Epicardial Activation in Patients with Coronary Artery Disease: Effects of Regional Contraction Abnormalities

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SUMMARY  To determine the correlation of regional contraction abnormalities with ventricular activation in patients with coronary artery disease, intraoperative epicardial mapping was performed in 24 patients who underwent surgery for coronary artery disease. The results were compared with ventriculographic findings. Nine patients had normally contracting ventricles, five had areas of hypokinesis and 10 had areas of akinesis or dyskinesis. Four patients with asynergy had documented ventricular tachycardia or fibrillation. The earliest epicardial activation occurred in the anterior right ventricle in patients with and without asynergy. Each patient with normal contraction or areas of hypokinesis had two left ventricular epicardial breakthrough sites, whereas patients with areas of akinesis or dyskinesis had an average of 1.2 ± 0.6 left ventricular epicardial breakthrough sites (p < 0.05). Breakthrough did not occur in areas of akinesis or dyskinesis. The latest epicardial activation occurred at the base of either ventricle in all patients with normal ventricles or areas of hypokinesis, but in only four of 10 patients with akinesis or dyskinesis, the latest activation was over an abnormally contracting segment. Regional activation time in hypokinetic zones was not significantly different from that in normal zones, but was significantly delayed in akinetic and dyskinetic zones. Among patients with asynergy, there was no difference in epicardial activation pattern between those with and those without malignant arrhythmias. We conclude that akinesis and dyskinesis, but not hypokinesis, are associated with marked changes in epicardial activation patterns.

THE SPREAD of electrical activation through the human heart has been studied in reperfused hearts and by electrical mapping at surgery. 1-3 These studies attempted to describe and quantitate the range of normality in epicardial activation sequence. Although several investigators have described delay of ventricular activation over ventricular aneurysms,4-6 there are few data, in a cross section of patients with coronary artery disease, on the effects of ventriculographic abnormalities on the pattern of ventricular activation. We performed epicardial mapping in 24 patients with coronary artery disease and correlated the electrophysiologic and ventriculographic findings.

Methods

Patients  
The clinical and electrocardiographic features of the 24 patients who underwent epicardial mapping are summarized in Table 1. There were 22 males and two females, mean age 52.9 ± 10.8 years. No patient had an intraventricular conduction defect, coexisting valvular heart disease, acute myocardial infarction or an acute ischemic syndrome. No patient was receiving antiarrhythmic medication. Patients 15, 19, 20 and 22 had a history of ventricular tachycardia or fibrillation that occurred without an acute cause.

Catheterization  
All patients underwent diagnostic catheterization by the Sones or Judkins technique before surgery. Ventriculography (40 ml of Renografin) was performed in the 20% right anterior oblique projection. All ventriculograms were reviewed by an independent observer. Only nonpotentiated beats in normal sinus rhythm were analyzed. Regional wall motion was analyzed by dividing the left ventricle as seen in the right anterior oblique projection into five segments (anterobasal, anterior, apical, inferior and inferobasal). Wall motion was classified as normal, hypokinetic, akinetic or dyskinetic according to established criteria.7,8 Akinetic and dyskinetic segments were analyzed together.

Epicardial Mapping  
The patients underwent operation through a median sternotomy. Mapping was performed during stable sinus rhythm, after cannulation of the great vessels, but before the institution of cardiopulmonary bypass. Simultaneous recordings were made of three body surface ECG leads, a bipolar reference ventricular electrogram and a bipolar electrogram from the exploring probe. The reference electrode consisted of two stainless-steel electrodes sutured to the anterior right ventricular wall. The roving electrode consisted of two silver electrodes embedded 2 mm apart in a plastic mesh.

Bipolar electrograms were recorded from 40-66 predetermined epicardial sites. Five to 15 right ventricular sites and 35-51 left ventricular sites were studied in each patient. Signals were isolated, amplified and recorded at a paper speed of 200 mm/sec on an Irex multichannel oscilloscopic recorder. Surface leads...
were recorded at 0.1–40 Hz and epicardial leads at 40–500 Hz. Mapping was completed within 5 minutes in each patient, and heart rate and QRS morphology remained stable throughout. No complications resulted from the mapping procedure.

