Precordial Electrocardiographic Mapping

A Technique to Assess the Efficacy of Interventions Designed to Limit Infarct Size

JAMES E. MULLER, M.D., PETER R. MAROKO, M.D., AND EUGENE BRAUNWALD, M.D.

The quantity of myocardium which becomes necrotic following coronary occlusion has been shown to influence both the acute and long-term consequences of myocardial infarction.1,2 Fortunately, experiments now indicate that the size of a myocardial infarct is not irrevocably determined immediately following a coronary occlusion, but can be altered substantially by a number of interventions.3-11 However, the clinical assessment of interventions designed to protect ischemic myocardium has posed considerable difficulty. Precordial electrocardiographic mapping, including analysis of both the ST segment and the QRS complex, which has been developed over the past several years, is now being used in studies on patients with acute myocardial infarction. In this review evidence will be presented which indicates that electrocardiographic mapping, when employed properly and with appropriate awareness of its limitations, can yield valid results and indicate whether or not an intervention modifies either the severity of ischemia itself or the eventual size of an infarction.

Epicardial Electrocardiographic Mapping

The electrocardiogram has been used in the study of myocardial ischemia and infarction for half a century. In 1918, in an effort to establish the utility of the electrocardiogram as an aid in the diagnosis of myocardial infarction, Smith conducted a systematic study in dogs of the changes in the electrocardiogram following coronary occlusion.12 These experiments demonstrated conclusively that ST-segment elevation appears following coronary occlusion; Q waves appeared in tracings recorded five days postocclusion but were not discussed. A detailed description of the epicardial QRS changes of infarction was then provided by Wilson and his colleagues,13,14 who postulated that a QS wave results from transmission of the negative cavity potential through necrotic myocardium. This theory of Q wave genesis was confirmed by Prinzmetal for some infarcts, but it was found that in other instances a QS complex resulted simply from a balance of vectors directed away from the injured area.15,16 Prinzmetal also noted that an epicardial QR complex was produced by a mixture of living and necrotic myocardium in the subjacent tissue.17

Conventional capacitor-coupled ECG amplifiers do not permit differentiation of ST-segment elevation from T-segment depression. Using a direct coupled ECG amplifier, Samson and Scher demonstrated in 1960 that the apparent ST-segment elevation observed following coronary occlusion can result from varying amounts of true ST-segment elevation and T-segment depression producing apparent ST-segment elevation.18 Furthermore, recordings from individual cells indicated that the TQ depression was accompanied by a loss of resting membrane potential while the true ST-segment elevation was accompanied by a shortening of the action potential. More recent studies have confirmed the presence of both TQ depressions and true ST-segment elevations during ischemia but stress the greater contribution of the former.19,20 Prinzmetal et al. investigated the subcellular events responsible for alterations in the monophasic action potential in ischemic myocardium. They demonstrated that perfusion of myocardium with a solution containing a high concentration of K+ causes TQ depression, leading to apparent ST-segment elevation.21 Johnson has recently proposed that...
the onset of ST-segment elevation, which occurs within seconds of coronary occlusion, could result from an inhibition of the active transport of K+ with a rapid accumulation of K+ in the transverse tubular system. Although K+ changes can account for alterations in the action potential of an ischemic cell, it has recently been shown that venous blood from an ischemic area contains an unidentified substance which can alter the electrical behavior of cells. Downar et al. demonstrated that blood from the veins draining an ischemic area of porcine myocardium shortened the action potential and reduced resting potential of cells in perfused cardiac muscle strips. These changes could not be totally accounted for by changes in K+ of the "ischemic" blood even in combination with hypoxia, acidosis, hypoglycemia or increased lactate.

Both Wilson's and Prinzmetal's groups used epicardial electrograms from numerous sites (epicardial maps) to study events following coronary occlusion. Later, Sayen reported that elevations occurred in ST-segment maps when myocardial oxygen tension, determined polarographically, declined by 35% or more from control values. The use of epicardial ST-segment mapping to evaluate interventions which could alter ischemic injury and necrosis following coronary occlusion began in 1969. Two separate methods of ST mapping were developed. The first is that in which the ST segment is used as an index of ischemic injury during sequential 20 minute coronary occlusions. An occlusion is placed on the left anterior descending (LAD) coronary artery of the dog. The ST-segment elevation in multiple epicardial sites is determined 15 minutes after occlusion. The occlusion is then released and the myocardium allowed to recover. Forty-five to sixty minutes later the artery is reoccluded in the same location but in the presence of the in-
tervention being tested for its ability to alter ischemic injury. The mean ST-segment elevation (ST) and the sum of ST-segment elevations in all epicardial sites (ΣST), as well as the number of epicardial sites with ST-segment elevation greater than 2 mV (NST) are then compared to the same parameters recorded during the first occlusion\(^3,26-28\) (figs. 1 and 2). The electrical manifestations of injury produced by 15 to 20 minutes of ischemia are reversible and several consecutive occlusions can be carried out in the same animal. When no intervention is interposed between occlusions the results are highly reproducible.\(^3,29\) The major advantages of this method are its simplicity and the fact that it permits each animal to serve as its own control. When animals do not serve as their own controls, comparison of results between animals requires large numbers of experiments because the naturally occurring variability of the coronary circulation leads to large differences in the size of the ischemic zone, and ultimately of the infarction following a "standard" coronary occlusion.

However, this approach has two serious inherent disadvantages: first, it is possible that the intervention being evaluated has a nonspecific effect on the ST segment and no effect on the ischemic injury itself; second, this method does not provide information about the relationship between ischemic injury occurring shortly after coronary occlusion and the final amount of myocardial necrosis.

The 24-hour occlusion method in which early ST-segment mapping is compared to the resultant necrosis overcomes both of these limitations. As with the first method, the LAD is occluded and the epicardial ST-segment map recorded 15 min later; the occlusion is maintained, and the chest is closed for 24 hr, reopened and transmural myocardial specimens are excised from the sites at which epicardial electrograms had been recorded 24 hr earlier. The biopsies are then coded and analyzed for histologic evidence of necrosis and decrease of tissue creatine kinase (CK) activity without knowledge of the origins of the specimens. In animals which receive no intervention, there is a predictable, highly significant inverse relationship between the height of the ST-segment 15 min after occlusion and the tissue signs of necrosis, i.e., the histologic, histochemical, electron-microscopic and biochemical (tissue CK activity) evidence of infarction 24 hr later.\(^30,32\)

Thus, with this technique, the epicardial electrogram serves as a predictor of subsequent tissue viability or infarction and the agent being evaluated is administered after the ST-segment map has been recorded. Since the ST-segment map is recorded before the intervention is applied, a nonspecific effect of the intervention on the electrogram can be excluded. Agents which alter the relationship between the amount of necrosis predicted (from a control group of animals) and that observed following administration of the agent can be said to alter the progression from ischemic injury to necrosis.\(^4,7,10,28,30\) (figs. 3-5).

Discussion of the limitations and potential difficulties of epicardial ST-segment mapping has centered on the following issues:

1) Does epicardial ST-segment elevation following coronary occlusion correlate with regional myocardial blood flow?

