Effect of Basic Drive Train Cycle Length on Induction of Ventricular Tachycardia by a Single Extrastimulus

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MORADY F, ET AL: Effect of Basic Drive Train Cycle Length on Induction of Ventricular Tachycardia by a Single Extrastimulus. *This study determined the effects of a wide range of basic drive cycle lengths on the induction of ventricular tachycardia (VT) by a single extrastimulus (S_2). Seventy-one patients with coronary artery disease and inducible sustained monomorphic VT underwent 121 electrophysiology tests either in the control state or during treatment with an antiarrhythmic drug. Ventricular basic drive trains were eight beats in duration and the intertrain interval was three seconds. Programmed ventricular stimulation was performed with S_2 using the longest possible basic drive cycle length rounded off to the nearest multiple of 100 msec, then using basic drive train cycle lengths that decreased in 100 msec steps to 400 msec, and finally using a basic drive cycle length of 350 msec. At each drive cycle length, an interval of > 50 msec beyond the effective refractory period (ERP) was scanned with S_2. Monomorphic VT was induced by S_2 in 52/121 studies (43%). The drive cycle length had a significant linear effect on the log odds of inducing VT ($P < 0.0001$). The highest yield of VT occurred with a drive cycle length of 350 msec (42/121, 34%), and with each increment in drive cycle length, the expected odds of inducing VT decreased by a factor of 1.7. In 88% of cases in which VT was induced at a particular drive cycle length but not at longer drive cycle lengths, the coupling intervals that induced VT exceeded the ERP measured at one or more of the longer basic drive cycle lengths. In conclusion, there is an inverse relationship between the basic drive cycle length and the yield of monomorphic VT induced by S_2. The use of shorter basic drive cycle lengths often facilitates the induction of VT by some effect other than critical shortening of the S_2 coupling interval.* (J Electrophysiol 3:111-116, 1989)

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Programmed ventricular stimulation typically is performed using basic drive trains that vary in cycle length between 400 and 600 msec.[1-9] The cumulative yield of ventricular tachycardia (VT) induced by single or double ventricular extrastimuli has been demonstrated to increase with the use of multiple basic drive cycle lengths spanning a range of at least 200 msec.[10] However, no prior studies have compared the inducibility of VT at various basic drive cycle lengths. The purpose of this prospective study was to determine the effects of a wide range of basic drive cycle lengths on the induction of VT by a single extrastimulus. The study protocol was limited to the use of a single extrastimulus in order to allow a direct comparison of the coupling intervals required to induce VT at different basic drive cycle lengths.

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Methods

Selection of Subjects

The following criteria were used to select the subjects for this study: (1) presence of coronary artery disease; (2) sinus rhythm; (3) a documented history of sustained, monomorphic VT; (4) sustained monomorphic VT inducible by programmed ventricular stimulation with 1, 2, or 3 extrastimuli; (5) hemodynamic stability during induced VT; and (6) ability to terminate induced VT by pacing. Because analysis of the effects of the basic drive cycle length on the induction of VT would be confounded by the induction of various types of VT, patients in whom more than one configuration of VT was induced by a single extrastimulus were excluded from this study. Also excluded were patients in whom induced VT was preceded by a bundle branch reentry beat, since the branch reentry beats may have served as a second extrastimulus.

Characteristics of Patients

Seventy-one patients with coronary artery disease met the inclusion criteria for this study. There were 67 men and 4 women, and their mean age was 64 ± 10 years (± standard deviation). The mean left ventricular ejection fraction, determined in 45 patients, was 31 ± 9. In 10 patients, the study protocol was performed only in the absence of antiarrhythmic drug therapy, in 17 patients the protocol was performed in both the control state and during antiarrhythmic drug therapy, and in 44 patients the study protocol was performed only during antiarrhythmic drug therapy because the induced VT was not hemodynamically stable in the control state. The antiarrhythmic drugs that were used included quinidine in 19 studies, mexiletine in 11 studies, quinidine plus mexiletine in 3 studies, encainide in 14 studies, amiodarone in 31 studies, and a combination of amiodarone plus one of the other antiarrhythmic drugs in 16 studies. Data from a total of 121 electrophysiology tests are included in this study.

Study Protocol

Electrophysiology studies were performed in the fasting, nonsedated state after informed consent was obtained. Three 6F quadripolar electrode catheters were inserted into a femoral vein and positioned in the right atrium, His bundle position, and right ventricular apex. A short 5F cannula inserted into a femoral artery was used to monitor the arterial pressure. Leads V_1, I and III, and the intracardiac electrograms were displayed in an oscilloscope and recorded with a Siemens-Elema Mingograf-7 recorder (Siemens-Elema, Solna, Sweden). Pacing was performed using a programmable stimulator (Bloom Associates, Ltd., Narbeth, PA, USA). The pacing stimuli were twice the diastolic threshold and 2 msec in duration.

