Analysis of Interectopic Activation Patterns During Sustained Ventricular Tachycardia

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SUMMARY We analyzed the patterns of interectopic continuous electrical activity recorded within interectopic intervals of sustained ventricular tachycardias. These arrhythmias were induced in dogs that were studied 4 days after left anterior descending coronary artery occlusion. Standard ECG leads and electrograms from the His bundle and left ventricular epicardium, both infract and normal zone, were recorded. In 19 of 24 dogs with transmural myocardial infarction, one to three ventricular paced beats induced sustained ventricular tachycardia, characterized by continuous electrical activity between the initiating and spontaneous ectopic beat and between successive ectopic beats recorded from the epicardium over the infarct zone but not from the normal epicardium. Continuous activity consisted of discrete potentials that were reproduced in each cardiac cycle, suggesting slow conduction within a reentrant circuit. The interectopic activity was divided into three distinct temporal periods, delineated by potentials occurring at the initial portion, the mid-interectopic portion and terminal portion or exit of the slow conduction segment of the presumed reentrant circuit. In some cases, sustained ventricular tachycardia was induced only if an appropriate initial potential was engaged. Spontaneous termination of the sustained ventricular tachycardia was associated with Wenckebach-like block of conduction in the initial or exit potential. Ventricular pacing caused alteration of the interectopic patterns and resulted in cessation of the arrhythmia. Procaimamide produced dose-dependent slowing of the ectopic rate due to depression of conduction in the mid-interectopic portion of the continuous electric activity. Inducibility of the sustained ventricular tachycardia was inhibited by decremental conduction in this compartment of the presumed reentry circuit.

The present study uses a preparation showing sustained ventricular tachycardia that is stable and regular. Functional analysis of the various portions of the continuous electrical activity during sustained tachycardias allows further insight into the mechanisms of initiation and termination of sustained ventricular tachycardias. The ability to localize the effect of antiarrhythmic drugs on specific portions of a possible reentrant circuit may provide important correlative data for the analysis and interpretation of detailed epicardial mapping studies.

IN RECENT YEARS increasing interest has been focused on sustained ventricular tachycardias, which have been extensively investigated in clinical and experimental studies. While most information about these arrhythmias in the clinical setting was obtained from observation of initiation and termination by applied stimuli,1 Josephson et al.2 recorded late diastolic potentials from a few patients with ventricular aneurysm and recurrent ventricular tachycardia using endocardial catheter electrodes.

In previous reports, we described two forms of ventricular arrhythmias in the infarcted canine heart 3–10 days after coronary artery occlusion. These arrhythmias may take the form of premature ventricular complexes or ventricular tachycardia. In the former, fractionated electrical activity was recorded on the epicardium overlying the infarct,3–5 which showed progressive delay in a Wenckebach-like fashion in the cycles leading to the occurrence of the ectopic beat. Ventricular tachycardia was associated with the occurrence of fractionated and continuous electrical activity. The continuous electrical activity was presumed to represent slow conduction of the impulse in abnormal epicardial cell layers, suggesting a reentrant phenomenon. This continuous activity was frequently regular, recordable from cycle to cycle and sometimes lacked a discernible pattern. The purpose of the present study was to analyze the regular patterns of continuous electrical activation observed during the interectopic intervals of sustained ventricular tachycardia. In this way, some of the functional properties of the presumed reentrant circuit could be characterized: mechanisms of initiation and termination of the arrhythmia by electrical stimulation and the actions of antiarrhythmic drugs on these arrhythmias.

