Intraoperative Electrophysiologic Mapping of the Ventricles During Sinus Rhythm in Patients with a Previous Myocardial Infarction

Identification of the Electrophysiologic Substrate of Ventricular Arrhythmias

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SUMMARY

To determine why only some patients with a previous myocardial infarction develop serious or life-threatening ventricular arrhythmias, we performed electrophysiologic ventricular mapping during sinus rhythm in 38 patients (31 men and seven women, mean age 51 years) during open heart surgery for coronary artery disease. Twenty-nine patients had a left ventricular aneurysm or dyskinetic area, eight had an akinetic area, and one had a severe hypokinetic area. Of 21 patients who had documented ventricular arrhythmias, 16 had recurrent, sustained ventricular tachycardia, two had ventricular tachycardia during exercise testing, and three had frequent premature ventricular complexes only. Seventeen patients were free of ventricular arrhythmias. Epicardial mapping was performed in all 38 patients. The endocardium was also mapped in 10 patients. In 20 patients with ventricular arrhythmias, an area of delayed activation (more than 100 msec after onset of the QRS complex) was found. This type of delay was present in only two of the 17 patients without arrhythmias. The mean latest epicardial activation in patients with arrhythmias was 137 ± 21 msec, whereas in patients without arrhythmias, the mean latest epicardial activation was 74 ± 21 msec (p < 0.001). Twenty of the 21 patients with arrhythmias had fractionated electrograms (three exclusively on the endocardium) and 13 patients had double potentials. Fractionation and double potentials were found in only one of the 17 patients without arrhythmias. The area where abnormal electrograms were recorded (i.e., the number of abnormal recording sites) was significantly larger in patients with recurrent sustained ventricular tachycardia than in patients who had premature ventricular complexes only or had no documented arrhythmias. We conclude that in patients with a previous myocardial infarction associated with serious or life-threatening ventricular arrhythmias, areas of significantly delayed epicardial activation, fractionation and double potentials are characteristic findings of ventricular mapping during sinus rhythm, and presumably constitute the substrate for development of these arrhythmias.

A CORRELATION between the incidence of ventricular arrhythmias in man and the extent of abnormally contracting myocardium caused by myocardial infarction has been observed by several investigators.1-3 The degree of myocardial fibrosis, as reflected by the number of abnormally contracting segments in the left ventricular angiogram and by abnormal Q waves of the ECG, was shown to be a useful predictor of frequent and complex ventricular arrhythmias in patients with coronary artery disease.4 In patients resuscitated from ventricular fibrillation, the left ventricular angiogram has demonstrated abnormal ventricular wall motion in 70% of cases studied.5 Thus, extensive myocardial damage may be important in establishing the milieu for life-threatening ventricular arrhythmias. However, many patients with large areas of abnormally contracting myocardium caused by myocardial infarction do not have ventricular arrhythmias. The present study was designed to determine whether electrophysiologic mapping of the ventricles in patients with abnormally contracting myocardium due to a myocardial infarction could help us to understand why some of these patients develop ventricular arrhythmias while others do not.

Methods

Selection of Patients

After obtaining informed consent, we used intraoperative electrophysiologic mapping techniques6-8 to study 38 patients (31 men and seven women, ages 31–67 years, mean 51 years) undergoing open heart surgery. All patients had coronary artery disease and had had a myocardial infarction a mean of 7 months before operation (range 1–96 months). Four patients had a myocardial infarction more than 3 years before surgery.

Preoperatively, all patients underwent standard left-heart catheterization, selective coronary angiography and biplane left ventricular angiography. One patient also underwent right-heart catheterization and biplane right ventricular angiography. The size of abnormally contracting segments was measured angiographically by superimposing the end-diastolic and end-systolic ventricular silhouettes and evaluated according to previously described techniques.9 In 29 patients, the an-
Giogram showed an aneurysm or a dysskinetic area, in eight patients an akinetic area, and in one patient severe hypokinesis. Often, ventricles with dyskinetic areas also demonstrated akinetic or hypokinetic segments. Twenty-one patients had significant three-ventricle disease, 10 patients had two-vessel disease and seven had one-vessel disease. The primary indication for surgery in 35 patients was angina pectoris or congestive heart failure. Three patients underwent surgery primarily because of recurrent episodes of sustained ventricular tachycardia unresponsive to antiarrhythmic medication with various antiarrhythmic agents, and three others for ventricular tachyarrhythmias and congestive heart failure.