The experimental results bearing on this issue are mixed and have recently been summarized.\(^28\) Wegria et al., who were the first to note a relationship between coronary blood flow and epicardial ST segment elevation, found that a 10 to

---

**OCCLUSION ALONE**

**EXPERIMENT 305**

- **A** - **AREA OF ST SEGMENT ELEVATION**
- **B** - **SITE OF BIOPSY**

---

**TABLE**

<table>
<thead>
<tr>
<th>SITE</th>
<th>ST (mv)</th>
<th>CPK I.U./mg prot</th>
<th>HISTOLOGY</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0</td>
<td>25.2</td>
<td>NORMAL</td>
</tr>
<tr>
<td>B</td>
<td>0</td>
<td>21.0</td>
<td>NORMAL</td>
</tr>
<tr>
<td>C</td>
<td>3</td>
<td>7.2</td>
<td>ABNORMAL</td>
</tr>
<tr>
<td>D</td>
<td>7</td>
<td>4.0</td>
<td>ABNORMAL</td>
</tr>
<tr>
<td>E</td>
<td>7</td>
<td>3.7</td>
<td>ABNORMAL</td>
</tr>
<tr>
<td>F</td>
<td>8</td>
<td>5.9</td>
<td>ABNORMAL</td>
</tr>
<tr>
<td>G</td>
<td>6</td>
<td>6.4</td>
<td>ABNORMAL</td>
</tr>
<tr>
<td>H</td>
<td>5</td>
<td>4.5</td>
<td>ABNORMAL</td>
</tr>
</tbody>
</table>

---

**FIGURE 3.** Relationship between ST-segment elevation 15 min after occlusion and CK activity and histologic changes 24 hours later in a dog without an intervention. Left) Schematic representation of the anterior surface of the heart. L.A. = left atrial appendage; L.A.D. = left anterior descending coronary artery. The shaded area represents the area of ST-segment elevation after occlusion. The circles represent sites from which specimens were obtained. Right) Comparison of ST-segment elevation with CK activities and histologic analysis 24 hours later in the same sites (from Circulation 45: 1160, 1972).
reductions of tissue flow by more than 65% led to a mean ST-segment elevation of 2.7 mV while flow reductions of 20 to 65% of normal produced a mean ST-segment elevation of only 0.5 mV. Smith et al. found a weak negative correlation between regional myocardial blood flow, as determined by microspheres and epicardial ST-segment elevation 15 minutes after occlusion. The inclusion of sites with severe ischemia (< 10% of normal blood flow) which had no epicardial ST-segment elevation weakened the correlation. This could be expected since sites with such severe ischemia often demonstrate local conduction delay, which invalidates the ST segment as an index of ischemic injury. Becker noted a great variability in the relation between ST-segment elevation following occlusion and coronary flow but found a correlation between areas of high, medium and low flow and ST-segment elevation. Irvin and Cobb found considerable scatter in the relationship between ST-segment elevation 15 min postocclusion and blood flow as determined by microspheres 2 hr postocclusion (r = 0.057), but noted that with only one exception ST-segment elevation exceeding 2 mV did not occur unless blood flow was less than 50% of normal. Kjekshus found a correlation between the ST-segment elevation 15 min after occlusion and both subendocardial and subepicardial flow 24 hr later, although the correlation between the ST segment and subendocardial flow was not linear.

Since myocardial oxygen consumption varies from dog to dog, and in the same dog from moment to moment, and since coronary blood flow correlates very closely with myocardial oxygen consumption, it would be surprising if a close correlation existed between local blood flow and epicardial ST-segment elevation. The latter, of course, does not reflect a reduction in blood flow per se, but rather an imbalance between the supply of oxygen provided by the coronary circulation and myocardial oxygen demand. If, at any level of coronary blood flow, oxygen demand rose, myocardial ischemia would be intensified and ST segments would be expected to rise.

35% reduction of coronary blood flow usually failed to produce electrographic changes while a 35 to 70% reduction produced 1.0 or 2.0 mV ST-segment elevation with T wave inversions. A reduction in coronary flow greater than 70% always produced more than 2.0 mV ST-segment elevation with concomitant T wave changes. When regional myocardial blood flow was measured by the microsphere technique,
On the other hand, numerous studies have demonstrated a close linkage between epicardial ST-segment elevation and ischemic injury. Scheuer and Brachfeld studied the relationships between myocardial production of lactate and ST-segment elevation in dogs with externally controlled coronary flow.41 They observed that whenever ST-segment elevation was present, myocardial lactate was produced. As ischemia was made progressively more severe, the ST-segment changes generally lagged behind the onset of lactate production. Karlsson et al. noted that sites with ST-segment elevations had much higher tissue lactate concentrations in either the inner half (14.8 ± 2.5 vs 1.6 ± 0.5 μ moles/g wet weight) or the outer half (12.5 ± 1.9 vs 1.6 ± 0.4 μ moles/g wet weight) of the ventricular wall. The sites with ST-segment elevations also showed significantly less adenosine triphosphate and creatine phosphate.42

Sayen et al. compared changes in the epicardial electrogram with myocardial oxygen availability as determined by the polarographic method.28, 43 ST-segment elevation appeared in the center of ischemic zones when the oxygen availability fell to less than 65% of the control level. Angell et al., using polarographic techniques, also found a significant correlation between intramyocardial oxygen tension and epicardial ST-segment elevation and concluded that “minute to minute variations in local myocardial oxygen balance thus appear to reflect the magnitude of epicardial ST elevation.”44 Khuri et al. have utilized a mass spectrometer to study the relationships between intramyocardial ST-segment changes and local intramyocardial oxygen and carbon dioxide tensions in dogs with coronary artery occlusion. Reductions of oxygen tension and elevations of carbon dioxide tension were both found to correlate with local ST-segment changes.45 Thus, while some uncertainty over the precise relationship between ST-segment elevation and ischemia persists, there is impressive evidence linking elevation of the epicardial ST segment to various well accepted markers of ischemic injury.

2) When an area of ischemia is enlarged, does epicardial ST-segment elevation increase or decrease?

In several studies epicardial ST-segment elevation has been observed to increase when the area of ischemia is enlarged.3, 37, 38, 46 In canine experiments the epicardial ST-segment elevation produced by occlusion of a branch of the LAD increased when a proximal LAD occlusion was added.37 However, in a subset of animals in which the area of ischemia was enlarged, local intraventricular block occurred and ST-segment elevations decreased. These changes, which are analogous to the well known secondary ST-segment changes produced by left bundle branch block, occur in accordance with the ventricular gradient theory.47 When the QRS duration in the dog exceeds 65 msec or the interval from the Q to the onset of the intrinsic deflection exceeds 40 msec, the relationship between the ST segment and ischemic injury is altered and the height of the ST segment no longer varies with the severity of ischemia in the subjacent myocardium. In similar studies in dogs in which occlusion of a branch of the LAD was followed by occlusion of the proximal LAD, ST-segment elevation was reported to decrease when the area of ischemia increased but changes in QRS duration were not considered.48, 49

As a corollary to the latter observation, it has been reported that ST-segment elevation is lowest in the center of an area of ischemia and increases as the electrode is moved from the center to the periphery.48 This diminution of ST-segment elevation in the center of an ischemic zone has not been noted in most studies of the spatial distribution of ST-segment elevation.10, 11, 87, 86 However, it might be accounted for by local conduction delay in the center of the ischemic area leading to a paradoxical decline in ST segment elevation.39

3) What is the relationship between subendocardial ischemia and changes in the epicardial ST segment?

This relationship has recently been clarified by the work of Guyton et al.31 Circumflex coronary flow was gradually diminished in dogs instrumented with endocardial and epicardial electrodes. When coronary perfusion pressure was reduced to 70 mm Hg, ST-segment elevation occurred in the endocardial lead. When the perfusion pressure was further diminished, the endocardial ST-segment elevation increased and reciprocal epicardial ST-segment depression appeared. This change occurred when epicardial flow remained unchanged from control values. Only when coronary perfusion pressure was reduced below 40 mm Hg did ST-segment elevation appear in the epicardial recordings. It is apparent, therefore, that epicardial ST-segment elevation reflects a balance of unknown amounts of subendocardial ischemia producing reciprocal epicardial ST-segment depression and subepicardial ischemia producing epicardial ST-segment elevation. However, the fact that epicardial ST-segment elevation cannot be dissected into its component parts (primary epicardial ST-segment elevation minus reciprocal epicardial segment depression) does not invalidate its use to assess interventions since the recorded epicardial ST-segment elevation has been found to correlate well with the amount of necrosis found in myocardial biopsy specimens 24 hr later.4-7, 10, 30-82

4) Does reduction in ST-segment elevation indicate a salvage of ischemic myocardium or an accelerated progression from ischemic injury to necrosis?

A distinction must be made between a reduction in the height of ST-segment elevation during a second temporary occlusion in the same dog, and a decrease in ST-segment elevation following a sustained occlusion. In experiments with two sequential occlusions the development of a reduced amount of ST-segment elevation on the second occlusion may be taken to indicate a reduction of ischemic injury if nonspecific effects of the intervention on the electrocardiogram can be excluded. In experiments with a single fixed occlusion, it is impossible to determine from the early ST-segment changes alone if a reduction in ST-segment elevation indicates salvage of myocardium or accelerated necrosis. However, if the animal survives 24 hr and the amount of necrosis is determined from the myocardial CK activity and histologic appearance of myocardial biopsy specimens, salvage of ischemic myocardium can be differentiated from accelerated necrosis.