Basic drive trains were eight beats in duration and separated by pauses of three seconds. Extrastimuli were scanned in steps of 10 msec. If there was atrioventricular dissociation during ventricular pacing, the atrium was paced synchronously with the ventricle in order to prevent interruption of the basic drive train by sinus capture beats.

The study protocol was performed upon completion of the standard, clinically used stimulation protocol, that consisted of programmed stimulation with 1, 2, and 3 ventricular extrastimuli using basic drive cycle lengths of 600 and 400 msec, first at the right ventricular apex, then if necessary, at the right ventricular outflow tract or septum. Sustained VT was defined as VT lasting > 30 seconds or requiring countershock or pacing to terminate; nonsustained VT was defined as VT 6 beats to 30 seconds in duration. In accord with the selection criteria for subjects, sustained monomorphic VT was inducible by 1, 2, or 3 extrastimuli in every patient in this study.

Because of time constraints, the study protocol was performed only at the right ventricular apex. Diastole was scanned with an extrastimulus during ventricular pacing, using the longest possible basic drive cycle length rounded off to the nearest multiple of 100 msec. Programmed stimulation with the single extrastimulus then was repeated using basic drive

train cycle lengths that decreased in 100 msec steps to 400 msec, and finally using a basic drive cycle length of 350 msec. At each basic drive cycle length, an interval of at least 50 msec beyond the effective refractory period (ERP) was scanned with the extrastimulus. Whenever VT was induced, programmed stimulation was continued at the same basic drive cycle length until all of the coupling intervals that resulted in the induction of VT were identified. The endpoint of the study protocol was completion of programmed stimulation using all of the basic drive train cycle lengths. If at any point in the protocol a hemodynamically unstable VT requiring countershock was induced, the study protocol was stopped and the patient was excluded from the study.

Data Analysis

To study the relationship between ventricular ERP and the basic drive cycle length, a random coefficient growth curve model was fit to the data.[11] For each of the 121 cases in the study, a regression of ERP on basic drive cycle length was fit. The 121 slopes and intercepts obtained from these regression lines were then analyzed. The effect of the basic drive cycle length on the induction of VT by a single extrastimulus was analyzed using logistic regression.[12] For this analysis, the log odds of inducing VT was modeled as a linear function of the basic drive cycle length. The effect of the basic drive cycle length on the range of coupling intervals that induced VT was analyzed using an analysis of variance. A P value < 0.05 was considered statistically significant.

Results

Ventricular Effective Refractory Periods

The mean ventricular ERPs are listed in Table 1. The basic drive cycle length had a significant linear effect on ERP ($P < 0.0001$), with each decrement in drive cycle length decreasing the expected value of the ERP by 11 msec.

Induction of VT by One Extrastimulus

Monomorphic VT was induced by a single extrastimulus in a total of 52/121 electrophysiology studies (43%). The VT was sustained in 48 of the studies and nonsustained in four. Polymorphic VT was never induced. Table 1 displays the incidence of monomorphic VT induced by one extrastimulus at each basic drive cycle length. The incidence of induced VT was highest when the basic drive cycle length was 350 msec (41/121, 34%). Among 52 studies in

TABLE 1

Effect of Basic Drive Cycle Length on Ventricular Refractoriness and Induction of Ventricular Tachycardia by a Single Extrastimulus

Basic Drive Cycle Length (ms)	No. of Studies	ERP (ms)	No. With Inducible VT	Range of CI's That Induced VT*	
				Range (ms)	Sample Size
350	121	244 ± 23+	41 (34%)	43 ± 24	25
400	121	253 ± 23	34 (28%)	41 ± 24	25
500	121	263 ± 22	19 (16%)	40 ± 19	17
600	121	274 ± 24	10 (8%)	38 ± 35	8
700	107	286 ± 25	6 (6%)	45 ± 34	6
800	83	300 ± 24	5 (6%)	27 ± 15	3
900	48	314 ± 29	2 (4%)	–	0
1000	24	318 ± 32	1 (4%)	–	0
1100	15	323 ± 25	0	–	0

+Mean ± standard deviation
*There were no significant differences between the various basic drive cycle lengths.
CI = coupling interval, ERP = effective refractory period, No. = number, VT = ventricular tacyhcardia.

which VT was induced by one extrastimulus, 350 msec was the only basic drive cycle length at which VT was induced in 15 (29%). The drive cycle length had a significant linear effect on the log odds of inducing VT ($P < 0.0001$), with each increment in drive cycle length decreasing the expected odds of inducing VT by a factor of 1.7.

The mean cycle length of VT induced by one extrastimulus, 427 ± 64 msec, was significantly longer than the mean cycle length of VT inducible only by 2 or 3 extrastimuli, 352 ± 80 msec ($P < 0.001$). Among the 69 electrophysiology studies in which VT was not inducible with a single extrastimulus, monomorphic VT was induced by two or three extrastimuli in 44 and 25 studies, respectively. A similar proportion of VTs induced by one versus two or three extrastimuli had a right bundle branch block configuration (60% vs 58%, respectively).