In 21 of the 38 patients, ventricular arrhythmias were documented preoperatively. Sixteen patients had recurrent sustained ventricular tachycardia or episodes of ventricular fibrillation that were unassociated with an acute myocardial infarction and required DC cardioversion. Two patients had ventricular tachycardia during exercise testing and also had complex ventricular arrhythmias at rest. Three patients had only frequent premature ventricular complexes. The remaining 17 patients had no history of ventricular arrhythmia, did not have premature ventricular complexes during preoperative ECG monitoring, and were not receiving antiarrhythmic medication. The ECG demonstrated a right bundle branch block pattern in two patients and left-axis deviation in six patients. No patient had a complete left bundle branch block pattern. Six patients required lidocaine therapy for malignant ventricular arrhythmias until the beginning of the operation, and in seven patients, antiarrhythmic treatment (with quinidine, disopyramide or procainamide) could only be discontinued 8–12 hours before surgery.

**Intraoperative Mapping Technique**

All patients underwent epicardial mapping during regular sinus rhythm before therapeutic surgery was performed. In 14 patients, this mapping was performed before cardiopulmonary bypass, and in 24 patients during cardiopulmonary bypass at 37°C. Either a tripolar hand-held electrode probe with an interelectrode distance of 2 mm or a fingertip-mounted tripolar electrode ring with an interelectrode distance of 2 mm was used to record three simultaneous bipolar ventricular electrograms from 40–42 predetermined epicardial sites on the left ventricle and the anterior wall of the right ventricle. In 10 patients (eight with a history of ventricular tachyarrhythmia, one with frequent premature ventricular complexes, and one without a history of arrhythmia), left ventricular endocardial mapping with a tripolar hand-held electrode probe was performed at 37°C after ventriculotomy through a myocardial scar was performed as part of the surgical therapeutic procedure. The endocardial grid was determined by the anatomic and clinical state and therefore varied somewhat from patient to patient. Special attention was directed to the left ventricular septum and the border zone of the endocardial fibrosis, and recordings were made from the endocardial equiv-

alents of the epicardial sites whenever possible. Bipolar endocardial electrograms were recorded from 20–25 sites.

For all studies, a bipolar reference electrogram recorded from a plaque electrode sewn on the anterior wall of the right ventricle and standard ECG leads I, II and III were recorded simultaneously with the three bipolar electrograms from the exploring electrode probe on an Electronics for Medicine DR-12 switched-beam oscillographic recorder. All bipolar electrograms were initially recorded at a calibrated gain of 1 cm/mV. The bipolar ventricular electrograms from the exploring electrode probes were recorded using an Electronics for Medicine VET amplifier calibrated so the gain of each of the simultaneously recorded signals could be adjusted to settings of 0.1, 0.2, 0.5, 1.0, 2.0, 5.0 and 10 cm/mV whenever appropriate, e.g., to obtain adequate signals from sites demonstrating low-amplitude potentials. All ventricular electrograms were recorded within a band pass of 12–500 Hz.

All data were recorded on photographic paper at a speed of 100 mm/sec. The data were also recorded on magnetic FM tape on a Honeywell model 5600 tape recorder for later playback and analysis. Ventricular activation times were determined by measuring the interval between the earliest onset of the QRS complex in ECG leads I, II or III and the first rapid deflection of the ventricular electrogram. All measurements were made with a vernier device with an accuracy of ± 1 msec at the recorded paper speed. Ventricular activation times were rounded off to the nearest 5 msec.