Methods

Experiments were performed in 24 adult mongrel dogs that weighed 10–20 kg. They were anesthetized with sodium pentobarbital, 30 mg/kg i.v. Under controlled ventilation and aseptic conditions, a left-sided thoracotomy was performed in the fourth intercostal space. The left anterior descending coronary artery (LAD) just distal to the septal artery was ligated with silk ligatures using the standard two-stage occlusion of Harris.6 The thoracotomy was closed and the dogs were allowed to recover. Before coronary artery ligation, 30 mg/kg of methylprednisolone, sodium succinate (Upjohn Co.) was administered intravenously. This procedure has been demonstrated to increase the occurrence of ventricular arrhythmias.7

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After 4 days, anesthesia was induced with sodium pentobarbital and standard electrocardiographic leads I–V₆ were recorded to obtain evidence for transmural myocardial infarction. This was indicated by the presence of QS patterns in the left precordial leads, V₅–V₆. All 24 dogs studied met these criteria for transmural myocardial infarction. The left thoracotomy was reopened and the pericardium split to expose the heart. Two bipolar composite electrodes were placed over the epicardial surface of the infarct zone (anteroapical wall) and the adjacent normal zone (posterior-lateral wall), to record subepicardial electrical activity.

A common carotid artery was exposed and a #5F or #6F electrode catheter with electrodes 10 mm apart was advanced into the aortic root to record His bundle activity. Electrocardiographic lead II was usually monitored continuously, as was peripheral arterial blood pressure from the femoral artery. A left ventricular endocardial recording close to the infarcted zone was obtained in some dogs by an additional electrode catheter inserted into a common carotid artery and placed in the left ventricular cavity. The vicinity of the infarct was identified by noting a marked reduction in the amplitude and fragmentation of the electrogram compared to closely adjacent normal zones. Ventricular pacing was achieved with a Grass S-88 stimulator and an SIU-5 isolation unit. Electrical stimuli of 2–10 V intensity, each lasting 0.5 msec, were delivered at a frequency of 20 Hz to the left vagosympathetic trunk to slow the heart and reveal underlying idioventricular automaticity. To increase the heart rate, twice-threshold stimuli of 2 msec duration were applied to the right ventricular outflow tract. Two plunger-wire electrodes served as the means of delivery for ventricular pacing stimuli.

All records were obtained on a multichannel oscilloscopic-photographic recorder (Electronics for Medicine VR-12) at paper speeds of 25–200 mm/sec with filter frequencies of DC–250 Hz for electrocardiographic leads and 30–250 or 100–250 Hz for electrographic leads. The high-pass filters for electrocardiographic leads were chosen to suppress the slower repolarization wave forms, whereas the higher-frequency depolarization potentials could still be recognized. Amplitudes of recorded potentials were compared with the underlying noise level, which averaged 3.4 ± 1.2 μV. In addition, continuous recordings were made in each experiment on an eight-channel tape recorder (Hewlett Packard) so that sections could be replayed and photographed for detailed analysis. Measurements were accurate up to 3 msec at a paper speed of 200 mm/sec.

Recordings were obtained during sinus rhythm. Ventricular stimulation was achieved by the introduction of three paced ventricular beats during sinus rhythm at pacing rates of 240–420 beats/min in an attempt to induce uniform sustained ventricular tachycardia, defined as a ventricular tachycardia with uniform QRS morphology consisting of 100 or more consecutive beats. During sinus rhythm and the initial pacing procedures, regions of maximum delay were identified within the infarct zone by varying the position of the composite electrode over the anterior-apical wall.

After induction of sustained ventricular tachycardia, all electrograms were continuously recorded. The tachycardia either ceased spontaneously or was terminated by introduction of electrically driven beats. The pacing protocol to induce and terminate the arrhythmia was repeated numerous times to initially establish an optimal composite electrode position, i.e., a recording which showed continuous electrical activity, and to verify the repeatability of the arrhythmia insofar as rate, QRS morphology and reproducibility of the pattern of continuous activity.

**Results**

In our study, 19 of 24 dogs exhibited sustained ventricular tachycardia at an average rate of 247 ± 78 following pacing protocols. A sustained ventricular tachycardia is illustrated in figure 1, in which the continuous electrical activation during the interectopic interval showed reproducible patterns of electrical potentials. For purposes of analysis, the initial third of the continuous activity is defined as the initial portion. This initial portion is followed by a mid-interectopic portion. A terminal portion just preceding the next QRS complex was designated as the exit.

