

Spontaneous Compared With Induced Onset of Sustained Ventricular Tachycardia

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Electrophysiological characteristics of the modes of initiation of 16 episodes of spontaneously occurring sustained ventricular tachycardia recorded in 16 patients by two-channel ambulatory electrocardiographic monitoring were compared with the characteristics of ventricular tachycardia induced by programmed electrical stimulation. Eleven episodes of spontaneous ventricular tachycardia began after a single ventricular premature depolarization (VPD), three episodes after two VPDs, and two episodes after five VPDs. By comparison, only four episodes of sustained ventricular tachycardia were induced with a single VPD. Each episode of spontaneous ventricular tachycardia was initiated by a late coupled VPD ($RR':QT$ ratio >1.0). The VPD was often morphologically similar to the ensuing ventricular tachycardia (eight of 11 episodes that began after a single VPD). No correlation was found between the modes of initiation of spontaneous and induced ventricular tachycardia. We hypothesize that concealed decremental slow conduction, reflected in the long coupling intervals of VPDs initiating ventricular tachycardia, is of critical importance in initiating ventricular tachycardia. We conclude that major differences exist in the timing and number of VPDs associated with the onsets of spontaneous and induced sustained ventricular tachycardia. (*Circulation* 1988;78:885-892)

Presently, investigators believe that the mechanism of sustained ventricular tachycardia in humans under most circumstances is reentry.¹⁻⁴ The basis for this conclusion includes animal and human studies demonstrating the reproducible initiation and termination of ventricular tachycardia by premature beats, the response of ventricular tachycardia to the delivery of extrastimuli, the ability to record continuous diastolic activity during ventricular tachycardia, and activation mapping.⁵⁻¹⁵ Although recent reports have suggested that some tachycardias are consistent with

triggered activity, the relative importance of this mechanism in humans is unclear at the present time.^{16,17} The available data is most consistent with reentry as the mechanism for most episodes of paroxysmal ventricular tachycardia associated with coronary artery disease.

Prerequisites for reentry include unidirectional block and slow conduction. Spontaneous ventricular premature depolarizations are thought to initiate sustained ventricular tachyarrhythmias by producing unidirectional block or slow conduction or both, which establishes the conditions necessary for reentry to occur. In an analogous fashion, programmed ventricular extrastimuli, which are the correlates of spontaneous ventricular premature depolarizations, are delivered in an attempt to provoke sustained ventricular tachycardia. Programmed stimulation has been used to determine mechanisms of and to help guide therapy for these arrhythmias.^{1,18}

This study was undertaken to compare the spontaneous onset of sustained ventricular tachycardia with the mode of induction required in the electrophysiology laboratory. We sought to determine whether there was any correlation between the spontaneous initiation of sustained VT and the requirements for initiation of the same arrhythmias by programmed ventricular stimulation.

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This data was presented in part at the 57th Scientific Sessions of the American Heart Association, November 1984, Miami, Florida.

Supported in part by grants from the American Heart Association, Southeastern Pennsylvania Chapter, Philadelphia, Pennsylvania; and National Heart, Lung, and Blood Institute, Bethesda, Maryland (HL-28093, HL-07346). M.E.J. is the Robinet Foundation Professor of Medicine (Cardiovascular Diseases).

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Received March 1, 1988; revision accepted June 2, 1988.

Patients and Methods

Patients

The patient population consisted of 16 men who ranged in age from 37 to 75 years (mean, 62 years) and had spontaneously occurring and inducible sustained ventricular tachycardia. Cardiac diagnoses included previous myocardial infarction in 13 patients, significant coronary artery disease without previous myocardial infarction in one patient, and no evidence of organic heart disease in two patients as determined by echocardiography and cardiac catheterization. For each patient, an episode of spontaneous sustained uniform ventricular tachycardia was recorded on a two-channel Holter monitor (Avionics, Los Angeles, California). In one patient, two episodes of spontaneous ventricular tachycardia were recorded. These episodes had the same electrophysiological characteristics, and only one was included in the analysis. No patients were taking antiarrhythmic medications at the time of the spontaneous onset of ventricular tachycardia.