**Definitions**

From the work of Durrer and colleagues, Wyndham et al., and Fontaine et al., we know that the latest normal epicardial activation time in the intact human heart rarely, if ever, exceeds 100 msec beyond the onset of the QRS complex. Accordingly, we defined delayed activation of the ventricles as that which occurs more than 100 msec after the onset of the QRS complex (fig. 1A). This definition excludes some areas that may, in fact, be activated considerably later than normal. We defined fractionation of the bipolar electrogram as polyphasic, primarily low-amplitude deflection (fig. 1B). We defined double potentials as electrograms with two clearly separated deflections (fig. 1C).

**Results**

**Presence and Extent of Delayed Activation**

An area of delayed epicardial activation was found in 22 patients, 20 of whom had ventricular arrhythmias. In one patient who had frequent premature ventricular complexes during preoperative ECG monitoring, no delayed activation was found. This patient also had an apical aneurysm and inferior akinesis, and the latest epicardial activation time recorded from the infarcted area of the anterior wall was 95 msec.

The area of latest activation time was determined for each patient. The mean latest activation time in patients with ventricular arrhythmias was 137 ± 21 msec.
Bipolar ventricular electrogram (VEG)

**FIGURE 1.** ECG leads II and III recorded simultaneously with a bipolar ventricular electrogram (VEG) in three patients recorded with an exploring electrode. (A) Delayed activation in which the ventricular electrogram occurs 145 msec after the onset of the QRS complex. (B) Fractionation of the ventricular electrogram. (C) A double potential in which the second deflection is separated from the initial deflection by 75 msec and occurs 140 msec after the onset of the QRS complex and 12 msec after the end of the QRS complex.

(range 95–190 msec). In patients without ventricular arrhythmias, the mean latest activation time was 75 ± 20 msec (range 55 ± 125 msec). The difference in mean latest activation time between patients with and without ventricular arrhythmias was significant (p < 0.001 by unpaired t test).

In patients with delayed activation, two patterns of epicardial activation occurred during sinus rhythm. One pattern was characterized by a marked difference in epicardial activation times between adjacent mapping sites (fig. 2). Eighteen of the 21 patients with and without known ventricular arrhythmias had this pattern of activation. The range of maximal difference between adjacent sites for these 18 patients was 60–135 msec (mean 99 msec). The second pattern (fig. 3), seen in four patients, was one of a relatively more gradual increase in epicardial activation time in the infarcted region. The maximal difference between sites activated relatively normally and adjacent sites in which activation was delayed was only 15–35 msec (mean 24 msec). The latest activation time in this group was never more than 125 msec after the beginning of the QRS complex (range 105–125 msec, mean 113 msec). Two of these four patients had ventricular arrhythmias (one had premature ventricular complexes and one had ventricular tachycardia), and two had no known ventricular arrhythmias.

Fifteen of the 17 patients without ventricular arrhythmias and one patient with frequent premature ventricular complexes showed only a minimally disturbed spread of ventricular activation (fig. 4), with the latest epicardial activation not more than 95 msec after the beginning of the QRS complex.

**Abnormal Electrogram Recordings**

Abnormal electrograms were not found exclusively at the border areas of a dyskinetic or akinetic myocardium, but rather, in almost any distribution throughout the abnormally contracting myocardium. However, fractionation and double potentials were always found near an area in which activation was delayed. When both fractionation and double potentials were recorded...

**FIGURE 2.** The sequence of epicardial ventricular activation in a 46-year-old man who had a large area of anteroapical dyskinesis. The area of latest epicardial activation, 180 msec after the beginning of the QRS complex, was adjacent to an area of relatively early (50 msec) activation. In this patient, bipolar ventricular electrograms recorded from mapping sites denoted by question marks were of such low amplitude that even with the highest possible amplification (10 cm/mV), the activation time could not be measured. This patient had ventricular tachycardia during exercise testing and had salvos of premature ventricular complexes and short runs of ventricular tachycardia during preoperative ECG monitoring. RA = right atrium; PA = pulmonary artery; LA = left atrium.