The experiments of Ergin et al. provide an opportunity for comparison of results of acute ST-segment mapping with direct measurement of completed infarct size.88 The LAD
was temporarily occluded in dogs and ST-segment elevation was measured 15 min postocclusion. One hour later the LAD was permanently occluded and ST-segment elevation was again measured 15 min postocclusion. In control animals the ST-segment elevation was not significantly different after each occlusion, while in animals given propranolol after the first occlusion the ST-segment elevation was markedly lower following the second. These ST-segment mapping results agreed with the results of direct measurement of the infarcted area several days later — 10.5 ± 2.2% by weight of the left ventricle in the propranolol group vs 18.5 ± 4.4% in the control group.

Additional support for the validity of ST-segment mapping as an index of alteration in myocardial damage is now available from the use of other techniques to evaluate infarct size. A method developed by Jennings et al. is based on histologic analysis of the amount of necrosis in the posterior papillary muscle of the dog following occlusion of the circumflex artery. Studies of the effect of propranolol on infarct size with this method produced results identical to those in a study of beta-blockade with the ST-segment mapping technique. A rat model of myocardial infarction has been developed in our laboratory which permits a quantitative assessment of infarct size totally independent of the electrocardiogram. In this model the left coronary artery of the rat heart is occluded and the size of the infarct measured 48 hr or 3 weeks later by analysis of the total CK activity of the left ventricle and the percent of the ventricle demonstrating histologic evidence of infarction. Studies in this model have demonstrated the effectiveness of hyaluronidase, cobra venom factor, an anticomplement agent, and glucocorticoids in limiting infarct size. These results are similar to and confirm those obtained in the dog with epicardial ST-segment mapping.

In summary, when appropriate attention is paid to its limitations, epicardial ST-segment mapping is a valuable technique which can be used to evaluate ischemic injury. It cannot be used in the presence of ischemia severe enough to produce local ventricular conduction delay. When accelerated necrosis or a nontoxic effect of the intervention on the electrocardiogram is a possibility, the 24 hour method with subsequent analysis of the subjacent myocardium must be employed along with acute ST-segment mapping. Finally, with the availability of totally different methods for assessing the efficacy of interventions designed to protect the ischemic myocardium, such as the rat model, results which support those obtained from ST-segment mapping in the dog have been obtained.

**Epicardial QRS Mapping**

It has been known since the work of Wilson and Prinzmetal and their respective collaborators that alterations in the epicardial QRS complex generally signify permanent changes in the subjacent myocardium. Kaiser et al. sought an electrographic method capable of detecting nonviable myocardium to assist with resection of scar tissue in patients with a ventricular aneurysm. Epicardial electrograms were recorded in 10 dogs from 10 days to one month postocclusion; the changes in the form of the electrogram were localized to tissue that demonstrated pathologic features characteristic of myocardial infarction. When it became evident that the extent of necrosis resulting from coronary occlusion could be modified, the relationship between early ST-segment elevations (an index of ischemic injury) and late QRS changes (an index of necrosis) was evaluated. It was found that the ST-segment elevation recorded 15 minutes following coronary occlusion was an excellent predictor of the development of epicardial Q waves 6 and 24 hr later (fig. 6). It was also demonstrated that these changes in the QRS complex could also be used to detect salvage of ischemic myocardium. The experiment was similar in design to the 24 hr ST-segment mapping method described previously, the sole difference being the recording of epicardial electrograms 24 hr following coronary occlusion, in addition to the analysis of myocardial histologic appearance and CK activity. In control (untreated) dogs there was a predictable relationship between the ST-segment elevation 15 min after coronary occlusion, and the development of Q waves and the loss of R waves (ΔQ + ΔR) 24 hr following occlusion (r = 0.81). A dose correlation was also present between ST-segment elevation 15 min after coronary occlusion and the development of Q waves 24 hr later (r = 0.83). Animals which received hyaluronidase or propranolol (agents shown in other studies to limit infarct size) demonstrated significantly less change (ΔQ + ΔR) than the control group. In addition, an extremely close correlation was present between the electrographic indices (ΔQ + ΔR) and tissue CK and histologic

![Figure 6](http://circ.ahajournals.org/)

**Figure 6.** The relationship between ST-segment elevation at 15 min following occlusion (ST<sub>15</sub>) and changes in QRS configuration at 24 hr ([ΔR + ΔQ]<sub>24h</sub>). The regression line for eight controls (continuous line) is: (ΔR + ΔQ)<sub>24h</sub> = (3.39 ± 0.75) ST<sub>15</sub> + (8.8 ± 1.9); N = 8, r = 0.81 ± 0.06. The regression line for eight hyaluronidase-treated dogs (dotted line) is: (ΔR + ΔQ)<sub>24h</sub> = (1.35 ± 0.37) ST<sub>15</sub> + (5.4 ± 1.7); N = 8, r = 0.60 ± 0.14. The regression line for the eight propranolol-treated dogs (dashed line) is: (ΔR + ΔQ)<sub>24h</sub> = (1.79 ± 0.41) ST<sub>15</sub> + (9.0 ± 2.5); N = 8, r = 0.68 ± 0.08. Note that for any level of ST<sub>15</sub> (ΔR + ΔQ)<sub>24h</sub> is less in the treated dogs than in the controls (P < 0.05), reflecting less myocardial necrosis. The values, which range from 8.1 to 60, indicate that the use of the technique should be confined to comparisons of groups of animals (from Circulation 54: 594, 1976).
appearance, the previously used markers of myocardial necrosis (fig. 7). The average correlation coefficient between \((\Delta Q + \Delta R)\) and tissue CK activity in eight dogs was found to be \(-0.86\). Ergin et al. have also demonstrated a close relationship between changes in the QRS complex four days following occlusion and the histologic evidence of cellular damage in the underlying myocardium.\(^{19}\)

The significance of epicardial QRS changes has also been studied in man. Kaiser et al. observed at operation that “in every instance in which the electrograms were clearly abnormal, excision of the tissue produced no bleeding from the cut surface.”\(^{20}\) Bodenheimer et al. studied the significance of the epicardial QRS recorded during cardiac operations in 25 patients who had previously undergone cardiac catheterization.\(^{21}\) During the catheterization two ventriculograms were obtained to identify segments of myocardium with asynergy which could be reversed by nitroglycerin. At the time of operation eight of the nine dyssynchronous segments which had improved with nitroglycerin showed initial R waves in the electrogram. Q waves were present in eight of the 11 dyssynchronous segments which failed to improve with nitroglycerin. A close relationship between epicardial Q waves and the presence of fibrosis in myocardial biopsy specimens has been observed.\(^{22,23}\) Local myocardial fibrosis, in turn, has been found to correlate well with the regional contraction pattern.\(^{24}\) This conclusion was reached after comparison of the amount of fibrosis in myocardial biopsy specimens obtained during coronary artery bypass surgery with the regional wall motion previously determined by ventriculography.

A potential difficulty in the analysis of R wave loss is the occurrence of a dramatic increase in R wave height sec-

ondary to a local conduction delay in areas of severe ischemia.\(^{25-27}\) In animal studies this difficulty can be overcome by use of the precocclusion R wave height for comparisons with the R wave height 24 hr later. If postocclusion QRS complexes are used as a baseline it is necessary to limit the application of this technique to sites at which such conduction delay does not occur or to record the height attained by the R wave prior to a fixed time (e.g., 60 msec) after the onset of the QRS complex. Sites excluded from R wave analysis should be analyzed for changes in Q wave development. If these sites were excluded entirely it would limit the utility of this method in detecting the effect of an intervention on the most severely ischemic areas.

The principal importance of these observations on the epicardial QRS complex is its validation as a marker of myocardial necrosis. They form a basis for the consideration of the use of surface leads.