Measurements were performed from the peak of the major deflection of the reference electrogram to the peak of the major deflection of the electrogram from the roving electrode. The interval from the earliest onset of the QRS in the body surface leads to the reference electrogram was added to the interval from the reference electrogram to the roving electrogram to determine local activation time. Local activation times were calculated as the mean of five to 10 beats in stable sinus rhythm. Measurements were considered accurate to within 5 msec, and measurements of individual beats at a given site were always within that range.

Epicardial breakthroughs were defined as sites of emergence of a radially propagating wave front at the epicardial surface, providing an island of early activation, completely surrounded by points of later activation. The latest epicardial activation was considered the site of latest recordable ventricular activation.

Each ventriculographic segment was correlated with the mapping grid. The correlation was verified by noting the contraction of the segments during the mapping procedure. Four to six epicardial points were recorded from each ventriculographic segment. The average epicardial activation time for a given myocardial segment was taken as the average of the activation times of the points corresponding to that segment. Activation times of sites within each segment were within 10 msec of each other.

Statistical analysis between the groups with normal, hypokinetic and akinetic or dyskinetic segments was done by analysis of variance. The unpaired t test was used to analyze pairs of groups.

Results

Ventriculographic Findings

Nine patients had normally contracting ventricles and 14 patients had areas of asynergy on ventriculography. The patients with asynergy included five patients whose most severe abnormality was hypokinesis, and 10 patients with at least one zone of akinesis or dyskinesis.

Electrophysiologic Findings

Examples of electrograms from two patients are shown in figures 1 and 2. Representative epicardial maps from three patients are shown in figures 3, 4 and 5. The ventriculographic and electrophysiologic data from all patients are summarized in table 2.

**Figure 1.** Epicardial recording from a patient with coronary artery disease and normal ventricular contraction. Surface leads I, II and III are displayed, followed by a bipolar recording from the reference electrode and from the probe. The paper speed was 200 mm/sec.
Epicardial Breakthrough

Normal Ventrices

In each patient with normal ventricular contraction, the earliest epicardial breakthrough occurred in the anterior paraseptal right ventricle. One patient had an additional breakthrough in the inferior right ventricle. Each patient had two subsequent breakthrough points on the left ventricular surface. The sites of breakthrough varied from patient to patient, but in each patient one breakthrough was in the anterior or anterolateral area and another was in the inferior or inferolateral area. Figure 3 is an epicardial map from a patient with normal ventricular contraction.

Ventricles with Areas of Hypokinesia

Five patients had ventricles that were normal except for one or more areas of hypokinesia. In each patient, the earliest epicardial breakthrough was in the anterior paraseptal right ventricle, followed by two left ventricular breakthrough points. The sites of breakthrough varied from patient to patient, but in each patient one breakthrough was in the anterior or anterolateral area and a second was in the inferior or inferolateral area. Figure 4 is an epicardial map of a patient with areas of hypokinesia. The pattern of epicardial breakthrough did not appear to be altered in ventricles with areas of hypokinesia.

Ventricles with Akinesis and Dyskinesia

Ten patients had more severe asynergy, including at least one area of akinesis or dyskinesia. In each patient, the earliest epicardial activation was in the anterior paraseptal right ventricle. One patient had an additional breakthrough site in the inferior right ventricle. The 10 patients with areas of akinesis or dyskinesia had an average of 1.2 ± 0.6 left ventricular breakthrough sites (p < 0.05 vs patients with normal ventricles or areas of hypokinesia). One patient had no left ventricular breakthrough points, six patients had single left ventricular breakthrough sites, and three had two left ventricular breakthrough sites.