Electrophysiological Study

All patients underwent electrophysiological evaluation while not taking antiarrhythmic medications. Electrophysiological study was performed within 3 days of the spontaneous episodes of tachycardia in 15 patients and within 6 days in one patient. Intracardiac electrophysiological evaluation was performed as previously described.¹ Briefly, three or four quadripolar or tripolar electrode catheters were inserted percutaneously or by cut down and positioned in the high right atrium, at the atrioventricular junction to record the His bundle electrogram, in multiple right ventricular sites, and in some patients, a catheter electrode was inserted in the coronary sinus. The electrophysiological stimulation protocol consisted of atrial pacing, atrial programmed electrical stimulation, single, double, triple, and, in some instances, quadruple programmed ventricular stimuli during sinus rhythm and multiple ventricular paced-drive cycle lengths (600, 500, and 400 msec) from two or more right ventricular sites, and rapid ventricular pacing at cycle lengths of 350–250 msec for 15–30 seconds. Stimulation was performed with rectangular pulses of 1-msec duration at twice diastolic threshold delivered with a custom-designed programmable stimulator with an optically isolated constant-current source (Bloom, Reading, Pennsylvania). Recordings were obtained with a sixteen-channel physiological recorder (VR-16, Electronics for Medicine, White Plains, New York) with real-time recordings on an ink-jet recorder (Elema mingo-*graf*, Siemens, Solna, Sweden). All data were stored on magnetic tape (5600 C, Honeywell, Denver, Colorado) for later retrieval.

For each patient, an episode of induced ventricular tachycardia was selected for subsequent evaluation. For patients in whom ventricular tachy-

cardia was induced with multiple-pacing techniques, the least aggressive mode of induction (the longest drive cycle length with the fewest number of extrastimuli required to induce ventricular tachycardia) was selected.

Evaluation of Spontaneous Onset of Sustained Ventricular Tachycardia

The onset of ventricular tachycardia was chosen as the first complex that morphologically resembled the ensuing complexes in a subsequent sustained uniform ventricular tachycardia. The initiating complex of ventricular tachycardia was chosen as the first ventricular premature depolarization (VPD), after sinus rhythm, occurring immediately before the onset of ventricular tachycardia. The onset of sustained ventricular tachycardia was evaluated with respect to 1) the mean sinus cycle length preceding the episode of ventricular tachycardia; 2) the coupling interval between the last sinus QRS and the initiating complex of ventricular tachycardia (RR'); 3) the number of VPDs preceding the onset of ventricular tachycardia (when the initiating complex was morphologically identical to the complexes of the subsequent ventricular tachycardia, this number was chosen to be one); 4) the ratio of the coupling interval between the last sinus QRS and the initiating complex of the ventricular tachycardia to the last RR before the initiation of ventricular tachycardia (RR':RR); and 5) the ratio of the RR' to the sinus QT interval (RR':QT).

For patients in whom only a single VPD preceded the onset of ventricular tachycardia, the VPDs were evaluated with respect to their morphological similarity to the ensuing ventricular tachycardia complexes.

Evaluation of Mode of Electrophysiological Induction of Sustained Uniform Ventricular Tachycardia

The electrophysiological induction of sustained ventricular tachycardia was evaluated with respect to 1) the ventricular paced-drive cycle length; 2) the number of ventricular extrastimuli necessary to induce ventricular tachycardia; 3) the coupling interval of the last beat of the drive to the first programmed ventricular extrastimulus responsible for ventricular tachycardia (S₁-S₂).

Statistical Analysis

For each patient, the cycle lengths of the spontaneous ventricular tachycardia and induced ventricular tachycardia were compared with a two-tailed *t* test for paired data.