**Precordial Electrocardiographic Mapping**

The exploration of the changes in precordial electrical potential produced by the heart began with the recording of the first electrocardiogram in man by Augustus Waller in 1889.\(^{28}\) The use of the surface electrocardiogram to characterize ischemia began with the observation by Pardee\(^{29}\) that a patient with acute myocardial infarction demonstrated ST-segment elevations in the standard limb leads. The correlation of a large Q wave in lead III with myocardial infarction was described by Fenichel and Kugell from a study of 35 autopsied cases.\(^{30}\)

The experimental and clinical basis for the use of the precordial electrocardiogram was presented by Wilson and colleagues in 1944.\(^{31}\) This classic paper presented the results of experiments in dogs and demonstrated "the close relation between the potential variations of a precordial electrode and the potential variations of the underlying ventricular surface." The electrocardiographic changes of anteroseptal, lateral and high lateral myocardial infarction were described, but no autopsy correlations were made. The relationship between the electrocardiographic changes and changes in the myocardium was studied by Myers et al. in a series of 161 autopsy cases. Patients who had developed Q waves in leads V\(_1\)–V\(_4\) were found to have anteroseptal necrosis.\(^{32}\) Patients with Q waves in V\(_3\)–V\(_4\) had necrosis in the anterolateral portion of the heart and those with pathologic Q waves in V\(_4\) and V\(_6\) only, were found to have necrosis in the lower lateral portion of the ventricle.\(^{33}\) \(^{34}\)

Another development in precordial electrocardiography of relevance to the need to assess changes in infarct size was the development of surface potential mapping. In 1963Tacardi utilized 240 precordial leads to demonstrate that multiple maxima and minima can exist on the precordial at any instant during the cardiac cycle.\(^{35}\) This finding supported Wilson's claim that the precordial leads yield information about local electrical events. Further development of isopotential surface maps permitted description of the movements of wavefronts through the heart and of the changes in the QRS complex following myocardial infarction.\(^{36}\) \(^{37}\) Thus, extensive experience with the precordial electrocardiogram and its close relationship to changes in the myocardium has been available to investigators searching
for a method to evaluate agents which could potentially limit infarct size.

**Precordial ST-Segment Mapping**

Early claims for the beneficial effects of an agent during myocardial infarction were made on the basis of the rapid normalization of ST-segment elevations in the standard 12 lead electrocardiogram,\(^\text{79, 80}\) even before the explicit development of the concept of the limitation of infarct size. The experimental foundation for the use of ST-segment elevations recorded from multiple precordial leads was established in 1972 in experiments in dogs with coronary artery occlusion.\(^\text{81}\) Interventions which caused an increase or decrease in epicardial ST-segment elevations produced similar directional changes in precordial maps. A 35 lead electrode blanket was devised to record precordial maps from patients with acute infarction. Several interventions, such as propranolol or intra-aortic balloon counterpulsation, resulted in rapid resolution of the precordial ST-segment elevation.\(^\text{82}\) The features of surface maps obtained with multiple precordial leads in patients with acute myocardial infarction were described and a reduction in ST-segment elevation following the administration of propranolol was reported.\(^\text{83, 84}\)

Recently, studies in dogs with simultaneously recorded epicardial and precordial maps have confirmed the presence of an extremely close relationship between changes in epicardial and precordial \(\Sigma ST\).\(^\text{85}\) Evidence indicating the sensitivity of precordial maps has also been obtained. In pigs, Capone et al. occluded the LAD in its midportion with a balloon-tipped catheter and recorded the total ST-segment elevation produced in a precordial map.\(^\text{86}\) They then withdrew the catheter an average of 1.6 cm to a more proximal location and again occluded the artery. The increase in the area of ischemia was reflected in a statistically significant increase in precordial ST-segment elevation.

In dogs, Abildskov and collaborators studied the precordial form of ventricular ectopic beats induced by stimulation of the heart with an epicardial electrode. Movement of the epicardial stimulation site by 1.5 cm produced easily recognizable changes in the form of VPBs in the precordial electrocardiogram.\(^\text{87}\)

Since patients with acute myocardial infarction ordinarily demonstrate progressive reductions of ST-segment elevation as a function of time alone, it is essential that results in a treated group be compared to results in a separate group of untreated control patients. This approach was employed in an investigation which demonstrated that patients with acute myocardial infarction who received hyaluronidase showed a significantly more rapid fall of ST-segment elevation than a control group.\(^\text{88}\)

Alternatively, the patient may be used as his own control; by this approach a control period is employed prior to the application of the intervention under investigation. Using this method it has been demonstrated that accelerated reductions in ST-segment elevation occur following intra-aortic balloon counterpulsation,\(^\text{89}\) propranolol plus intra-aortic balloon counterpulsation,\(^\text{90}\) propranolol alone,\(^\text{91, 86}\) nitroglycerin with and without phenylephrine,\(^\text{92, 93}\) and inhaled oxygen.\(^\text{94}\) An infusion of nitroprusside in patients with acute myocardial infarction was found to increase ST-segment elevation.\(^\text{95}\) The results of this approach are most persuasive when a postintervention control period is employed and the ST segments revert to their previous elevations. However, since it is possible that the beneficial effects of an intervention can persist after the intervention is terminated,\(^\text{96}\) it is not essential for a demonstration of efficacy that ST-segment elevation increase after cessation of treatment. ST-segment mapping has also been useful in detecting extensions of the original area of ischemic injury.\(^\text{81, 90, 97}\)

Since the technique of precordial ST-segment mapping has many limitations, it is not surprising that its use has led to differing assessments of its validity. Discussion has centered on a number of questions.

1) **How does the normal variability of the course of precordial ST-segment elevation during acute myocardial infarction affect the method?**

Large, rapid fluctuations in ST segment may occur in the course of infarction in individual patients without obvious cause\(^\text{98}\) and in a group of patients there is a progressive fall in the average ST-segment elevation as a function of time. The occurrence of these spontaneous changes in \(\Sigma ST\) precludes generalization from changes of ST-segment elevation in a single patient. However, conclusions can be drawn from comparison of ST-segment changes in groups of patients randomly assigned to control or treatment protocols. Alternatively, pre and postintervention control periods can be compared with the intervention period, as described above. Madias and Hood demonstrated the relative stability of mean \(\Sigma ST\) in a group of 28 patients with acute myocardial infarction. From 6 to 7 hours after onset of pain, mean \(\Sigma ST\) changed only slightly (from 65.8 ± 8.4 to 63.8 ± 8.7 mm).\(^\text{99}\)

2) **Does the sensitivity of precordial ST-segment elevation to stimuli other than a change in ischemic injury invalidate the method?**

Events which alter the conducting properties of the chest, such as the development of a pneumothorax, or which alter the relationship of the ST segment to ischemic injury, such as a change in plasma \([K^+]\) or the development of pericarditis, can cause nonspecific changes in precordial ST-segment elevation. These events must be actively searched for and when identified, the use of ST-segment mapping must be discontinued. Thus, frequent examinations can eliminate most cases of pericarditis, while inattention to this detail will tend to invalidate the results of ST-segment mapping. It is likely that the few remaining cases of nonspecific variation in ST-segment elevation which cannot be identified will occur in a random manner in both the control and the treated groups. When a specific intervention causes a change in ST-segment elevation unrelated to a change in ischemic injury (as may occur with glucose-insulin-potassium), the ST-segment mapping method should not be used.

The major value of precordial ST-segment mapping is to provide an index of changes in ischemic injury that can occur
within minutes of an intervention. When its use is confined to brief intervals of time, the effects of pericarditis or changes in plasma [K+] may be minimized.

3) How do differences in chest geometry affect the height of precordial ST-segment elevation?

The distance between the exploring electrode and the ischemic zone, and variations in chest thickness and configuration weaken the correlation between ST-segment elevation and other markers of infarct size. However, the precordial ST-segment mapping method has not been proposed as a method to measure infarct size, but rather as a method to determine if an intervention alters ischemic injury. The objective is to detect differences in the rate of resolution of ST-segment elevation between treated and untreated patients, or the immediate effects of the intervention using pre and postintervention control periods. These applications of the method largely negate the variations in ST-segment elevation due to variations in chest thickness and configuration.

4) What is the effect of changes in ST-segment elevation in other parts of the heart on precordial ST-segment elevation produced by anterior ischemia?

The surface electrocardiogram results from a balance of diversely oriented electrical forces. The posterior extension of an anterior infarct will reduce the ST-segment elevation in anterior leads. This difficulty can be avoided by restricting the use of ST-segment mapping to infarcts in which the boundaries of the ischemic injury can be encompassed. Thus, patients with concomitant acute anterior and posterior wall myocardial infarctions should be excluded from study by this method. A 35 lead precordial map utilized in several clinical studies extends from the left mid axillary line to the right sternal border horizontally and the length of the sternum vertically. This map completely encompasses the zone of ST-segment elevation of anterior infarctions.

