ST-Segment Mapping
Realistic and Unrealistic Expectations

DURING THE LAST FEW YEARS considerable interest has developed in the possibility that some of the myocardial damage consequent to coronary occlusion may be averted. To explore this possibility there is a critical need for techniques capable of testing the hypothesis that a given intervention is capable of protecting ischemic myocardium. Since it has long been appreciated that myocardial ischemia produces changes in the ST segment, it was natural to attempt to utilize this portion of the electrocardiogram as an index of ischemic injury. The purpose of this editorial is to review the electrophysiologic basis for deviation of the ST segment and to place into perspective its potential value and limitations in assessing the efficacy of interventions designed to limit infarct size.

In 1920, Pardee directed attention to this portion of the electrocardiogram when he described elevation of the ST segment as a clinical sign of myocardial ischemia following coronary occlusion. Wilson, Bailey, Rakita and their respective collaborators noted that following experimental ligation of a coronary artery, epicardial leads showed ST-segment elevation. Sometimes ST-segment depressions occurred at the junction of the cyanotic and normal zones.

The electrophysiologic basis of changes in the ST segment in myocardial ischemia has not been completely clarified, and there is a great need to obtain an electrical model of the sequential changes that take place from the onset of ischemia to the stage of chronic infarction. It has been postulated that following repolarization of normal tissue the resting membrane potential of ischemic cells is lower than that of normal cells and for this reason a "current of injury" flows across the boundary between the normally polarized region and the ischemic zone. According to this concept this current disappears when the entire heart is depolarized during excitation and the elevated ST segment results from a depressed T-Q segment.

It has also been suggested that ST-segment elevation may occur as a result of failure of the injured area to depolarize during excitation, which results in current flow during depolarization across the boundary between the partially polarized, injured region and the depolarized normal zone.

A closely related possible mechanism of ST-segment elevation is an altered waveform of the transmembrane action potential of ischemic tissue, with loss of the normal plateau portion so that current flows between such an area and normal tissue during inscripation of the action potential.

Conventional electrocardiographic techniques prevent differentiation of downward displacements of T-Q segments from elevations of ST segments; both phenomena appear as ST-segment elevations. Recent studies using the magnetocardiogram have shed light on the genesis of ST-segment elevations. This approach allows the recording at the body surface of magnetic fields produced by the ionic currents in the heart, and can be used to detect both depolarization and the flow of direct current without the difficulty usually encountered in conventional electrocardiography. Coronary occlusions in closed chest dogs result in the appearance of a steady direct current magnetic field, of opposite polarity to the simultaneously occurring ST-segment elevations. These findings would appear to indicate that the major change after coronary occlusion is a flow of diastolic injury current that lowers the T-Q segment, producing apparent ST-segment elevation. The magnetocardiogram also revealed some shortening of the duration of the transmembrane action potential or failure of normal depolarization in the ischemic zone which is polarized in resting muscle, indicating the participation of true ST-segment shifts.

It is likely that alterations in the permeability of myocardial cell membranes, which modify ion transport and thereby alter the magnitudes of the resting potential, the transmembrane potential during the plateau, and the voltage time course of repolarization represent the ultimate cause of the ST-segment shift during acute myocardial ischemia.

It is critical to recognize that factors other than ischemia can affect the ST segment. These changes in the electrical activity of nonischemic cells include, but are not limited to, alterations in pH and ion concentrations, temperature changes, drugs such as quinidine and digitalis, the development of localized intraventricular conduction defects (a common occurrence in severe ischemia), sympathetic stimulation of the heart and epicardial injury due to pericarditis. Consequently, it would be misleading to attribute changes in ST segments exclusively to alterations due to ischemia. However, at a time when a noninvasive, easily applicable method for the assessment of myocardial...
ischemia in patients is sorely needed, it is important to recognize that the ST segment is influenced profoundly by the perfusion of the myocardium. Indeed, a wealth of data indicate the sensitivity and usefulness of the ST segment in this regard, and it is appropriate to review this information.