Possible relations between the mode of onset of spontaneous ventricular tachycardia and the mode of induction of induced ventricular tachycardia were evaluated with two-tailed *t* tests for unpaired data and with Fisher's exact test when the data were discrete. The descriptive variables analyzed, for spontaneous ventricular tachycardia, were the sinus

TABLE 1. Electrophysiological Variables of Spontaneous Ventricular Tachycardia Onset Compared With Ventricular Tachycardia Induction

		VT induced			
		Extrastimuli			
Spontaneous VT	(n)	EPS paced-cycle length (msec)	Single (n)	Multiple (n)	S ₁ -S ₂ (msec)
Sinus cycle length					
<774	9	467 ± 100	3	6	274 ± 53
≥774	7	557 ± 79	1	6	281 ± 28
VPD Preceding VT					
1	11	490 ± 100	1	10	278 ± 47
>1	5	540 ± 90	3	2	276 ± 36
VPD morphology					
Same	8	480 ± 100	1	7	278 ± 49
Different	3	530 ± 120	0	3	290 ± 52
RR'					
<499	11	500 ± 100	2	9	276 ± 47
>499	5	520 ± 110	2	3	280 ± 35
RR':QT ratio					
<1.2	8	500 ± 110	0	8*	270 ± 53
>1.2	8	510 ± 100	4	4	285 ± 31
RR':RR ratio					
≤0.66	9	478 ± 97	2	7	262 ± 51
>0.66	7	486 ± 107	3	4	280 ± 18

Values are mean ± SD. n is number of episodes.

VT, ventricular tachycardia; EPS, electrophysiological programmed stimulation; VPD, ventricular premature depolarization.

*p = 0.038.

cycle length (dichotomized to less than and greater than or equal to the mean value of 774); the number of VPDs before the onset of ventricular tachycardia (dichotomized to single and multiple VPDs); the RR' (dichotomized to less than and greater than the mean value of 499); the RR':QT ratio (dichotomized to less than and greater than the median value of 1.20); the RR':RR ratio (dichotomized to less than or equal to and greater than the mean value of 0.66); and for episodes of ventricular tachycardia initiated by a single VPD, the VPD morphology (dichotomized as similar to or different from the ensuing ventricular tachycardia complexes).

The analyzed variables for induced ventricular tachycardia were the paced-drive cycle length, the number of extrastimuli necessary to induce ventricular tachycardia (dichotomized to single and multiple extrastimuli), and S₁-S₂.

Possible correlations between the continuous spontaneous and induced variables were evaluated by linear regression with the independent variables of sinus cycle length, RR', RR':QT ratio, and RR':RR ratio and the dependent variable of S₁-S₂.

All data are expressed as mean ± SD unless otherwise specified. A p value less than 0.05 was considered statistically significant.

Results

Spontaneous Ventricular Tachycardia Compared With Induced Ventricular Tachycardia

Sixteen episodes of spontaneous and induced ventricular tachycardia were analyzed. The mean

cycle length of the spontaneous ventricular tachycardia was 388 ± 87 msec, whereas the mean cycle length of the induced ventricular tachycardia was 340 ± 84 msec (p = NS).

Sinus Cycle Length as Predictor of Ventricular Tachycardia Induction Variables

The mean sinus cycle length preceding spontaneous initiation of ventricular tachycardia was 774 ± 137 msec. With the dichotomization described above, the mean electrophysiological variables, paced-drive cycle length and S₁-S₂, for the two groups were compared. Possible differences between these groups in the number of extrastimuli necessary to induce ventricular tachycardia (dichotomized to single and multiple) were evaluated. No significant differences in ventricular tachycardia induction variables could be detected between these two groups (Table 1).

Number and Morphology of Ventricular Premature Depolarizations Preceding Ventricular Tachycardia as Predictor of Electrophysiological Induction Variables

Eleven episodes of ventricular tachycardia began spontaneously after a single VPD, three episodes after two VPDs, and two episodes after five VPDs. By comparison, only four episodes of sustained ventricular tachycardia were induced with one VPD. Nine episodes were induced with two VPDs and three episodes with three VPDs. In only three instances were fewer programmed ventricular