5) Do initial or peak precordial ΣST correlate with other indices of infarct size?

Morris found that ST-segment displacement in the anterior or inferior leads 48 hr after the onset of the infarct correlated directly with maximum SGOT. In addition, a significant correlation was observed between ΣST and the area of an infarct as determined by pyrophosphate scan, although the relationship was curvilinear. However, Thompson et al. found poor correlations between ΣST and peak or estimated total CK released. A close quantitative relationship between ΣST and other indices of infarct size does not exist and would not be expected for several reasons. First, precordial ST-segment elevation is influenced primarily by one part of the heart (i.e., the anterior wall). Thus, if varying degrees of infarction occur in the other walls of the heart, they will not be detected by precordial mapping but will be measured by other methods such as serum CK activity. Second, as already mentioned, differences in the geometry of the chest and of the position of the heart within the chest of each patient will lead to varying degrees of precordial ST-segment elevation for the same degree of epicardial ST-segment elevation. Third, varying amounts of tissues with differing electrical resistances lie between the epicardial surface and the pericardium, further weakening the relationship. Finally, since ST-segment elevations may decline rapidly with time, variable intervals from onset of pain to the initial recording of the precordial electrocardiographic map will further diminish the correlation.

6) What is the relationship between precordial ΣST and clinical condition or prognosis?

No correlation between ΣST and radiographic evidence of pulmonary venous hypertension has been observed in a group of unselected patients including some with, and others without, a previous infarction. However, in another study in which patients without a previous infarction were analyzed separately, patients with higher ΣST on admission were found to have higher scores by the Killip classification for clinical condition. The division of patients with anterior infarction into groups with ΣST in the six precordial leads ≥ 0.5 mV or < 0.5 mV revealed that the former displayed a higher incidence of cardiac arrest, congestive heart failure, second or third degree A-V block, atrial fibrillation, shock, death, premature ventricular contractions and ventricular tachycardia. It has also been shown that increases in ST-segment vector magnitude during the course of a myocardial infarction presage new ischemic injury and sudden death. Despite these correlations, we believe that it is unlikely that the absolute value of the ΣST will prove useful as a prognostic indicator since it does not correlate well with infarct size, as indicated above. It may be useful, however, in patients in whom myocardial necrosis is limited to the anterior left ventricular wall.

7) What changes occur in precordial ST-segment elevation when an area of ischemia enlarges?

In dogs in which multiple epicardial and precordial leads were recorded simultaneously, the ΣSTs showed parallel changes when the area of ischemia was modified. In pigs, on the other hand, it has been reported that epicardial ST-segment elevation decreased while precordial ST elevation increased as an area of ischemia became larger. However, in that investigation only a single epicardial electrode was used, and it could have been strongly influenced by local events. In any event, clinical studies have shown that extension of infarction, as identified by re-elevation of serum CK and chest pain, is accompanied by an increase in precordial ST-segment elevation.

8) Does an accelerated rate of fall of precordial ST-segment elevation reflect reduction of ischemic injury or accelerated progression from ischemic injury to necrosis?

As already noted, reductions of epicardial or precordial ΣST due to salvage of ischemic tissue cannot be distinguished from accelerated necrosis by ST-segment mapping alone. However, although all the pharmacologic interventions that reduced ST-segment elevations were found...
to reduce necrosis and not to accelerate it, only an independent assessment of myocardial necrosis can confirm tissue salvage or necrosis. The close relationship between myocardial necrosis and changes in the QRS complex\textsuperscript{15,60} suggests the usefulness of analysis of the QRS complex in the interpretation of rapid resolution of ST-segment elevation.

In summary, when applied with appropriate controls and with attention to invalidating factors, precordial ST-segment mapping can produce helpful information concerning the efficacy of interventions designed to limit infarct size. Important additional information can be obtained with precordial QRS mapping, as described below.

**Precordial QRS Mapping**

This technique is based on the following three considerations:

1) QRS evolution following coronary occlusion is predictable.\textsuperscript{18,69}

2) Changes in the epicardial QRS correlate closely with the amount of necrosis observed in subjacent myocardial biopsy specimens.\textsuperscript{19-63}

3) Changes in epicardial potentials are closely reflected by changes in precordial electrical potentials.\textsuperscript{67}

With the use of these relationships, salvage of ischemic myocardium has been detected in dogs by precordial QRS mapping.\textsuperscript{107} A group of dogs in which an LAD occlusion was maintained demonstrated a greater loss of R wave voltage in precordial leads exhibiting ST-segment elevation than did a group of dogs in which ischemic myocardium was salvaged by early reperfusion (fig. 8).

The value of this method rests upon the accuracy with which the precordial QRS complex reflects the actual condition of the myocardium. It is therefore essential to review the evidence that the development of Q waves or loss of R wave voltage in the precordial leads indicates the development of myocardial necrosis. It is theoretically possible, and has been reported, that Q wave development may be reversible.\textsuperscript{108-111} In such instances, the Q wave cannot, by definition, serve as an index of necrosis. However, reversal generally occurs in Q waves which are present only a short time, i.e., less than several hours. In addition, in many instances Q waves may be lost when left anterior hemiblock or other conduction abnormalities develop.\textsuperscript{108,112} The number of instances in which early Q wave reversal occurs in the absence of a conduction change is extremely small and unlikely to influence mapping results in a large group of patients. Finally, it is well known that Q waves may disappear months or years after an infarction.\textsuperscript{112} This disappearance would not affect the use of QRS mapping as proposed here since the last ECG would be recorded only one week postinfarction, before this type of change could have occurred.

As has already been noted, epicardial R wave height may increase in severe ischemia secondary to local conduction delay. A similar though attenuated increase in R wave height also occurs in precordial leads,\textsuperscript{113} but can be recognized by a delay in the onset of the intrinsicoid deflection. Therefore, intraventricular conduction disturbances invalidate, or at the least cloud, the interpretation not only of the ST segment but also of the QRS complex.

Clinicians have long been aware of the close relationship between QRS changes in the precordial electrocardiogram and the condition of the underlying myocardium. In 1945 Rosenbaum, Wilson and Johnston\textsuperscript{114} described a patient with recurrent chest pain several days after an anteroseptal infarction; simultaneously QS complexes were noted to appear in leads V\textsubscript{4} and V\textsubscript{6}, and the R wave height fell in V\textsubscript{4}. They reasoned that "since the changes in the QRS complexes are now recorded from a much larger area, it is evident that the initial zone of infarction has grown larger by lateral extension." There is abundant autopsy evidence that abnormal Q waves are related to myocardial necrosis and scarring. As already mentioned, Myers et al. described an excellent correlation between the development of Q waves in specific precordial leads and the pathologic evidence of infarction in the corresponding regions of the heart.\textsuperscript{72,73} In a similar study comparing autopsy and electrocardiographic findings in 1184 patients, Horan et al.\textsuperscript{113} found 51 patients with Q waves > 0.03 sec in leads I, V\textsubscript{5}–V\textsubscript{6}. Forty-eight of these patients had autopsy evidence of infarction in the anterolateral myocardium, indicating the high specificity of Q waves in these leads for myocardial damage. Savage et al. recently compared QRS changes with infarct size as measured by planimetry in 24 patients who were found to have a myocardial infarction at autopsy.\textsuperscript{116} A loss of R wave voltage in V\textsubscript{4}–V\textsubscript{6} was found to indicate increasingly extensive infarction of the apex of the heart.

