be recognized by the QRS duration and/or Q to intrinsic deflection intervals which exceed the upper limit of normal by more than 50%, and can be excluded from studies in which ST-segment elevation is summed to provide an index of myocardial injury. Indeed, it has been our practice to eliminate all such sites from consideration and calculation. Elimination of these sites does not compromise the usefulness of epicardial ST-segment mapping since the electrograms can still be used to define the margins of the ischemic area. In these areas of severe ischemic injury with marked local conduction delay, the delayed peak of the epicardial R wave corresponds to an R' in the overlying precordial lead. Thus, ST segments recorded in precordial leads with an RSR'
configuration and/or QRS prolongation might also be expected to underestimate ischemic injury.

Although the epicardial technique has been most useful in animal studies, it is applicable to patients only during or following thoracotomy. The readily accessible variations in electrical potential on the human precordium, since their first demonstration by Waller,53 have been widely used for clinical studies. A "semi direct" relationship of precordial electrocardiograms to epicardial electrograms was first described by Wilson, who noted that QRS complexes recorded from the right or left side of the dog's chest was remarkably similar to those recorded directly from the right or left side of the canine heart.6 Caruso et al. subsequently extended these observations to patients undergoing thoracotomy.54 Numerous autopsy studies have confirmed the relationship between the location of precordial electrocardiographic changes and the anatomic position of myocardial infarction.21, 22

The use of the precordial electrocardiogram to define ischemic injury in a more quantitative manner was anticipated over 30 years ago by Wilson who stated: "We must determine more exactly what the different electrocardiographic patterns seen in infarction mean in terms of the size of the infarct . . . ."6 More recently it has been proposed that the $\Sigma$ST recorded from multiple precordial leads can be used to assess alterations in myocardial ischemic injury in man.8 It has been shown in the dog that interventions known to increase or reduce epicardial ST-segment elevations following occlusion exert similar directional effects on precordial ST segments. Also, interventions which had previously been demonstrated in animal experiments to reduce ischemic injury such as betaadrenergic blockade,1, 8, 10, 13, 14 nitroglycerin,12 intracoronary balloon counterpulsation,9, 13, 36 and verapamil19 have been shown to reduce precordial ST-segment elevations in patients. However, simultaneous recordings of Epi$\Sigma$ST and Pre$\Sigma$ST have not been made previous to this study. As expected from Gauss' law, epicardial voltages were about tenfold higher than precordial voltages. The exact relationship between the two varied for each dog, depending on factors such as location of the ischemic zone, the degree of hemopneumothorax, and the configuration of the chest. In several instances coronary occlusion produced ST-segment elevations in epicardial maps only, which is in accord with the greater sensitivity of the epicardial sites and with previous observations that small infarcts may not be reflected in routine surface electrocardiograms.55

The results of the present study demonstrate an extremely close and consistent relation between changes in epicardial and precordial $\Sigma$ST, regardless of whether the coronary occlusion producing the ischemic injury was sustained, was reduced by release of one of the two occluded vessels, was increased by occlusion of an additional coronary artery, or was increased by an infusion of isoproterenol. The correlations observed were between changes in the sum of ST-segment elevations from multiple precordial and epicardial leads, and not between specific precordial and epicardial sites. In dogs in which reperfusion of a portion of the ischemic zone was carried out, Epi$\Sigma$ST and Pre$\Sigma$ST fell in parallel and in sites at which epicardial ST segment elevation fell to normal following the reperfusion, myocardial CPK activity and histologic appearance 24 hours later were normal. Thus, not only did reduction of Epi$\Sigma$ST correctly reflect the prevention of myocardial necrosis, as reported previously,1 but more importantly, from the point of view of the present investigation, reduction of Pre$\Sigma$ST reliably signaled a reduction of actual tissue necrosis.

A reduction in the epicardial R wave electromotive force within four hours of experimental coronary occlusion was first demonstrated by Wilson and his associates.56 Later it was demonstrated that a reduction of epicardial R wave voltage was found in sites in which ischemia produced a mixture of viable and necrotic myocardium, as determined by histologic study.57, 58 In the present study, the 31.0 ± 7.9% decrease of epicardial R wave height between 15 and 60 minutes following coronary occlusion in the non-reperfused sites which exhibited ST segment elevation after coronary occlusion and which later showed CPK depletion and abnormal histologic appearance is in accord with these observations.

Similar R wave changes could be detected by precordial mapping. In the seven dogs with a fixed occlusion, the presence of ST-segment elevations exceeding 0.15 mV 15 min following occlusion from precordial leads on the left chest correlated well with the reduction of R wave height over the ensuing 45 min. In the partially reperfused group, threatened myocardium was protected, as documented by CPK activity and histologic appearance, 24 hours later. This group of dogs could be identified by the greater retention of R wave voltage than that of the control, i.e., the nonreperfused, group.

Canine and human torsos exhibit a different configuration and the spatial relationship between the heart and chest wall differ in these two species. However, the demonstration of a close correlation between epicardial and precordial maps for dogs of widely differing chest geometries suggests the applicability of this correlation in man. This is in accord with the semidirect nature of the human precordial leads.5, 21, 22

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While the findings of the present investigation strongly support the use of serial precordial electrocardiographic mapping in patients with acute myocardial infarction to assess the effects of any specific intervention on alterations in the extent of myocardial ischemic injury, it is important to recognize the following limitation of the method:

1. **Patient selection.** The method is applicable only to patients with acute anterior or lateral transmural myocardial infarctions. It is not applicable to patients with subendocardial infarction, diaphragmatic, and/or true posterior infarctions.

2. **Changes in electrocardiographic measurements without changes in ischemic injury.** Numerous factors such as conduction defects, marked variations in serum electrolytes, or the development of pericarditis, pericardial effusion, or pneumothorax can alter ST-segment elevation or R wave voltage independent of changes in ischemic injury.

3. **Changes in ischemic injury unrelated to the intervention being evaluated.** The patient with an acute myocardial infarction is subject to a myriad of influences which may alter ischemic injury. Progression of a partial coronary occlusion, resolution of a thrombotic occlusion, the development of arrhythmias, secondary thrombosis, congestive heart failure, hypotension, fever, the administration of positive and negative inotropic agents, oxygen, and other as yet undefined factors all contribute to an unpredictable time course for ST-segment elevation and QRS changes in any given patient. The effect of these uncontrolled variables must be countered by comparison of electrocardiographic changes between patients randomly assigned to control and treatment groups when the effects of a specific intervention are being investigated.

4. **Nonquantitative.** A percentage fall in ST-segment elevation cannot be directly related to grams of myocardium salvaged nor can the reduction of R wave height be converted to the quantity of myocardium infarcted. The efficacy of an intervention is based on the demonstration of significant differences between precordial ST segment and R wave changes in control and treated groups.

In view of the potential usefulness of precordial electrocardiographic mapping on the one hand and its limitations on the other, it would seem reasonable to utilize this method for clinical trials aimed at the limitation of infarct size, but at the same time continue the search for other methods of detecting changes in ischemic injury in patients with acute myocardial infarction.

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Evaluation of precordial electrocardiographic mapping as a means of assessing changes in myocardial ischemic injury.

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