The pattern of activation during induction of sustained ventricular tachycardia is illustrated in figure 2. In the upper panel, three ventricular pacing impulses at a rate of 300 beats/min caused fractionation of the composite electrogram recorded from the epicardial infarct zone. The last potential of the fractionated electrogram is negative. Also, ventricular activation time did not exceed the T wave (complete activation time 110 msec), as indicated by horizontal bars below the electrogram, and no arrhythmias occurred. In the lower panel, three paced beats at the same rate but at a shorter coupling interval to the sinus beat induced fractionated potentials, the last of which shows a large positive deflection after the QRS and preceding the first ectopic beat. Total activation time increased to 190 msec, exceeding the QT interval. Correspondingly, sustained ventricular tachycardia at a cycle length of 185 msec ensued. During the tachycardia, a recognizably regular pattern of continuous electrical activity was recorded in the infarct zone electrogram but not in the normal zone electrogram, where the pattern was regular but discontinuous. This suggests that initiation of sustained ventricular tachycardia was associated with a particular activation sequence in the viable but sick epicardial layer after the last stimulated QRS complex. The slanted arrows indicate the exit potential during each interectopic period. Repeated attempts to induce sustained ventricular tachycardia resulted in the same QRS morphology and the same patterns of continuous electrical activity. Only when the late positive deflection in the infarct zone electrogram was observed would delay and fractionation result in sustained ventricular tachycardia.

Termination of sustained ventricular tachycardia
was observed in association with a Wenckebach-like conduction pattern in a discrete portion of the continuous electrical activity. This phenomenon is illustrated in figure 3, obtained during spontaneous termination of a sustained ventricular tachycardia. The first two interectopic intervals shown have a regular pattern of continuous electrical activity. The time intervals between the initial and exit potentials are shown above and the duration of the initial potential is shown below the infarct zone epicardial tracing. After the third QRS, the initial potential was slightly delayed by 3 msec, inducing a notch in the upstroke. However, activation time to the exit potential and the RR interval were unchanged, 65 and 160 msec, respectively. After the next QRS complex, there was a more pronounced delay of the initial potential from the preceding QRS complex, which was accompanied by a loss of amplitudes of the initial and exit potentials showed only slight alterations. The fifth ectopic beat was followed by an isoelectric potential in the recorded epicardial electrogram. The sequence of activation reflected a Wenckebach periodicity in the initial portion of the interectopic activity followed by cessation of tachycardia. The RR interval increased only by 10 msec, whereas the delay in the initial potential was 15 msec. The possible mechanism of this dissociation will be discussed below. During the last two beats in figure 3, normal sinus rhythm, indicated by a normal sequence of A, H and V potentials in the His bundle electrogram, resumed and no late electrical activity could be detected.

Another form of Wenckebach-like conduction associated with termination of a sustained ventricular tachycardia could be demonstrated during interruption of the tachycardia by ventricular pacing. Figure 4 demonstrates cessation of a sustained ventricular tachycardia in another animal by rapid ventricular pacing, which alters the QRS morphology, the pattern of continuous activity and finally results in a different but unstable tachycardia. The top trace shows the regular pattern of continuous electrical activity in the first two interectopic intervals, indicated by arcs. After the first ectopic beat of the sustained tachycardia, five ventricular stimuli at a rate of 180 beats/min were introduced, which caused marked alteration of this pattern of continuous electrical activity in the infarct zone electrogram. The interectopic electrical activity was not interrupted, but the pattern was altered and irregular. After cessation of pacing, the first spontaneous beat was preceded by a different interectopic pattern and had a new QRS morphology. No stable pattern ensued, but a gradual change in the continuous activity accompanied by a shift from left to right bundle block pattern in ECG leads was seen. Perpendicular dotted lines indicate the onset of the QRS complexes, which are similar in the last three beats of the tachycardia. All are preceded by a similar exit potential. The interval from the beginning of this exit potential to the succeeding QRS gradually increased in a Wenckebach fashion. Although the initial portion of the continuous activity occurred after the last QRS complex, block in the exit potential or between the initial portion and the exit potential would explain the termination of the arrhythmia. There is a loss of mid-interectopic activity during