Correlations have also been noted between precordial Q waves and ventricular performance in patients with coronary artery disease. Miller found that patients with pathologic Q waves had significantly higher left ventricular end-diastolic pressures than patients without pathologic Q waves.\textsuperscript{117} Williams compared the location of asynchrony as determined by ventriculogram with the QRS signs of transmural anterior infarction and concluded that the electrocardiogram can be used as an index of the location and

**Figure 8.** Retention of R wave voltage as a sign of salvage of ischemic myocardium. In seven control dogs permanent occlusions were placed on two branches of the LAD and 30 lead precordial maps were obtained 15 and 60 minutes later. In the seven partially reperfused dogs, identical measurements were made but one of the two occlusions was released after the 15 minute map, salvaging a portion of ischemic myocardium. The mean fall of R wave voltage (\(\bar{R}\)) of sites with ST-segment elevations of 0.15 mV or greater 15 minutes after occlusion is shown. From 15 to 60 minutes postocclusion the group in which ischemic myocardium was salvaged, as documented by retention of myocardial CK activity and histologic appearance 24 hr later, showed significantly greater retention of R wave voltage (\(P < 0.05\)).
severities of ventricular wall lesions. In a similar study Miller found that the electrocardiogram reliably predicted the presence or absence of dysynergy in 88% (108 of 123) of patients with coronary disease.18 Furthermore, they found that in patients with anterior myocardial infarction, the most lateral precordial lead to which pathologic Q waves extended was related to the severity of dysynergy. In patients undergoing cardiac surgery it has been shown that precordial Q waves generally overlie epicardial Q waves and that epicardial Q waves indicate the presence of myocardial fibrosis.19 Awan et al. recently found a correlation coefficient of \(-0.87\) between the number of Q waves in a 35 lead precordial map and the angiographically determined ejection fraction.\(^{20}\) In addition, a correlation with one year mortality was found: less than 15 Q waves \(-9\%\), 15 to 25 Qs \(-19\%\) and 26 to 35 Qs \(-60\%\). An intervention which reduced the number of Q waves appearing in a precordial map could by inference be expected to have an effect on ventricular function and mortality. Although less attention has been directed to the relationship between the loss of R wave and ventricular function, the sum of R wave voltage in the precordial V leads has been demonstrated to correlate with the ejection fraction.\(^{21}\)

These considerations led to a study in patients with acute myocardial infarction of the relationship between ST-segment elevation in precordial leads on admission to the coronary care unit and subsequent changes in the QRS complex (R wave loss and Q wave development).\(^{22}\) Precordial leads with ST-segment elevation \(\geq 0.15\) mV on admission exhibited a 63.7 \(\pm\) 3.8% loss of R wave voltage over the ensuing five days. Four-fifths of this fall occurred during the first 24 hours after admission.

From these observations the following method of precordial QRS mapping is proposed for use in patients with acute myocardial infarction. First, precordial electrocardiograms from 35 sites on the patient's chest (a precordial map) are obtained as soon as the patient comes under observation. The patient is then randomly assigned to a control or treatment group. A second precordial map is recorded one week later in order to evaluate the changes of the QRS complex in the sites at risk (i.e., those sites which had exhibited ST-segment elevations on the first map), and the extent of the change in the control and treatment groups is compared. This method has been used to evaluate the effect of hyaluronidase in limiting myocardial necrosis in patients with acute myocardial infarction.\(^{23}\) Ninety-one patients with an anterior myocardial infarction who were studied within 8 hr of the onset of chest pain were randomly assigned to control or hyaluronidase treatment groups. Sites with ST-segment elevation \((\geq 0.15\) mV) on the initial ECG which exhibited an R wave were considered vulnerable for the development of electrocardiographic signs of necrosis. The sum of R wave voltages of vulnerable sites fell more in the control group than in the hyaluronidase group \((70.9 \pm 3.6\% \text{ vs } 54.2 \pm 5.0\%, P < 0.01)\). Q waves appeared in 59.3 \(\pm\) 4.9\% of the vulnerable sites in the control patients vs 46.4 \(\pm\) 4.9\% in the hyaluronidase patients \((P < 0.05)\). Sites with ST-segment elevation \(< 0.15\) mV on the first map also showed more favorable evolution in the treatment group. With hyaluronidase there was diminished loss of R wave voltage \((30.7 \pm 4.3\% \text{ vs } 39.7 \pm 4.0\%)\).

Derrida et al. have also used this method of QRS analysis to study the effect of nitroglycerin on the electrocardiographic signs of necrosis in patients with acute myocardial infarction.\(^{24}\) Forty-six patients with acute anterior myocardial infarction were randomly assigned to control or nitroglycerin treatment groups 10.1 \(\pm\) 0.9 hr after the onset of ischemia. The nitroglycerin group lost less R wave \((32.4 \pm 8.1\% \text{ vs } 64.0 \pm 12.7\%)\) and developed fewer Q waves \((30.0 \pm 7.3\% \text{ vs } 56.2 \pm 14.0\%)\) than the control group. An additional value of these studies is the demonstration that even with relatively small sample sizes, QRS mapping can be used to detect protection of ischemic myocardium.

In summary, it is possible to predict the evolution of the QRS complex of patients observed in the early phases of an acute myocardial infarction. Differences in evolution between a treated and control group can then be sought. There is strong evidence indicating that these changes in the QRS complex reflect changes in the extent of necrosis and viability of the underlying myocardium. These changes are related to localized wall motion, ventricular function, and less directly to morbidity and mortality.

**Technical Aspects of Precordial Mapping**

At the present time the use of mapping is so varied that each group of investigators using the technique can be identified by the number or types of electrocardiographic leads employed. Since improvement in the method is needed, this pluralistic approach is desirable and likely to aid its development. In the following section we will describe the mapping technique which we utilize, not to urge its universal acceptance, but to present an example of a method which has already been tested in a group of patients with acute myocardial infarction.\(^{25}\)

**Patient Selection**

The use of the method is restricted to patients with all of the following conditions: 1) an acute transmural myocardial infarction by clinical, standard electrocardiographic and enzymatic (determined retrospectively) criteria; 2) an interval of less than 8 hr from the start of the pain signaling the onset of ischemia; 3) acute anterior or lateral myocardial ischemia, as indicated by a total ST-segment elevation of at least 2.5 mV (25 mm at normal electrocardiographic standardization) in 35 precordial leads with at least five leads each having 0.15 mV or more of ST-segment elevation; 4) no evidence of left bundle branch block or QRS duration exceeding 0.10 sec on the initial ECG; 5) no record of pre-existing "persistent" ST-segment elevation; 6) no significant abnormalities of serum electrolyte concentration.

**Mapping Technique**

A commercially available* 35 lead electrode blanket is used to facilitate recording (fig. 9). Electrodes (Hewlett-Packard 14057) with felt attached are located in fixed positions in a grid of five horizontal rows with seven leads in each row. The electrode nearest the patient's head and right arm is placed in the second right intercostal space at the

---

*Manufactured by Mr. Richard Peters, 5 Janice Road, Stoughton, Mass. 02702.
right parasternal line. The distance between the first two vertical columns is 7 cm, and the distance between the other adjacent vertical columns is 4.5 cm. The distance between adjacent horizontal rows is 4 cm. The electrodes lead to a switch box which in turn is connected to a commercial electrocardiographic recorder through the "V" lead. The limb leads are connected in the routine manner. Since results are based on comparison between maps it is of the utmost importance that all maps be recorded from the same location of the individual patient's chest. To minimize shifts of location an outline of the borders of the map is drawn on the patient's chest.

A 0.1 mV standardization is placed at the beginning and end of each tracing. The six limb leads are recorded to detect changes in axis and conduction of the depolarization wave which could affect the precordial QRS complex. Each of the 35 precordial leads is then recorded sequentially. Three to four complexes which have a stable baseline and are free of interference are recorded from each lead; at least one complex is recorded at a paper speed of 50 mm/sec to facilitate analysis of Q wave width and the timing of the intrinsicoid deflection. Immediately after the first map is recorded the patient is randomized and treatment or placebo administered. One week later a second precordial map is recorded in identical fashion.

**Analysis of the Electrocardiographic Maps**

Patients who demonstrate an increase in QRS duration of greater than 0.02 sec between the two tracings or the appearance of fixed left anterior hemiblock or bundle branch block are excluded from analysis.

1) **ST-segment elevation.** The difference between the baseline (the TQ segment) and the ST-segment height (recorded 40 msec after the end of the QRS complex) in millivolts is recorded for each of the 35 sites.

2) **R wave loss.** The sum of R wave voltage ($\Sigma R$) is determined for sites with ST-segment elevation $\geq 0.15$ mV, for sites with ST elevation $< 0.15$ mV, and for all 35 sites in both tracings. The percentage fall in $\Sigma R$ between the two electrocardiograms is then determined for each of these three groups of leads.