Coupling Intervals at Which VT Was Induced

Whenever ≥ 2 coupling intervals induced VT at a particular basic drive cycle length, the range of coupling intervals that induced VT was determined; the mean range of extrastimulus coupling intervals that induced VT at each basic drive cycle length are listed in Table 1. The range of coupling intervals that induced VT did not differ significantly among the various drive cycle lengths. When VT was inducible at a particular drive cycle length, the shortest coupling interval that induced VT was within 10 msec of the ventricular ERP in 52% of cases, and > 20 msec beyond the ventricular ERP in the remaining cases.

In 88% of cases, when VT was induced at a particular drive cycle length but not at longer drive cycle lengths, the coupling intervals that induced VT exceeded the ERP measured at 1 or more of the longer basic drive cycle lengths.

Effect of Antiarrhythmic Drug Therapy

A comparison of electrophysiology tests performed in the control state and those performed in the presence of antiarrhythmic drug therapy demonstrated no significant difference in the relative yield of VT at the various basic drive cycle lengths.

Discussion

Yield of Ventricular Tachycardia with a Single Extrastimulus

Among 121 cases of sustained monomorphic VT inducible by programmed stimulation with 1–3 extrastimuli, the use of multiple basic drive cycle lengths resulted in a 43% yield of inducible VT when a single extrastimulus was used. In contrast, in prior clinical studies that have used only two basic drive cycle lengths between 600 and 400 msec, the percentage of monomorphic VTs induced by a single extrastimulus has been 16%–28%.[2,4,5,7,9] In the present study, had the basic drive cycle lengths been limited to 400 and 600 msec, as is typical in clinical stimulation protocols, the yield of VT with a single extrastimulus would have been 28%. Therefore, the use of multiple basic drive cycle lengths increases the yield of monomorphic VT during programmed stimulation with one extrastimulus.

Effect of Basic Drive Cycle Length

The results of this study demonstrate an inverse relationship between the basic drive cycle length and the yield of monomorphic VT induced by a single extrastimulus. The shortest basic drive cycle length used in this study (350 msec) resulted in a 34% yield of VT during programmed stimulation with one extrastimulus, and there was a progressive fall in the yield of VT as the basic drive cycle length increased.

Coupling Intervals Associated with VT Induction

As expected, there was a progressive shortening of the ventricular ERP as the basic drive cycle length decreased. Therefore, the shorter basic drive cycle lengths allowed the use of extrastimulus coupling intervals that would not have resulted in ventricular capture at longer

basic drive cycle lengths, and this may have been a factor accounting for the higher yield of VT at the shorter basic drive cycle lengths. However, in more than 80% of cases, VT was induced by coupling intervals that exceeded the ERP at longer basic drive cycle lengths and that nevertheless had not induced VT at the longer drive cycle lengths. Therefore, the use of shorter basic drive cycle lengths often facilitates the induction of VT by some effect independent of the extrastimulus coupling interval. As has been suggested previously,[13] shortening the basic drive cycle length may facilitate the induction of VT by resulting in more slowing of conduction and/or greater heterogeneity in refractory periods within the reentrant circuit.

Comparison with Prior Studies

In this study, the basic drive cycle length did not have an effect on the range of coupling intervals that induced VT. In contrast, Breithardt et al.[13] reported that a decrease in the basic drive cycle length resulted in a widening in the range of coupling intervals capable of inducing VT. These disparate results may be attributable to differences in study design. Breithardt et al.[13] compared the sum of coupling intervals that induced VT with one or two extrastimuli at basic drive cycle lengths of 500 or 430 msec versus 370 or 330 msec. However, in the present study only one extrastimulus was used and the extrastimulus coupling intervals that induced VT were compared at individual drive cycle lengths ranging between 350 to 1100 msec.

Limitations

The subjects in this study were limited to patients who had hemodynamically-tolerated VT, and therefore the conclusions of the study may not apply in patients with rapid and hemodynamically unstable VT.

Many of the subjects in this study were being treated with antiarrhythmic drugs at the time of electrophysiological testing, and these drugs may have influenced the results. For example, it is possible that programmed stimulation with one extrastimulus is more likely to induce VT in the presence of antiarrhythmic drugs than in the control state. However, no difference in the relative yield of VT among the various drive cycle lengths was found when comparing control studies with studies performed during therapy with antiarrhythmic drugs.

The results of this study suggest that clinical programmed stimulation protocols should incorporate the use of a basic drive cycle length of 350 msec, because this will significantly increase the probability of inducing VT with one extrastimulus. The induction of monomorphic VT by one extrastimulus not only shortens the duration of electrophysiological testing but also may improve specificity by obviating the need for programmed stimulation with multiple extrastimuli, which are more likely to induce nonclinical forms of VT. However, the relative sensitivity and specificity of stimulation with one extrastimulus at a basic drive cycle length of 350 msec as compared to two and three extrastimuli at conventional drive cycle length of 400 and 600 msec remains to be determined.

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