**Figure 1.** Regular patterns of electrical activity during the interectopic interval of sustained ventricular tachycardia. Horizontal dashed line indicates electrical zero potential and vertical dotted lines indicate onset and termination of the QRS complex in the ECG. L-2 = ECG lead II; Hbeg = His bundle electrogram; IZ epi = composite epicardial electrogram from the infarct zone. The interectopic activity consisted of an initial portion (IP), a mid-interectopic portion (MIP) and a terminal portion (exit). Horizontal bars refer to their respective time intervals during the interectopic interval. See text for discussion.

**Figure 2.** Initiation of sustained ventricular tachycardia by ventricular stimulation. (A) The paced beats fail to induce sufficient delay of activation (bar below IZ epi) in the infarcted epicardium and no arrhythmia ensues. (B) Appearance of a late positive potential (arrowhead) after the third paced beat (associated with marked prolongation of activation) is followed by onset of sustained ventricular tachycardia. There is a regular pattern of fractionated potentials (arrows) recorded during the interectopic interval. PI = pacer impulses; NZepi = composite epicardial electrogram from the normal zone; other abbreviations as in figure 1.
the ventricular tachycardia, shown in the lower panel of figure 4.

In 60% of the induced sustained ventricular tachycardias, regular, reproducible patterns of interectopic activity were recorded from the epicardial surface overlying the infarct. In 40%, continuous electrical activity was recorded with no apparent pattern or with interectopic activity that was not regularly reproducible in each cardiac cycle. Figure 5 is an example of induced sustained ventricular tachycardia in which seemingly random activation occurs continuously in the composite recording from the infarct zone. Similar continuous activity has been found during sustained ventricular tachycardia in patients with myocardial infarction and ventricular aneurysm.10

Using this experimental model of sustained ventricular tachycardia, localization of antiarrhythmic drug action could be determined. Figure 6 is an example of the antiarrhythmic effects of procainamide in this experimental setting. Panel A was obtained after induction of sustained ventricular tachycardia. In the composite electrogram from the infarct zone, the regular pattern of continuous electrical activity was consistent and could be separated into the three compartments: the initial portion, mid-interectopic portion and exit. In panel B, procainamide, 10 mg/kg, was administered intravenously before registration. Compared with the control state (A), there was a marked slowing of heart rate (the RR increased from 340 to 425 msec). Correspondingly, the mid-interectopic interval was markedly prolonged; initial and exit potentials are only moderately affected. The decrease in the ectopic rate from 176 to 142 beats/min is completely accounted for by slowing of conduction in the mid-interectopic portion of the electrogram.
In panel C, the dose of procainamide was increased to 20 mg/kg. Progressive slowing of the tachycardia allowed the sinus node to capture the ventricles. Rapid atrial pacing was used in an attempt to induce the ventricular tachycardia. After the first sinus beat in panel C, three atrial paced beats were introduced at 340 beats/min, which induced fractionated activity that bridged the interval to the first ectopic beat. Both the ectopic beats and the exit potentials just before them are the same as in the sustained ventricular tachycardia above. The first interectopic interval showed marked prolongation of the mid-interectopic portion,
followed by the same exit potential and the same QRS configuration. The His bundle recording indicates that this QRS complex is the result of a fusion beat. Although another initial potential ensues, normal sinus rhythm resumes before very slow conduction reaches the exit potential. The very slow conduction can be deduced by the long interectopic interval (five asterisks). Results were reproduced in eight additional dogs in which procainamide was administered during sustained ventricular tachycardia.