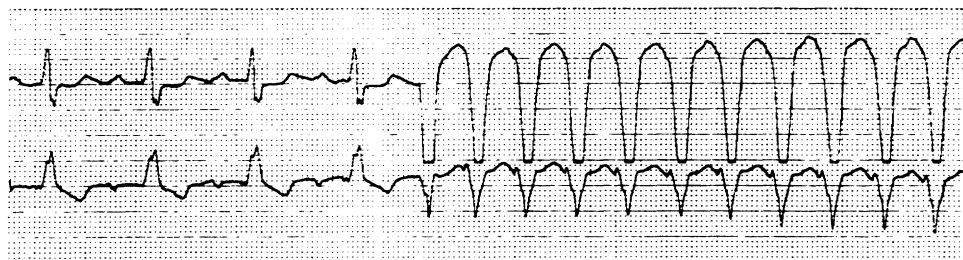


FIGURE 1. *Electrogram of spontaneous onset of sustained ventricular tachycardia after a single ventricular premature depolarization of morphology similar to the ensuing ventricular tachycardia. Eight episodes of sustained ventricular tachycardia began after a single ventricular premature depolarization having a morphology similar to the ensuing ventricular tachycardia. Representative example is shown.*

extrastimuli required than were required by spontaneous VPDs to induce ventricular tachycardia ($p=0.063$, Table 1).

With the dichotomization described above, no significant differences in ventricular tachycardia induction variables between the two groups could be detected (Table 1).

Two different patterns were observed during spontaneous initiation after a single VPD. Eight episodes began after a single VPD that was morphologically similar to the complexes of the subsequent ventricular tachycardia (Figure 1). Three episodes of sustained ventricular tachycardia began after a single VPD with a morphology different from that of the sustained ventricular tachycardia (Figure 2). Five episodes of ventricular tachycardia began after multiple VPDs (Figure 3).

Analysis was performed for patients with only one VPD preceding ventricular tachycardia. The groups were defined by whether the VPD was morphologically similar to or different from the ensuing ventricular tachycardia. No significant differences in ventricular tachycardia induction variables could be found between the two groups (Table 1). Also, there was no difference in the mean sinus cycle length, RR' , $RR':RR$ ratio, or $RR':QT$ ratio

between those episodes in which the initiating VPD morphology was the same compared with those in which it was different from the ventricular tachycardia morphology (Table 2).

Coupling Interval of the First Ventricular Premature Depolarization as Predictor of Electrophysiological Induction Variables

The mean RR' was 499 ± 98 msec. With the dichotomization described above, the electrophysiological induction variables for the two groups were compared. No statistically significant differences were found (Table 1).

$RR':QT$ Ratio as Predictor of Electrophysiological Induction Variables

The median ratio between the RR' and the sinus QT interval ($RR':QT$) for the initiation of spontaneous ventricular tachycardia was 1.20. With the dichotomization described above, the electrophysiological induction variables were compared. Although neither the mean electrophysiological paced cycle length nor the mean S_1 - S_2 were significantly different for the two groups, the number of extrastimuli necessary to induce ventricular tachycardia was significantly less in the group of patients