In 1949, Wegria first reported on the correlation in experimental animals between ST-segment changes in the electrocardiogram and coronary blood flow. Reduction in flow by two-thirds or more always produced marked ST-segment changes, while minor changes occurred when coronary blood flow was reduced by between one-third or two-thirds of control; no changes were noted with reductions in coronary flow by less than one-third. Becker et al. measured regional myocardial perfusion with radioactive microspheres and correlated the results with epicardial electrogroms. ST segments were substantially elevated in most, though not all, sites overlying low flow zones. Smith et al. also noted a significant correlation between epicardial ST-segment elevation and blood flow reduction, but no precise correlation or simple quantitative relation between ST-segment elevation and reduction in total or subendocardial coronary blood flow occurred early after coronary occlusion. In contrast, Kjekshus et al. reported a linear relation between the degree of ST-segment elevation recorded 15 min after coronary occlusion and reductions in subepicardial blood flow measured 24 hours after coronary occlusion. However, the relation between ST-segment elevation and the reduction in subendocardial blood flow was not linear. Indeed, it would be surprising if there were an excellent correlation between ST-segment elevation and coronary blood flow under a wide variety of circumstances since the severity and extent of ischemic injury are dependent not only on myocardial perfusion, but also on myocardial oxygen needs, i.e., on the balance between supply and demand.

The correlations between ST-segment changes and myocardial metabolism have been examined in several studies. When global ischemia of the left ventricle was produced, ST-segment changes occurred almost simultaneously with the first biochemical indices of ischemia, i.e., reduction of myocardial lactate extraction and efflux of K+ from the heart. In a correlation of epicardial ST-segment changes with metabolic alterations in the underlying myocardium following occlusion of the anterior descending coronary artery in dogs, Karlsson found that at sites with definite ST-segment elevations, biopsies showed lactate accumulation, as well as depletion of ATP and creatine phosphate. This study indicated that ST-segment elevation reflected subendocardial and subepicardial ischemia with anaerobic metabolism. Sayen et al., using polarographic measurements of intramyocardial oxygen tension, found that ST-segment elevations in the epicardial electrocardiogram promptly followed reduction of oxygen tension below 65% of control. More recently, Angell et al. compared the magnitude of ST-segment elevations in surface electrograms with the intramyocardial oxygen tension in the subjacent tissue recorded by means of platinum-iridium electrodes. The ST map correlated closely with the oxygen tension as the latter was varied by altering coronary perfusion pressure. In a similar investigation, Khuri and associates varied coronary blood flow and recorded myocardial PO2 and pCO2 using a mass spectrometer. When regional ischemia was produced, epicardial ST-segment elevations correlated with changes in myocardial gas tensions. However, intramyocardial ST segments proved to be even more sensitive than those recorded from the epicardium.

We have noted consistently in the open-chest anesthetized dog that epicardial ST-segment elevation recorded shortly after occlusion of the left anterior descending coronary artery, or one of its major branches, is an excellent predictor of the loss of myocardial viability, as judged by histologic appearance as well as depletion of cardiac creatine phosphokinase (CPK) activity 24 hours later. A linear inverse correlation was found between the log of myocardial CPK activity and the degree of local ST-segment elevation. Myocardial CPK activity has been found to be reduced 24 hours following occlusion whenever epicardial ST-segment elevation exceeded 2 mV 15 min following occlusion. In some sites where mild ST-segment elevation of 1 to 2 mV had been present, CPK was normal in the subepicardial regions while subendocardial CPK depletion occurred 24 hours later. Thus, it is apparent from this observation, as well as the aforementioned correlations of the epicardial and intramyocardial ST segment with myocardial gas tensions, that a limitation of the epicardial ST-segment measurement is its relative insensitivity to the more extensive subendocardial ischemic damage. A linear relation was found between local myocardial blood flow and log CPK activity 24 hours after coronary occlusion for both the subendocardial and subepicardial samples.

Unipolar epicardial ECG maps, recorded from fixed sites, both in the open-chest dog and in the conscious closed-chest dog, can be used to detect changes in the size of an ischemic region. We have found that epicardial ST-segment elevations and their sum in a number of leads (ΣST) are quite reproducible during serial coronary occlusions, with intermittent periods of reflow. Hirshfeld and associates have also found an excellent correlation between intramyocardial ST-segment elevations and myocardial CPK depletion 24 hours later. Furthermore, the acute ST-segment elevation 15 min after coronary occlusion correlates not only with CPK depletion at 24 hours, but also with the extent of myocardial damage determined by histologic and electron microscopic examination one day or one week later.