3) **Q wave development.** The precise quantification of increases in Q wave depth is more complex for precordial than for epicardial leads because of occasional discontinuity in Q wave changes. In leads recorded from the area of $V_2$ and $V_4$, the total loss of a very small R wave can convert a deep S wave into a deep Q wave. This increase in Q wave depth is not directly comparable to an equivalent Q wave increase in $V_1$ or $V_6$. This difficulty can be minimized by the use of the scoring system described below. Another approach is to record the changes in the maximum negative deflection, be it an S wave or a Q wave.

The following scoring system has been developed to categorize and weigh the relative degree of necrosis indicated by various QRS configurations:

- **Score 0** = a QRS complex with normal appearance, i.e., Q wave $< 0.2$ mV and $< 40$ msec.
- **Score 1** = a decline in R wave amplitude by $> 0.2$ mV and $> 50\%$ from that recorded on the first map; Q wave $< 0.2$ mV and $< 40$ msec. By definition this score cannot be applied in analyzing the initial map.
- **Score 2** = a QRS complex with Q wave amplitude $\geq 0.2$ mV, duration $\geq 40$ msec, and a Q/R ratio $\leq 1.0$.
- **Score 3** = a QRS complex identical to that defined for a score of 2, except for a Q/R ratio $> 1.0$.
- **Score 4** = a QS complex.

The QRS complex from each of the 35 sites is assigned a score from 0 to 4 for the initial and final maps. The number of sites which demonstrate an increase in score by 1 or more and by 2 or more are determined for each patient. As with the percentage fall in $\Sigma R$, this calculation is made for sites with and without 0.15 mV ST-segment elevation on admission and for all sites regardless of the ST-segment elevation.

The final results of this analysis are expressed as a percentage fall in $\Sigma R$ and a percentage of sites with a change in score of 1 or more or 2 or more. These three indices are analyzed separately for sites with $\geq 0.15$ mV or $< 0.15$ mV ST-segment elevation on admission and without regard to ST-segment elevation (fig. 10). It is then possible to compare these quantitative descriptions of the QRS signs of necrosis for control and treated groups.

**Limitation of Method**

The greatest disadvantage of electrocardiographic mapping (ST and QRS) is its restriction to patients with transmural anterior or lateral myocardial infarction. In addition, patients must be free of significant intraventricular conduction defects. For QRS mapping the patient must sur-
After 1 Week

I II III aVR aVL aVF caL

%ΔR=100.0 %Δ score≥1=100.0 %Δ score≥2=100.0

FIGURE 10. An example of the use of 35 lead precordial electrocardiographic mapping to evaluate the development of myocardial necrosis in a patient with an anterior myocardial infarction. The sites with ST-segment elevation ≥ .15 mV on admission are outlined. Note the unfavorable progression from ischemic injury to necrosis with 100% loss of R wave voltage by 1 week of sites within the outline.

Another limitation of both QRS and ST mapping is that they provide information only about the response of the epicardial half of the anterior left ventricular wall to an intervention, and provide no direct information concerning the effect of an intervention on the subendocardium or of the posterior and diaphragmatic walls of the ventricle. This limitation may not be a serious one since interventions beneficial to one portion of the heart are likely to be beneficial to ischemic myocardium regardless of its location. Finally, electrocardiographic mapping in its present form does not yield quantitative results in terms of grams of myocardium infarcted or salvaged. Therefore, the demonstration of a difference in QRS evolution between two groups of patients cannot be translated into the actual amount of myocardium preserved. However, it can be concluded that an intervention which produces a favorable change in mapping results is more beneficial than one which fails to do so.

Future Development of Precordial Electrocardiographic Mapping

The precordial mapping method is still in an early stage of its development and numerous improvements are likely to
be made. First, it is probable that additional information can be gained from greater experience with the method as it is presently applied. For instance, multiple maps could be obtained after the onset of pain to define the rate of evolution of the QRS complex. It may also prove useful to compare the results of QRS measurements in patients with infarction with the known QRS variation in a normal population as has recently been reported for changes in the R/S ratio.\textsuperscript{126} In addition, analysis of absolute changes may well strengthen the linkage of QRS changes with measurements of ventricular function, and with morbidity and mortality from myocardial infarction.

Second, certain relatively straightforward modifications of the method are needed. For instance, it may well be that a substantial reduction in the number of leads will result in only a minimal loss of information. It must be determined if the inferior leads (II, III, aV\textsubscript{F}) are adequate for evaluation of diaphragmatic infarctions. Also, the value of computer techniques to measure the ST segment and the QRS complex and to analyze these measurements must be investigated. The use of a computer to analyze precordial ST-segment elevation has already been demonstrated.\textsuperscript{128}

Third, two approaches to mapping which differ from that described in this review may be of great value in the future. The ST-segment vector in the vectorcardiogram has been shown to correlate with 2ST derived from the scalar electrocardiogram in dogs and in patients with acute myocardial infarction.\textsuperscript{127, 128} This would offer a simplified method of following changes in 2ST. The vectorcardiogram has been shown to be superior to the scalar ECG in detecting asynchrony of the anterior wall of the heart.\textsuperscript{129} Indeed, the vectorcardiogram has been shown to be capable of detecting a 1 cm area of akinesia, as determined by ventriculography with a sensitivity of 85\%.\textsuperscript{130} Therefore, it is logical to study the use of analysis of changes in the QRS loop of the vectorcardiogram as a method of assessing the amount of myocardium infarcted.

An interesting use of precordial mapping has been the recording by McLaughlin et al.\textsuperscript{131} of the difference in the precordial isopotential distribution map before and one week following experimental coronary occlusion. This difference represents an electrical picture of the infarct. In clinical studies a pre-occlusion map is usually unavailable, but these investigators are now obtaining control maps on a large number of patients at high risk of developing a myocardial infarction. If appropriate serum CK measurements could be obtained during infarction, the maps obtained in these patients postinfarction could yield valuable information concerning the relationship between the electrical deficit produced by the infarction and the extent of loss of myocardial tissue.

Comparison of Precordial Mapping with Other Techniques

Two approaches other than precordial electrocardiographic mapping have been taken to assess changes in infarct size: the analysis of serum creatine kinase (CK) curves, as developed by Sobel and colleagues\textsuperscript{133-137} and radionuclide imaging of ischemic and infarcted myocardium.\textsuperscript{138, 139} Both methods have certain advantages over electrocardiographic mapping, but also have certain limitations which hinder their use in clinical studies.

**Serum CK curves can be used to measure or to predict infarct size.** Infarct size can be calculated from a knowledge of the level of serum CK activity, the rate of release of CK from the necrotic myocardium, the CK distribution space and the rate of disappearance of CK activity from the serum. However, a recent study in dogs with experimental myocardial infarction does not confirm the results of earlier investigators.\textsuperscript{140} In man it has been shown that infarct size calculated from CK curves conforms closely to infarct size measured morphologically at autopsy in patients who died of acute myocardial infarction.\textsuperscript{141}

Even if the conflict in the results of animal studies is disregarded two problems remain with the clinical use of this method to assess the effect of an intervention on infarct size: 1) the biologic variation in size of infarcts is so great that large numbers of control and treated patients are needed since patients do not serve as their own controls; and 2) interventions may alter the amount of CK released from infarcting tissue, giving a falsely elevated serum CK.\textsuperscript{142}

The number of patients required for a study can be markedly reduced by a modification of the serum CK method — the prediction method. With this method serum CK samples are collected for 7 hr prior to intervention. Each patient can then be used as his own control to project future changes in serum CK activity. Since serum CK levels do not begin to rise for about 3 hr after the onset of myocardial ischemia and since a delay of 7 hr from the start of CK elevation is required to permit prediction of the entire curve, the intervention to be evaluated cannot be applied until at least 10 hr after the onset of ischemia. By that time it is likely that most of the injured cells would have progressed to necrosis. An improvement in the CK method which is of benefit when a noncardiac cause of CK elevation is suspected is the measurement of the MB isoenzyme of CK which is specific for myocardial tissue.\textsuperscript{130, 142}

The CK method may also be used to assess the presence and size of extensions of infarction. It has recently been shown that propranolol attenuates the late rise in CK observed in approximately 50\% of patients with infarction.\textsuperscript{143}

The advantages of the CK method over precordial mapping as are as follows:

1) The CK method can yield quantitative results (if the intervention can be shown not to alter the fraction of CK released from infarcting myocardium) while mapping cannot.