The data on individual patients are presented in Table 2. Four patients had breakthrough sites in the anterior or anterolateral left ventricle, three with normal or hypokinetic anterior walls and one patient with akinesis of the anterior wall who had a breakthrough in a normally contracting anterobasal segment. Of six patients with no anterior wall breakthrough points, five had anterior wall akinesis or dyskinesia. Eight patients had breakthrough sites in the inferior wall, six with normal or hypokinetic inferior segments and two with akinetic or dyskinetic inferior segments who had breakthrough sites in normally contracting inferobasal segments. Two patients had no inferior breakthrough sites, both of whom had akinesia of the inferior wall. Left ventricular breakthrough sites were never observed in areas of akinesis or dyskinesia.

Figure 2. Epicardial recording from a patient with coronary artery disease and ventricular aneurysm. Same format as figure 1. Activation over the aneurysm occurred after the QRS complex. This patient did not have a history of ventricular tachycardia or fibrillation. The paper speed was 200 mm/sec.

Figure 3. Epicardial map of a patient with coronary artery disease and normal ventricular contraction. The anterior, left lateral and inferior aspects of the heart are displayed. Codes for each 10-msec interval are displayed under the QRS (lead III). Areas of epicardial breakthrough are seen in the anterior right ventricle, anterolateral left ventricle and inferior left ventricle.
not directly determined, coronary anatomy did not appear to affect the pattern of epicardial activation.

Correlation of Surface ECG with Ventricular Contraction and Epicardial Breakthrough

Nine patients had Q waves in the anterior precordial leads. Three patients had anterior wall hypokinesis and all three had epicardial breakthrough sites in the anterior wall. Six patients had anterior akinesis or dyskinesis and only one had an anterior wall epicardial breakthrough (in a normally contracting anterobasal segment).

Four patients had significant Q waves in the inferior leads. Three patients had inferior wall hypokinesis and all three had epicardial breakthrough points in the inferior wall. One patient with inferior wall akinesis had no inferior wall breakthrough point.

In summary, five of nine patients with an ECG pattern of anterior myocardial infarction had no anterior wall breakthrough site and one of four patients with an ECG pattern of inferior myocardial infarction had no inferior wall breakthrough site.

Correlation of Activation Pattern with Arrhythmias

Four of the 10 patients with akinesis or dyskinesis had a history of ventricular tachycardia or fibrillation occurring without acute cause. The abnormalities in epicardial activation did not differ between patients with and those without these arrhythmias. In one pa-

Effects of Coronary Anatomy on Epicardial Activation

There was no difference in the number or severity of coronary obstructions in patients with normal ventricles, patients with hypokinesis and patients with akinesis and dyskinesis. While coronary perfusion was

Latest Epicardial Activation

The latest epicardial activation was recorded at the base of one of the ventricles in all nine patients with normal contraction, all five patients with hypokinesis, and four of 10 patients with akinesis or dyskinesis ($p < 0.05$). In six patients, the latest epicardial activation was over a dyskinetic area. In two of these patients, activation over the aneurysm occurred after the end of the QRS.

Regional Activation Time and Contractile Status

The average activation times for the anterobasal, anterior, apical, inferior and inferobasal segments were correlated with the contraction status of these segments (table 3). There was no significant difference, for any location, between normal and hypokinetic segments. However, for each location where a sufficient sample was available (i.e., anterior, apical and inferior), akinetic and dyskinetic segments were activated significantly later than normal and hypokinetic segments.

Effects of Coronary Anatomy on Epicardial Activation

There was no difference in the number or severity of coronary obstructions in patients with normal ventricles, patients with hypokinesis and patients with akinesis and dyskinesis. While coronary perfusion was

FIGURE 4. Epicardial map of a patient with coronary artery disease and anterior, apical and inferior hypokinesis. Same format as figure 3. Areas of epicardial breakthrough are seen in the anterior right ventricle, anterobasal left ventricle and inferior left ventricle.