**Discussion**

**Experimental Models of Sustained Ventricular Tachycardia**

Numerous experimental models have been developed to study the mechanisms of and therapeutic approaches to ventricular tachycardia. All of these models have certain advantages and limitations in regard to simulating clinical pathophysiologic phenomena. We studied dogs pretreated with methylprednisolone, 30 mg/kg before operation, that underwent ligation of the left anterior descending coronary artery four days before investigation, because of certain advantages not achieved by other models: (1) Pretreatment with methylprednisolone results in a high percentage of dogs prone to develop sustained ventricular tachycardia. This finding was limited to dogs with "transmural" myocardial infarction determined electrocardiographically. (2) These tachycardias occur at relatively slow rates and do not hemodynamically compromise cardiac function. They can be easily induced and terminated with two to three ventricular paced beats at a constant rate. (3) Most of these tachycardias are related to abnormal electrical activity in the epicardial layers (viable but abnormal) overlying the infarct zone. Fortuitously, these areas are readily accessible to our recording techniques, i.e., composite electrograms.

**The Mechanisms of Sustained Ventricular Tachycardia**

Experimentally, some definitive requirements for reentry proposed by early investigators included demonstration of unidirectional block, slow conduction, identification of a continuous circus movement and the termination of the arrhythmia by cutting the circuit. Recently, with the aid of complex multielectrode systems, extensive mapping studies have been undertaken in the infarcted dog heart. Demonstration of the above-mentioned criteria for reentry have not been readily achieved. Specifically, El-Sherif et al. mapped the activation front on the epicardial surface of the 4-day infarcted heart in 21% of ectopic beats that were analyzed. Wit et al. reported that they did not locate reentrant pathways in the 3–7-day infarcted hearts with sustained ventricular tachycardias. On the other hand, more support of reentry has been the finding of continuous electrical activity connecting sinus beats and ectopic beats as well as consecutive ectopic beats recorded from infarcted hearts. Such recordings have been obtained experimentally using composite electrodes placed over the infarct. Recordings from catheters in patients with left ventricular aneu-

**Analysis of Continuous Electrical Activity**

In the present study we attempted to analyze the recorded interectopic electrical activity to determine the functional properties of these tachycardias. These properties, in turn, may have a bearing on the underlying mechanisms of sustained ventricular tachycardia. The very tachycardia, with a path of lesser delay being used to activate the heart through the exit potential. The designation of the clinical syndrome as recurrent ventricular tachycardia carries with it the implicit idea of a regular rhythm that spontaneously terminates and abruptly starts.

Recordings from electrocardiographic in patients with left ventricular aneurysms revealed continuous electrical activity during sustained ventricular tachycardia. The concept of a continuous wave of excitation causing ventricular arrhythmias was initially proposed by McWilliam in 1897. Harris and Guevara Rojas stated that the demonstration of continuous electrical activity would indicate the operation of reentry; however, they did not document such activity. In accordance with Waldo and Kaiser, who first observed interectopic activity in dogs with ventricular arrhythmias after acute myocardial ischemia, we designated continuous electrical activity as a marker of reentry or more cautiously, as strong presumptive evidence for reentry.

We do not believe that continuous electrical activity can simply be equated with reentry. We and others have demonstrated that portions or all of the continuous electrical activity may be dissociated from the ongoing rhythm and may even represent artifact. The latter was particularly a problem in patients studied using electrode catheter recordings in the left ventricle. The examples in the present studies associating continuous electrical activity with the slowly conducting portions of a reentrant circuit were based on cause-and-effect relationships between the functional properties of the continuous electrical activity and the behavior of the ventricular tachycardia. This was particularly evident in the ventricular tachycardia documented in figure 3, in which the spontaneous termination of sustained ventricular tachycardia followed a Wenckebach-like conduction in the initial portion of the continuous interectopic activation. The progressive delay in the initial portion from the preceding QRS began before slowing of the tachycardia. This sequence provides evidence of functionally dissociated pathways in that a slight perturbation in the reentrant pathway i.e., initial portion, can destabilize the tachycardia, with a path of lesser delay being used to activate the heart through the exit potential. The designation of the clinical syndrome as recurrent ventricular tachycardia carries with it the implicit idea of a regular rhythm that spontaneously terminates and abruptly starts.
tained reproducible patterns of interectopic activity from epicardial recordings overlying the infarct zone. We do not know why two patterns, random or reproducible, were recorded during sustained ventricular tachycardia. One possibility might be the way the composite electrode is placed over the infarct zone. Another may relate to more than one reentry pathway being involved in a given sustained ventricular tachycardia. The overlap of activation patterns from different reentrant circuits could mask a common exit from the area of slow conduction.10 Also, we cannot exclude the possibility that, in some cases, the random activity was not associated with reentry. However, continuous electrical activity in all our cases was seen only during sustained ventricular tachycardia and not during sinus rhythm.