2) The CK method can be applied to more patients than mapping, including those with diaphragmatic, posterior or subendocardial infarctions.

On the other hand, electrocardiographic mapping has certain advantages over the CK method:

1) With mapping, the intervention can be applied immediately after the initial electrocardiogram is recorded.

2) Each patient serves as his own control for the amount of necrosis expected, radically decreasing the sample size needed to detect significant differences between control and treatment groups.

3) Since the ECGs are recorded before and long after the intervention is administered, it is possible to prevent a temporary nonspecific effect of the intervention on the electrocardiogram from invalidating the results.

On the other hand, with the CK method samples could be
affected by the intervention since they are collected while it is being administered. The possibility that an intervention such as reperfusion during the collection period could alter the amount of CK released from infarcting tissue has been mentioned above.

Radionuclide techniques can also be used to assess myocardial ischemia and infarction. They are conveniently described as “cold spot” or “hot spot” methods. Following intravenous injection, cold spot agents, such as radio potassium and its analogs, are distributed in the myocardium in proportion to regional myocardial blood flow. Since there is limited distribution of the radioactive material to an ischemic area, an external detector demonstrates a cold spot of decreased radioactivity over the ischemic area in comparison to the activity recorded over well perfused areas.139 Many radiopharmaceuticals can be used to obtain cold spot myocardial images after intravenous injection.144–147 Among these, thallium-201 has emerged as the most promising because of its energy level, its long half-life, its avidity for normal myocardium and its ability to delineate a myocardial infarction within 6 hr of the onset of symptoms. Extensive use of thallium-201 has been limited by its high cost and limited availability.

In addition to potassium analogs, macroaggregated albumin,149, 150 radiolabeled microspheres,151 and xenon-133152–154 have all been used to identify areas of decreased myocardial perfusion. However, all three of these techniques require a direct intracoronary injection which limits their clinical usefulness. Finally, cold spot methods all measure areas of hypoperfusion rather than damaged myocardium and therefore are unable to distinguish areas of fresh ischemia from areas with reduced blood flow secondary to chronic scarring.

Hot spot imaging is based on the selective accumulation of an agent in ischemic and/or infarcted myocardium. Both 99mTc-tetracycline155, 156 and 99mTc-pyrophosphate157, 158 have been used to obtain direct images of myocardial changes caused by local ischemia. The resolution capabilities of currently available equipment hinder exact quantification of ischemic damage. The primary disadvantage of 99mTc-tetracycline is the 3-day interval from onset of ischemia to the optimal period for scanning. The use of 99mTc-pyrophosphate scans is complicated by accumulation of the agent in bone,158 false positive scans,159 accumulation of the agent in ischemic as well as infarcted myocardium160 and poor accumulation in areas of low flow. A major factor limiting the quality of imaging techniques is the distortion produced by representing a three-dimensional space on a two-dimensional plane. All of the cold spot and hot spot techniques presently available have limitations of resolution, repeatability, or interpretation which limit their present value for clinical studies of limitation of infarct size.

Several new imaging techniques have been employed in experimental animals. These have not yet been applied clinically but are mentioned here because they hold substantial promise for the future. Radiiodidine-labeled antibodies to myosin selectively accumulate in infarcted myocardium and can be used to obtain images of the infarction.161, 162 Also, emission computerized tomography (CT) can be used to obtain images of ischemic or infarcted myocardium. Positron-emitting monovalent cations with extremely short half-lives can be used for sequential determination of myocardial blood flow.163 Substrates such as 11C-labeled glucose,164 octanoate, and palmitate,165 and 13C-labeled amino acids,166 can be used to assess the integrity of certain well understood metabolic pathways, if it can be determined that failure of uptake occurs because of cellular injury and not because of low flow. A major disadvantage of these techniques is the requirement for cyclotron-produced radionuclides.

Finally, transmission CT may be of great value for the noninvasive evaluation of infarcting myocardium. In the nonbeating heart, with the problem of cardiac motion eliminated, transmission CT can be used to distinguish between normal myocardium, edematous ischemic myocardium and dense necrotic myocardium.166, 167 Transmission CT or radionuclide techniques168, 169 may also be useful for obtaining sequential measurements of an index of left ventricular function, such as the ejection fraction in patients with myocardial infarction.

Acknowledgment

We are grateful for the assistance of Patricia Kadlick in the preparation of this manuscript.

References

1. Braunwald E (ed): Symposium on Protection of the Ischemic Myocar-
dium. Circulation 53 (suppl I): 1–1, 1976
2. Sobel BE, Brensahan GF, Shell WE, Yoder RD: Estimation of infarct
3. Maroko PR, Kjekshus JK, Sobel BE, Watanabe T, Covell JW, Ross J,
Braunwald E: Factors influencing infarct size following experi-
4. Maroko PR, Libby P, Sobel BE, Bloor CM, Sybers HD, Shell WE,
Covell JW, Braunwald E: The effect of glucose-insulin-potassium in-
fusion on myocardial infarction following experimental coronary artery
occlusion. Circulation 45: 1160, 1972
5. Maroko PR, Libby P, Bloor CM, Sobel BE, Braunwald E: Reduction
by hyaluronidase of myocardial necrosis following coronary artery
Reduction of experimental myocardial infarct size by corticosteroid
7. Kjekshus JK, Mjøls OD: Effect of inhibition of lipolysis on infarct size
after experimental coronary artery occlusion. J Clin Invest 52: 1770,
1973
8. Reimer KA, Rasmussen MM, Jennings RB: Reduction by propanolol
of myocardial necrosis following temporary coronary artery occlusion
tion in the canine heart. Arch Pathol 97: 380, 1974
Reduction in severity and extent of myocardial infarction when nitro-
glycerin and methoxamine are administered during coronary occlusion.
Circulation 49: 291, 1974
11. Epstein SE, Kent KM, Goldstein RE, Borer JS, Redwood DR: Reduc-
tion of ischemic injury by nitroglycerin during acute myocardial infarc-
12. Smith FM: The ligation of coronary arteries with electrocardiographic
study. Arch Intern Med 22: 8, 1918
13. Wilson FN, Macleod AG, Baker PS, Johnston FD, Klostermeyer LL:
The electrocardiogram in myocardial infarction with particular refer-
ce to the initial deflections of the ventricular complex. Heart 16:
155, 1933
in experimental MI. II. The early effects produced by ligation of the
anterior descending branch of the left coronary artery. Ame Heart J 10:
889, 1934
15. Prinzmetal M, Kennamer R, Maxwell M: Studies on the mechanism of
ventricular activity. VIII. The genesis of the coronary QS wave in
16. Maxwell M, Kennamer K, Prinzmetal M: Studies on the mechanism of
ventricular activity. IX. The mural-type coronary QS wave. Am J Med
17: 614, 1954
17. Shaw CMcK Jr, Goldman A, Kennamer R, Kimura N, Lindgren I,
Maxwell MH, Prinzmetal M: Studies on the mechanism of ventricular
activity. VII. The origin of the coronary QR wave. Am J Med 16: 490,
1954
and pathologic findings in anteroseptal infarction. Am Heart J 36: 535, 1948


107. Muller JE, Maroko PR, Braunwald E: Use of precordial R wave mapping to detect changes in myocardial ischemic injury. (abstr) Am J Cardiol 35: 159, 1975


118. Williams RA, Cohn PF, Yokonas PS, Young E, Herman MV, Gorlin R: Electrocardiographic, arteriographic and ventilographic cor- relations in transmural myocardial infarction. Am J Cardiol 31: 595, 1975


121. Askenazi J, Freedman WB, Cohn PF, Braunwald E, Parisi AF: The predictive value of the QRS complex in assessment of left ventricular function. (abstr) Circulation 54 (suppl II): 11-125, 1976


158. Lesch M, Tanaka T, Holman BL: Comparative accuracy of 99mTc pyrophosphate, 99mTc-tetracycline, and 99mTc-glucoponate for the scintigraphic diagnosis of acute myocardial infarction. (abstr) Circulation 52 (Suppl II): II-51, 1975


Precordial electrocardiographic mapping. A technique to assess the efficacy of interventions designed to limit infarct size.
J E Muller, P R Maroko and E Braunwald

Circulation. 1978;57:1-18
doi: 10.1161/01.CIR.57.1.1

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1978 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/57/1/1.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/