**FIGURE 3.** Gradual increase in epicardial activation time over the posterior wall of the left ventricle. The latest epicardial activation is 110 msec after the beginning of the QRS complex. The left ventricular angiogram of this 53-year-old woman without arrhythmia showed an area of posterior dyskinesis.
in the same patient, they were always very close together. In seven of the 10 patients in whom endocardial mapping was performed, fractionated electrograms and double potentials were recorded from abnormal myocardial tissue on the ventricular septum. Also, areas on the endocardium where fractionation or double potentials were recorded did not necessarily correspond with the area of epicardial delay or fractionation. In one patient who had recurrent episodes of sustained ventricular tachycardia, most of the area in which fractionation and double potentials were recorded was in the right ventricle.

Fractionation

Fractionation of the bipolar ventricular electrograms was observed in 21 patients, 20 of whom had ventricular arrhythmias. One patient with fractionated electrograms had no ventricular arrhythmias, and one patient with ventricular arrhythmia did not show fractionation. The latter patient, who had one preoperative episode of ventricular tachycardia, did not undergo endocardial mapping. In one patient with frequent ventricular premature complexes in whom epicardial activation never occurred 100 msec or more after the onset of the QRS complex, mapping clearly showed fractionated electrograms. In all patients in whom both epicardial and endocardial mapping was performed, when fractionation of the epicardial electrograms was observed, electrograms recorded from some endocardial sites also showed fractionated activity. In three patients with ventricular arrhythmias, fractionated activity was only found in endocardial electrograms.

Double Potentials

Double potentials were observed in 14 patients. Thirteen of these patients had documented recurrent episodes of sustained ventricular tachycardia and one had no known ventricular arrhythmias. In two patients, double potentials were only found in endocardial recordings. The 13 patients with double potentials and documented ventricular arrhythmias also had both fractionation and delayed activation. The patient with double potentials but no known ventricular arrhythmias was the same patient who also showed fractionated electrograms, but in whom no area of delayed epicardial activation was found.

Low-amplitude Electrograms

Abnormal electrograms that consisted of deflections of very low amplitude (fig. 5) or were virtually flat even at the highest amplification (10 cm/mV) were recorded from the region of the myocardial infarction in all patients. This confirms observations in experimental animals6. 13. 14 and in man.6. 7 Thus, low-amplitude electrograms alone do not provide the necessary basis for generation of ventricular arrhythmias.

Number of Abnormal Recording Sites

Double potentials or fractionated electrograms were recorded at five to 11 sites (mean eight sites) in 17 patients with ventricular tachycardia, at two to three sites (mean two sites) in the three patients with frequent premature ventricular complexes, and at four sites (two epicardial and two endocardial) in one pa-
tient who had no known ventricular arrhythmia. One patient who had a single episode of ventricular tachycardia before surgery had no double potentials or fractionated electrograms. This patient, whose area of latest activation was 105 msec and whose maximal difference in activation time between adjacent sites was 15 msec, did not undergo endocardial mapping. Thus, with one exception, relatively large areas of abnormally conducting myocardial tissue were associated with serious and life-threatening arrhythmias.

**Discussion**

Simple intraoperative electrophysiologic mapping during sinus rhythm can delineate abnormalities associated with life-threatening ventricular arrhythmias. These abnormalities probably reflect markedly abnormal local conduction. Because most chronic ventricular arrhythmias associated with myocardial infarction are reentrant and because local abnormalities of conduction (i.e., slow conduction and unidirectional block) are requirements of reentrant rhythms, it is logical to presume that the abnormalities we recorded in these studies constitute the electrophysiologic substrate of ventricular arrhythmias.

**Delayed Activation**

In our patients with serious ventricular arrhythmias, the finding of areas of markedly delayed activation, particularly when adjacent to areas that were activated normally or only somewhat later than normal, is striking. These data suggest that there is either direct, but slow, conduction from the normal area to the adjacent area of delayed activation or indirect conduction, and the impulse ultimately gets to the area of delayed activation by a roundabout means. Thus, markedly delayed activation of areas adjacent to ones activated normally or relatively normally may be an important indicator of risk for serious or life-threatening ventricular arrhythmias, as it appears to represent either one or both of the important requirements for reentrant rhythms, slow conduction and unidirectional block.