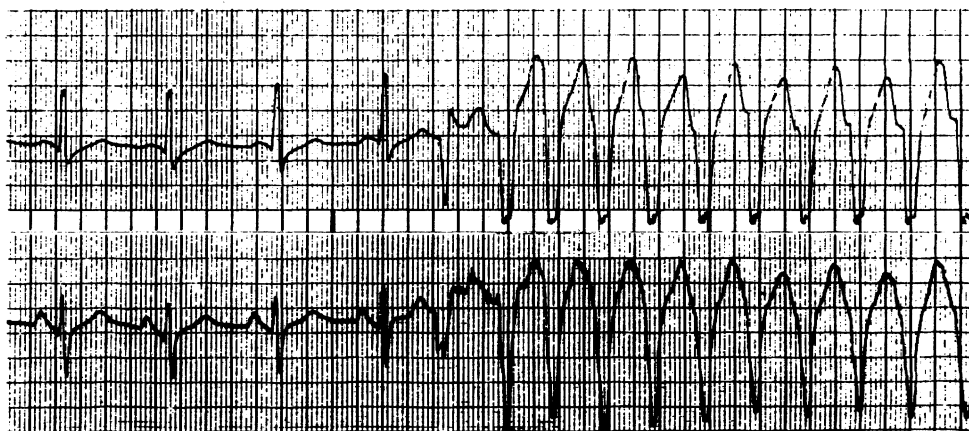


FIGURE 2. *Electrogram of spontaneous onset of sustained ventricular tachycardia after a single ventricular premature depolarization of morphology different than the ensuing ventricular tachycardia. Three episodes of sustained ventricular tachycardia began after a single ventricular premature depolarization with a morphology different from that of the ensuing ventricular tachycardia. Representative example is shown.*

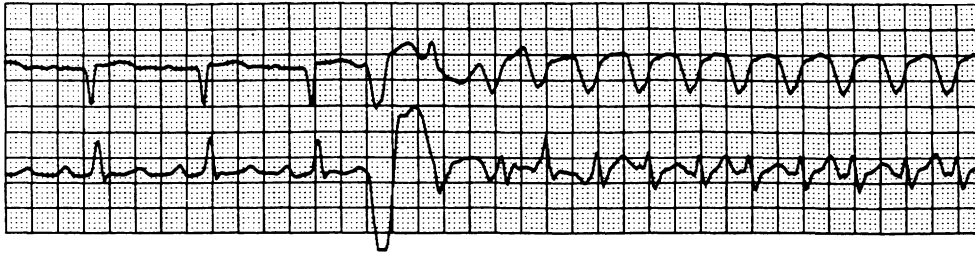


FIGURE 3. Electrogram of spontaneous onset of sustained ventricular tachycardia after multiple ventricular premature depolarizations. Five episodes of sustained ventricular tachycardia began after multiple ventricular premature depolarizations. Representative example is shown.

with the longer $RR':QT$ ratio ($p = 0.038$, Table 1). Of note, in all episodes of sustained ventricular tachycardia, the $RR':QT$ ratio was greater than one.

RR':RR Ratio as Predictor of Electrophysiological Conduction Variables

The mean ratio of RR' and the preceding RR interval ($RR':RR$) was 0.66. With the dictotomization described above, electrophysiological induction variables were compared. No significant differences between the groups could be found (Table 1).

By linear regression with the continuous independent variables of sinus cycle length, RR' , $RR':QT$ ratio, $RR':RR$ ratio and the dependent variable of S_1-S_2 , no correlation was found (correlation coefficients all <0.33).

Therefore, in most instances, spontaneous ventricular tachycardia began with a relatively late VPD that was frequently similar in morphology to that of the sustained ventricular tachycardia that followed. In most patients, more VPDs were required during electrophysiological study to induce ventricular tachycardia than were observed to occur spontaneously. Patients whose spontaneous episodes of ventricular tachycardia occurred after earlier first VPDs, relative to the QT interval, tended to require more extrastimuli to induce ventricular tachycardia. With this exception, none of the descriptive variables analyzed for spontaneous ventricular tachycardia, including the sinus cycle length, the number and morphology of the VPDs preceding ventricular tachycardia, the timing of the first VPD, and the timing of the first VPD relative to the sinus cycle length accurately predicted electrophysiological induction variables.

Discussion

Most episodes of sustained ventricular tachycardia are considered to be reentrant in nature.¹⁻⁴ This conclusion is based upon the ability to reproducibly initiate and terminate these arrhythmias by programmed stimulation, the response of the tachycardia to stimulation, the effect of drugs on the tachycardia, and by activation mapping during ventricular tachycardia.^{1,2,5,9,19}

Ventricular premature depolarizations are believed to trigger sustained ventricular tachyarrhythmias by

creating unidirectional block or slow conduction or both. The ventricular premature depolarization induced by programmed extrastimuli in the electrophysiology laboratory is the counterpart of the spontaneous ventricular premature depolarization. Therapy for ventricular tachycardia has been directed at suppressing the VPDs.^{20,21} Holter monitoring has been used to document these spontaneous events and their response to medical therapy.²¹