FIGURE 5. Epicardial map of a patient with coronary artery disease and anterior and apical dyskinesis. Same format as figures 3 and 4. Areas of epicardial breakthrough are seen in the anterior right ventricle and inferior left ventricle.
## Table 2. Ventriculographic and Electrophysiologic Data

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<td>D</td>
<td>H</td>
<td>N</td>
<td>15  28  43</td>
<td>83</td>
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Abbreviations: A = akinetic; AB = anterobasal; ALLV = anterolateral left ventricle; ALV = anterior left ventricle; ANT = anterior; AP = apical; ARV = anterior right ventricle; D = dyskinetic; H = hypokinetic; IB = inferobasal; INF = inferior; ILLV = inferolateral left ventricle; ILV = inferior left ventricle; LEA = latest epicardial activation; N = normal.

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tient with and one patient without malignant arrhythmias, activation over an aneurysm extended beyond the end of the QRS.

### Discussion

In 1970, Durrer et al.1 performed epicardial and intramural mapping on seven reperfused human hearts from patients with no history of cardiac disease and a normal ECG. The epicardial excitation pattern reflected the movement of the endocardial and intramural fronts, and the earliest epicardial breakthrough occurred in the anterior right ventricle adjacent to the septum. The left ventricular epicardial breakthrough sites were more variable: Sites of early
TABLE 3. Mean Activation Time of Epicardial Segments
by Anatomic Segment and Contraction Pattern

<table>
<thead>
<tr>
<th>Segment</th>
<th>Normal (ms)</th>
<th>Hypokinetic (ms)</th>
<th>Akinetic/dyskinetic (ms)</th>
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<td>Anterobasal</td>
<td>42.9 ± 11.7</td>
<td>46.5 ± 8.7</td>
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<tr>
<td>Anterior</td>
<td>38.2 ± 5.4</td>
<td>41.0 ± 6.1</td>
<td>73.3 ± 16.7</td>
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<tr>
<td>Apical</td>
<td>36.7 ± 4.0</td>
<td>37.5 ± 4.2</td>
<td>62.8 ± 9.3</td>
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<td>Inferior</td>
<td>34.1 ± 8.0</td>
<td>35.3 ± 6.2</td>
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<td>Inferobasal</td>
<td>43.9 ± 7.4</td>
<td>44.4 ± 6.1</td>
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Values are in milliseconds (mean ± SD). Numbers in parentheses represent number of patients with a given combination of findings.

activation occurred on the anterior surface para-septally, close to the atroventricular sulcus; in an anterior paraseptal area halfway between the apex and the base; and in a posterior paraseptal area halfway from apex to base. In 1979, Wyndham et al. studied the epicardial activation of 11 patients without conduction defect at surgery. Ten of these patients had coronary artery disease, but patients with previous myocardial infarction or dyskinesis on ventriculogram were excluded. Wyndham et al. found the earliest epicardial activation in the anterior right ventricle, followed by subsequent breakthrough points in the inferior right ventricle, anterolateral left ventricle and inferior left ventricle.

In the dog heart, chronic myocardial infarction is associated with characteristic changes in the sequence of ventricular activation. Durrer et al. found that the epicardial surface of all but the smallest subendocardial scars was activated later than normal for the region studied. This delay was due to the slow spread of activation both through and around the scar. In at least one dog with a nearly complete transmural infarction, epicardial activation after the completion of the QRS complex was noted. Daniel et al. found similar delays and documented that delay was due to slow conduction through areas of scar.