In our studies, the efficacy of an intervention designed to minimize myocardial ischemic damage following coronary occlusion has been based on observing significantly less morphologic damage and reduction of CPK activity 24 hours following coronary occlusion for any level of ST-segment elevation occurring immediately after coronary occlusion, compared with those in nontreated controls. This approach has been extended to precordial electrocardiograms in the closed-chest dog and pig. Despite theoretical objections, a close correlation has been found between ΣST from epicardial and precordial leads during acute interventions. Furthermore, both precordial and epicardial ST-segment shifts soon after coronary occlusion predict myocardial CPK activity measured 24 hours later. The exact relation between precordial and epicardial ΣST varied for each dog but in general the precordial electrocardiogram was less sensitive than the epicardial electrocardiogram in detecting ischemia. Capone et al., however, have reported that even slight changes in the pig in the severity of ischemia were readily recognized in the precordial ΣST.
sence of other changes capable of influencing the ST segment (e.g., electrolyte concentration, intraventricular conduction disturbance, sympathetic stimulation, pericarditis). ST-segment elevation recorded directly at a given epicardial site reflects ischemia of the subjacent myocardium, and that when such elevation is present 15 to 20 min after the onset of a permanent coronary occlusion, some degree of myocardial damage will be encountered 24 hours or more later unless a favorable intervention is interposed. However, it must be noted that the epicardial lead appears to be a rather insensitive detector of ischemia, when the latter is limited to the subendocardium. The sensitivity of the method is further reduced when ST segments are recorded from the precordium. In precordial leads interpretation is complicated by the effects of reciprocal changes in the ST-segment vector and the lack of homogeneity of the conducting medium between the voltage generator and the recording electrode.

Since the site and number of leads used for ST-segment mapping in experimental animals have been arbitrary and the topographic relation between the infarct and the location of the recording leads has not been fixed, the epicardial or precordial ST-segment map cannot be expected to provide precise information concerning the absolute size of an area of ischemic injury. For example, a large zone of ischemia in the posteroinferior region of the left ventricle might produce ST-segment depression only in anterior epicardial or precordial leads, while a smaller ischemic zone in the anterolateral region of the left ventricle might result in ST-segment elevations in precordial leads. Therefore, it is unrealistic to expect absolute infarct size, or infarct size as estimated by enzyme release into blood or radionuclide scanning, to correlate well with the precordial or the epicardial ST-segment map in its current state of development. The precordial and epicardial maps can provide information concerning the zone of injury and its rate of resolution, while other techniques such as CPK washout and radionuclide scanning provide totally different information. However, with the more extensive and systematic sampling of the epicardium or precordium, it is possible that these methods might provide some useful information about infarct size.

Precordial ST-segment mapping provides a useful noninvasive approach for the assessment of acute directional changes in ischemic injury that appears to be a reliable clinical indicator of particular therapeutic interventions. More rapid reductions of ST-segment elevations were observed in patients with the inhalation of oxygen and the use of drugs such as hyaluronidase, nitroglycerin (with and without phenylephrine), as well as with intra-aortic balloon counterpulsation, than in untreated patients. The same interventions have been shown to reduce infarct size in experimental animals, and these changes in the ST segment appear to correlate well with the salvage of myocardium.

The interpretation of accelerated resolution of ST-segment elevations in patients by various modes of treatment will ultimately require correlation with other measurements of the size of the damaged region. One such measure that is readily available clinically is the QRS complex. A reduction in the electromotive force of the epicardial R wave within four hours of experimental coronary occlusion was first demonstrated by Wilson and his associates. Later it was demonstrated that a reduction in epicardial R wave voltage was found at sites in which ischemia produced a mixture of viable and necrotic myocardium, as determined by histologic study. To apply this method clinically, we would propose to use the precordial ST segment soon after the onset of the clinical event as a predictor of the ultimate fate of the tissue, in a manner analogous to the epicardial ST segment in the experimental animal. This precordial ST segment, recorded soon after the clinical event, may then be compared to the changes in the QRS complex that occur subsequently such as the developing or deepening of Q waves and the reduction of R waves; these changes in the QRS complex could then be employed in a manner analogous to the alterations in CPK activity or histological appearance of the myocardium subjacent to the epicardial electrode in the experimental animal. Indeed, recent experiments in our laboratory have confirmed the existence of a very close correlation between changes in the QRS complex of epicardial leads and of myocardial CPK activity.

The further refinement of electrocardiographic techniques for the assessment of the efficacy of interventions designed to reduce infarct size is a fruitful area of future research. For example, vectorcardiographic methods or isopotential mapping may provide additional information not readily available in the ordinary scalar precordial electrocardiograms. Regardless of which recording techniques are utilized, however, ST-segment mapping should be utilized only with a clear appreciation of how it can be influenced by factors other than ischemia. It should not be used in isolation but in conjunction with other methods of assessing tissue injury such as analysis of changes of the QRS complex. Nevertheless, until more accurate and convenient methods for assessing ischemic injury have been developed and validated, changes in ST segments are likely to continue to provide extremely helpful information concerning the presence and extent of ischemic damage of the myocardium, both in experimental animals and in patients.

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