Ventricular premature depolarizations have been graded with respect to frequency, complexity, and the so-called "R-on-T" phenomenon. Very early ventricular premature depolarization or the R-on-T phenomenon has been ascribed particular significance in its ability to induce sustained ventricular tachycardia.^{22,23} However, based on animal and human studies, investigators have questioned the clinical significance of early ventricular premature depolarizations.²⁴ Based on clinical studies, investigators have questioned the ability of the R-on-T phenomenon in the setting of the coronary care unit to predict the later occurrence of malignant ventricular arrhythmias.^{25,26} Similarly, it has been reported that most episodes of paroxysmal nonsustained ventricular tachycardia observed during Holter monitoring began with relatively late ventricular premature depolarizations.²⁷

Since the original descriptions of R waves interrupting T waves by Smirk,^{28,29} there have been several attempts to quantify this phenomenon. The prematurity index is one of the simplest measurements and is merely the $RR':QT$ ratio with a value

TABLE 2. Spontaneous Onset of Ventricular Tachycardia After Single Ventricular Premature Depolarization (VPD) Relation to Morphology of VPD

Morphology of VPD	Similar to VT (n = 8)	Different from VT* (n = 3)
Sinus cycle length	731 ± 151	777 ± 86
RR'	508 ± 125	517 ± 100
RR'/QT	1.28 ± 0.35	1.29 ± 0.25
RR'/RR	0.69 ± 0.13	0.67 ± 0.14

Values are mean ± SD; n is number of episodes.
VPD, ventricular premature depolarization; VT, ventricular tachycardia.

*p = not significant.

of less than one corresponding to an R wave interrupting the previous QT interval. In the present study, we observed the spontaneous onset of sustained ventricular tachycardia in 16 patients. Most of the episodes began with a single premature ventricular depolarization with a relatively long coupling interval. In most instances, the initial ventricular premature depolarization resembled the morphology of the subsequent sustained ventricular tachycardia. The mean prematurity index was 1.25 ± 0.27 , and in each episode, it was greater than one. The mean coupling interval was 499 ± 98 msec. Thus, by these criteria, premature beats initiating ventricular tachycardia were not early R-on-T phenomena. The present study lends further credence to the more and more widely accepted concept that the R-on-T phenomenon is not a predictor of malignant ventricular arrhythmias in chronic ischemic disease.³⁰

When systematically analyzed, none of the variables describing the mode of spontaneous initiation of ventricular tachycardia could be used to accurately predict variables of programmed electrophysiological stimulation required in the laboratory to induce ventricular tachycardia. We observed that during intracardiac electrophysiological study very different modes of stimulation; that is, drive cycles, number of premature stimuli, and coupling intervals of extrastimuli were often required for the induction of arrhythmias similar to those observed clinically.

Although this study does not contain data to support any specific mechanistic claim, our observations can be interpreted in light of our current understanding of the mechanisms of ventricular tachycardia. It has been observed in experimental models of subacute ischemia that conduction delays often precede the onset of ventricular arrhythmias.³¹ Sinus rhythm mapping in patients with ventricular tachycardia and coronary artery disease reveals electrogram fractionation.^{32,33} These fractionated electrograms have been shown to be related to slow conduction due to the uncoupling of relatively normal cells in tissues exhibiting nonuniform anisotropy.^{34,35} Thus, patients with ventricular tachycardia have slow conduction, a prerequisite for reentry.

Concealed decremental slow conduction may explain the observation that many episodes of ventricular tachycardia begin as late coupled ventricular depolarizations. As the sinus impulses reach the diseased tissue, progressive local delay occurs. When local conduction is sufficiently slow, the depolarization wavefront encounters adjacent tissue that has recovered excitability, thereby leading to a reentrant rhythm. The slow conduction in an infarcted area could account for the appearance of a relatively late ventricular premature depolarization.