Most studies of the electrophysiologic effects of coronary artery disease on ventricular activation in humans were concerned primarily with the correlation of unipolar epicardial leads with precordial leads. There are few data on the effects of coronary artery disease on ventricular conduction. Durrer et al. and Boineau et al. showed, in individual cases, that activation was delayed over human myocardial infarction. Daniel et al. performed epicardial mapping on 20 patients with coronary artery disease at coronary bypass surgery. Although areas of epicardial delay were usually found over areas of anterior infarction, data were provided on only two patients who fit this generalization and one (with conduction system disease) who did not. Two patients with infarction were studied using plunge electrodes, and fragmentation and delay of conduction similar to that in dogs was found. Gallagher et al. described activation after the end of the QRS over an anterior aneurysm in a patient with recurrent ventricular tachycardia, but Fontaine et al. found delayed potentials in only one of 10 patients with ventricular tachycardia and ventricular aneurysm. Spear et al. performed microelectrode studies on tissues removed from human aneurysms and found a mix of normal and abnormal cells with areas of slow current and areas of inexcitable cells.

Our findings in patients without asynergy are similar to those of Durrer et al. and Wyndham et al. Breakthrough points in the anterior right ventricle, anterior left ventricle and posterior left ventricle appear to correspond to the termination of the right bundle branch, the left anterior fascicle and the left posterior fascicle. Unlike Wyndham et al., but similar to Durrer et al., we did not find a consistent breakthrough point in the inferior right ventricle. Wyndham et al. could deduce no anatomic explanation for this breakthrough site.

Our study shows that areas of hypokinesis had a pattern of epicardial activation similar to that of normally contracting areas, whereas areas of akinesis and dyskinesis had marked changes in epicardial activation. Patients with akinesis and dyskinesis did not have breakthrough sites in the asynergic zone. Breakthrough sites were either absent or located in a myocardial segment adjacent to the abnormal zone. Activation times for hypokinetic zones did not differ from those in normally contracting zones, but akinetic and dyskinetic zones were activated much later. In patients with akinesis and dyskinesis, the latest recorded epicardial activation was frequently over the abnormal area, rather than at the base of the heart.

Areas of asynergy on the ventriculogram represent the effects of chronic ischemia with or without fibrosis. Areas of akinesis and dyskinesis, especially with an infarction pattern on the ECG, represent areas of transmural necrosis. Areas of hypokinesis may represent chronic fibrosis or normal myocardium with chronic ischemia. The absence of changes in epicardial activation in hypokinetic zones is compatible with the lesser degree of ischemic damage in these zones. Preservation of electrical function after deterioration of contractile function has been seen in the animal model of acute ischemia. By analogy with the animal model, absence of breakthrough sites in zones of akinesis and dyskinesis may be due to slow spread of activation through the scar, with activation of the epicardium from adjacent tissue. Epicardial breakthrough in normal or hypokinetic zones bordering akinetic zones might be due to survival of Purkinje fibers in the zone of infarction, with subsequent endocardial-to-epicardial spread in the border of the akinetic segment. Survival of Purkinje fibers in zones of myocardial infarction has been reported in dogs and in cellular studies of human tissue.

Further studies are necessary to directly correlate epicardial and intramural findings with pathologic state. Using unipolar recordings, Bodenheimer et al. found epicardial r-waves over areas of hypokinesis in which < 10% muscle loss was present on histologic examination. Epicardial Q waves were found over areas of akinesis and dyskinesis. The bipolar recordings used in our study reflect underlying tissue more directly. We found no changes in areas of hypokinesis but marked changes in areas of akinesis and
dyskinesis, consistent with the findings of Bodenheimer et al. Further studies are necessary to determine whether electrical recordings are useful in predicting areas in which coronary grafting will improve contraction pattern.

Four of our 10 patients with akinesis and dyskinesis had a history of malignant arrhythmias. There was no discernible difference in the degree of epicardial delay between patients with and those without arrhythmias. One patient with and one patient without malignant arrhythmias had latest epicardial activation after completion of the QRS. Our findings are at variance with those of Klein et al., who showed that marked epicardial delay was a marker for the presence of arrhythmias, but are consistent with those of Horowitz et al., who reported that only three of 31 patients with recurrent sustained ventricular tachycardia had latest epicardial activation after the QRS. That epicardial delay did not distinguish patients with arrhythmias from those without is consistent with the hypothesis that these arrhythmias may have an endocardial origin.

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