**Fractionation**

Durrer and colleagues first described fractionation of electrograms recorded from within the area of an infarct, although they did not use the term “fractionation.” Waldo and Kaiser demonstrated the association of fractionated ventricular electrograms (but used the term “continuous electrical activity”) with the occurrence of ventricular tachycardia and ventricular fibrillation after acute coronary artery occlusion in the canine heart. Since then, there has been ample demonstration of these abnormal recordings in the chronic canine model of ventricular arrhythmia and in man. What these recordings represent is unclear, although desynchronized activation, localized fibrillation, and localized reentry have been suggested. Recently, El-Sherif et al. demonstrated that fractionated signals recorded from a large composite electrode may be associated with reentrant wave fronts or with several wave fronts invading an area simultaneously in association with several areas of block. However, regardless of their pathogenesis, fractionated electrograms indicate abnormal local conduction in the area from which the recording was obtained.

**Double Potentials**

Double potentials were first described by Durrer et al. (although they did not use that term) in studies of myocardial infarction in the canine heart. They later recorded double potentials from a large ventricular aneurysm in a patient during open heart surgery. Fontaine et al., in a series of studies, most of which were in patients without a previous myocardial infarction, emphasized the association of double potentials with ventricular arrhythmias. In fact, they called this relationship the postexcitation syndrome, and used the term “synchronized potential” for the first deflection because it was associated with the inscription of the QRS complex, and the terms “epsilon or E wave,” “delayed potential” or “late potential” for the second potential. Double potentials have also been recorded by others during intraoperative studies of patients with ventricular tachycardia not associated with myocardial infarction.

Fontaine et al. used signal averaging techniques to record a bipolar ECG from the precordium of seven patients with ventricular tachycardia (only one associated with myocardial infarction) and a demonstrated double potential on epicardial mapping, found an equivalent in the body surface recording. Rozanski et al. also used signal averaging and detected delayed ECG wave forms from the body surface well after the QRS complex in eight patients with ventricular aneurysms and chronic ventricular tachycardia. These observations are consistent with our findings in recordings made directly from the heart.

What double potentials represent is not entirely clear, although one might speculate that they are a direct manifestation of local reentry. Support for this comes from the experimental studies of Durrer et al., who demonstrated apparent reentry in studies of conduction after myocardial infarction in the dog. Even stronger support comes from the studies of Wit et al., who demonstrated during epicardial mapping with multiplexing techniques that two discrete electrograms recorded at one site and associated with one QRS complex indeed resulted from reentry of the same impulse, which returned to that site from a different direction.

**The Critical Mass of Abnormal Tissue**

Garrey was the first to emphasize that a critical mass of abnormal tissue was required to generate rapid ventricular arrhythmias. Any investigator who has tried to study acute or chronic ventricular arrhythmias in the experimental animal is keenly aware of the importance of producing a large infarct to produce ventricular arrhythmias. Conversely, those who have studied aspects of myocardial infarction unrelated to arrhythmias understand the importance of keeping the infarct small to avoid arrhythmias. The recent studies of Kaplinsky et al. in the experimental animal again
emphasize the importance of size in determining the presence or absence of ventricular arrhythmias. Many observations in man suggest that there is a critical mass of abnormal tissue required to produce ventricular arrhythmias,\textsuperscript{1,4} as the data from the present study confirm. However, our data also indicate that a large infarct alone is not enough to cause ventricular arrhythmias. Our patients with significant life-threatening ventricular arrhythmias not only had relatively large areas of abnormal myocardium, but also had large areas from which double potentials or fractionation were recorded. Thus, it appears that the abnormal myocardial tissue must include a large enough area of abnormally conducting tissue to provide the substrate for reentry and the generation of ventricular arrhythmias. However, we did not record from the endocardium in all patients or from intramycardial sites in any patient.