The initiating ventricular premature depolarizations were often morphologically similar to the ensuing ventricular tachycardia. The morphologically similar VPDs most likely represent the first

tachycardia beats exiting from the circuit. The RR' would then encompass the conduction time of the previous sinus impulse through the area of locally slowed conduction and through the tachycardia circuit until the point of exit. Episodes of ventricular tachycardia after a single VPD of different morphology might reflect an initial different exit from the same tachycardia circuit. Alternatively, the VPDs of different morphology may establish the slow conduction necessary for subsequent tachycardia initiation.

Marked differences in the mode of spontaneous initiation of ventricular tachycardia and ventricular tachycardia induction were found. The number of ventricular premature depolarizations necessary for the spontaneous initiation tended to be less than the number of programmed extrastimuli necessary for ventricular tachycardia induction. This observation may also be understood in terms of slowed and inhomogenous conduction.

Conduction velocity and conduction block in ischemic myocardium have been shown to be rate dependent.⁷ Intermittent ischemia and rate changes in the ambulatory state may facilitate the development of the local conduction delays necessary to provoke ventricular tachycardia. More extrastimuli may be necessary in the laboratory to duplicate the slowing of conduction and block that occur in the clinical state secondary to ischemia, rate changes, and other neurogenic and hemodynamic factors not yet well understood. Further elucidation of the relative contributions of these factors to conduction velocity and block in the clinical state is necessary. This might be pursued by endomyocardial mapping to evaluate local conduction and variations in electrogram fractionation as functions of ischemia, rate, and autonomic tone.

Limitations

Of necessity, the measurements made during the observed spontaneous onset of ventricular tachycardia were somewhat subjective in nature. Deciding which beat is responsible for ventricular tachycardia initiation is, at times, difficult and subject to interpretation. This was particularly important during those episodes that seemed to begin after multiple spontaneous ventricular depolarizations. In those instances, because only two electrocardiographic leads were observed, it was difficult to differentiate ventricular premature depolarizations with morphologies different from those of the sustained tachycardia. Nevertheless, most episodes began after a single ventricular premature depolarization having a morphology identical to that of the ventricular tachycardia, at least in the limited number of leads available. Similarly, because the number of electrocardiographic leads monitored was limited during the spontaneous onset of ventricular tachycardia, we cannot be sure that the observed tachycardia was identical to that induced in the electrophysiology laboratory.

Although we cannot definitively exclude the site of stimulation as an important factor in the induction of ventricular tachycardia, we have observed that the site of stimulation with respect to the site of ventricular tachycardia origin is not an important determinant of the mode of induction of ventricular tachycardia in the electrophysiology laboratory.³⁶ Stimulation close to the site of ventricular tachycardia origin, as determined by catheter endocardial mapping techniques, is not necessarily associated with an easier mode of ventricular tachycardia induction.

Conclusions

Despite the above limitations, we believe that these data suggest major differences in the timing and number of ventricular premature depolarizations associated with the spontaneous onset of ventricular tachycardia compared with that used in the electrophysiology laboratory. The observation that ventricular premature depolarizations initiating sustained ventricular tachycardia are frequently late coupled is consistent with our understanding that concealed decremental slow conduction precedes reentrant ventricular tachycardia. The discrepancies between the modes of initiation of spontaneous and induced ventricular tachycardia support our belief that factors other than the mere timing of spontaneous ventricular premature depolarizations and the presence of a ventricular tachycardia substrate are of prime importance in causing clinical sustained ventricular tachycardia. The further elucidation of these other factors may explain the discordances found between the ambulatory electrocardiographic and invasive electrophysiological assessment of antiarrhythmic drug efficacy and our abilities to predict arrhythmia recurrences by these methods.

Acknowledgments

We are grateful to Faith Marie Hope and Carol A. Davis for their technical assistance in the preparation of this manuscript.

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KEY WORDS • spontaneous sustained ventricular tachycardia
 • induced sustained ventricular tachycardia • programmed electrical stimulation • ventricular premature depolarization

Spontaneous compared with induced onset of sustained ventricular tachycardia.

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Circulation. 1988;78:885-892

doi: 10.1161/01.CIR.78.4.885

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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