The recording of reproducible patterns of continuous electrical activity during sustained ventricular tachycardia provides a basis for the regularity of the timing and uniformity of the QRS complexes during the arrhythmia. Such reproducible continuous activation was the exception during coupled ectopic beats observed by El-Sherif et al.4 even when these beats were induced by similarly coupled premature stimulation. Sustained ventricular tachycardia, on the other hand, shows that a given pathway can be used repetitively with remarkable regularity. At the same time, the tentative nature of conduction found in these same areas was frequently observed. Procainamide, for example, suppressed the amplitude of the mid-interectopic portion of the continuous electrical activity and caused progressive delay between the initial and exit potentials with increasing dosage (fig. 6). In our studies, the mid-interectopic potentials appeared to be the weak link in regard to the depressant action of antiarrhythmic drugs.

In a recent clinical report of patients with coupled premature depolarizations, Giardina and Bigger reported that increasing plasma concentrations of procainamide were associated with progressive prolongation of the coupling intervals until the arrhythmia was abolished.29 They speculated that procainamide “prolongs conduction in a depressed portion of a reentrant pathway such that conduction is further depressed and block finally occurs, thereby terminating the arrhythmias.” Other drugs may exert their antiarrhythmic action on different parts of the reentrant pathway. This may determine the differential effect of drugs on inducibility, rate and stability of recurrent ventricular tachycardia.30

The division of continuous electrical activity into temporal components was based on empirical observations, but is not unprecedented. Previous studies from our laboratory22 provided evidence that fractionated potentials could be observed consistently before the beginning of the QRS complex in runs of ventricular tachycardia. A recent study by Kabell et al.31 has shown that the exit potential was distinct for each sustained ventricular tachycardia, i.e., specific QRS morphology. In some cases in which one sustained ventricular tachycardia spontaneously changed to another form, the exit potential changed before the change in QRS morphology.

Clinically, similar “exit” potentials have been noted during sustained ventricular tachycardia in patients with a recurrent form of this syndrome.32,33 The earliest sites of endocardial or epicardial activation were referred to as “the site of origin of ventricular tachycardia.” That these sites were part of continuous activity occurring in areas of slow conduction can be inferred by noting the continuous electrical activity recorded in patients with sustained ventricular tachycardia by Horowitz et al.33 and the designation by Josephson et al.32 of more than one “site of origin” for a given ventricular tachycardia. We have used the term “exit potential” to describe that part of the slow conducting wave that just precedes activation of normal tissue, thus initiating a QRS complex. In patients with reproducible interectopic activity, we could consistently identify uniform exit potentials in the composite recording. However, the initial and mid-interectopic portions of the continuous activation pattern were not as consistently identifiable. Alternation of potentials from one cardiac cycle to another may occur in the interectopic activation pattern.31 In any event, on the basis of functional properties, three portions of the interectopic activity could be consistently characterized.

Boineau and Cox34 constructed a hypothetical scheme to describe the reentrant circuit presumed to occur in patients with sustained ventricular tachycardia. Coincidentally, this theoretical representation included three separate components: an area of slow, desynchronized conduction with a region of maximal delay, the area of origin of tachycardia and the reentrant pathway linking the two areas. These authors, using activation data, independently arrived at an analysis of the reentrant circuit remarkably similar to our interpretation based on experimental observations.

Our studies indicate that in 60% of sustained ventricular tachycardias, the association between reproducible patterns of continuous electrical activation and functional changes in the tachycardia, i.e., initiation, termination, slowing due to antiarrhythmic drugs, can be consistently and repeatedly observed. Analysis of these patterns of electrical activation may further define the nature of these arrhythmias.

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