Clinical Implications

Since ventricular mapping during sinus rhythm at the time of open heart surgery permits one to identify easily and quickly the areas of abnormal conduction conducive to ventricular arrhythmias, this simple mapping technique can be used by the surgeon to identify the tissue responsible for generating ventricular tachyarrhythmias. The surgeon can then excise or otherwise exclude the abnormal tissue from the rest of the ventricle in an effort to treat these arrhythmias effectively. Body surface ECG signal averaging techniques\textsuperscript{26,36} and endocardial mapping during cardiac catheterization\textsuperscript{27,39,40} may help in identifying patients in whom sinus mapping may be useful.

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CONDUCTION SYSTEM IN DMD/Sanyal and Johnson 853


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Cardiac Conduction Abnormalities in Children with Duchenne’s Progressive Muscular Dystrophy: Electrocardiographic Features and Morphologic Correlates

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SUMMARY  The ECGs of 50 boys, 5–18 years old, with Duchenne’s muscular dystrophy were studied for evidence of cardiac conduction system abnormalities. Among the 24 patients with positive findings (48%), most had intraatrial conduction defects: 16 an abnormally prolonged PV, index, 12 a short PR interval with a normal QRS and two coronary sinus rhythm. Five patients had infranodal conduction defects: One had right bundle branch block, three left anterior fascicular block and one right bundle branch block with left anterior fascicular block. Only one child had first-degree atrioventricular (AV) block. About one-third of the patients had more than one type of defect. The conduction abnormalities were progressive in some patients.

Morphologic features of the conduction systems of three patients were studied systematically to find correlates for the observed ECG changes. Compared with normal controls matched for age and sex, each of these three hearts showed multifocal areas of degenerative changes, characterized by vacuolization, fatty infiltration, nuclear pyknosis, loss of myofibers and moderate-to-severe fibrosis. These dystrophic changes were similar in all patients and (with differing severity) involved the sinoatrial node, “atrial preferential pathways,” approaches to the AV node, the AV node including the upper portion, the bundle of His, and subendocardial as well as infranodal right and left bundle branches.

Our observations indicate a high prevalence of ECG evidence of cardiac conduction abnormalities in patients with Duchenne’s dystrophy. Multifocal dystrophic involvement of the cardiac conduction system furnishes the anatomic basis for such changes and may account for the persistence of an infantile pattern of accelerated conduction, which may sometimes manifest clinically as Lown-Ganong-Levine syndrome with or without sinus tachycardia.

PATIENTS with Duchenne’s muscular dystrophy (DMD) have a distinctive ECG, characterized by a tall R wave with an abnormal R/S ratio over the right precordial leads and deep but narrow Q waves over leads I, aV, and V, . This classic profile, seen in 70–80% of patients with DMD, has been attributed to multifocal dystrophic involvement of the left ventricular myocardium with a peculiar predilection for the posterobasal segment and contiguous lateral or inferior walls. Other ECG findings, such as short PR interval and left-axis deviation of the mean electrical force, which imply involvement of the cardiac conduction system in the disease, are seldom recognized, and their prevalence is unknown. In a study of 34 patients, Ronan et al. found no atrioventricular (AV) or intraventricular conduction disturbance and concluded that impairment of AV conduction was an unlikely manifestation of DMD. Perlloff et al. in contrast, observed prolonged AV conduction in seven of 35 patients with DMD. Reports of the prevalence of short PR intervals

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Received September 18, 1981; revision accepted February 19, 1982. Circulation 66, No. 4, 1982.
Intraoperative electrophysiologic mapping of the ventricles during sinus rhythm in patients with a previous myocardial infarction. Identification of the electrophysiologic substrate of ventricular arrhythmias.

H Klein, R B Karp, N T Kouchoukos, G L Zorn, Jr, T N James and A L Waldo

Circulation. 1982;66:847-853
doi: 10.1161/01.CIR.66.4.847

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