Reentrant Ventricular Tachycardia

Interpretations of Electrophysiologic Findings and Its Applications

Yoshifusa AIZAWA, MD, Yasutaka TANABE, MD,
and Masayuki YAMAURA, MD

SUMMARY

Monomorphic sustained ventricular tachycardia (MSVT) was revisited in relation to the electrophysiologic findings and their relation to the drug efficacy. Old myocardial infarction is less common cause of MSVT in Japan, and the majority (about 2/3) of MSVT is unrelated to coronary artery disease but, the mechanism shared a common mechanism: reentry with an excitable gap as others. The reentrant mechanism was supported from the inducibility, the terminability of VT by electrical stimulation, and by the ability to entrain with rapid pacing. In MSVT associated with underlying heart diseases, diseased myocardium showed low amplitude and fragmented electrograms and the area was considered to participate as the central common pathway of reentrant circuit. The area of slow pathway showed a decremental conduction or all-or-nothing conductive property. The width of the excitable gap seemed to be determined by the maximal conductive frequency but not by the duration of action potential: effective refractory period. As to the drug efficacy, there was no baseline characteristics in predicting the efficacy. However, the significant narrowing of the width of the excitable gap was associated with the drug efficacy and VT became non-inducible after addition of the same drug. The response pattern of the excitable gap to specific drug including class III, was not predictable. Further electropharmacological studies will be warranted. (*Jpn Heart J* 1998; 39: 121-137)

Key words: Sustained ventricular tachycardia, Electrophysiologic study, Reentry, Excitable gap, Electropharmacology, Central common pathway

PATIENTS having monomorphic sustained ventricular tachycardia (MSVT) are good candidates for electrophysiologic study since the same VT as the clinically documented one can be reproducibly induced by programmed electrical stimulation and MSVT has been most well studied for the mechanism.^{1,2)} Though most MSVT has been shown to be reentry with an excitable gap,²⁻⁴⁾ the drug efficacy is limited⁵⁻⁸⁾ and the selection of drugs can be done in trial-and-

From the First Department of Internal Medicine, Niigata University School of Medicine, Niigata, Japan.

Address for correspondence: Yoshifusa Aizawa, MD, The First Department of Internal Medicine, Niigata University School of Medicine, Asahimachi, Niigata 951, Japan.

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error way. There is no parameter which enables us to predict the efficacy of a specific drug for a specific patient. In this paper, we review MSVT in relation to the electrophysiologic study and their relation to drug efficacy based on our experiences.

MECHANISM OF MSVT

MSVT associated with coronary artery disease has been most extensively studied,^{1,2,9)} however, in Japan, MSVT associated with coronary artery disease; actually old myocardial infarction, occupies only 1/3 and the rest (about 2/3) of MSVT is unrelated to coronary artery disease.^{4,5)} Furthermore, in about 1/4, we were unable to detect an abnormality of the heart by the routine non-invasive or invasive examinations. The underlying heart diseases at our institution were shown in Table I. When MSVT was documented, the same MSVT can be induced by programmed electrical stimulation in >90%. Exception was MSVT in some non-ischemic heart disease or that which developed during antiarrhythmic therapy. Though we had diverse underlying heart diseases, we were able to demonstrate evidence which can be most well explained by a reentrant mechanism.⁴⁾

Most direct proof of reentry is to demonstrate the whole circuit on which wave fronts revolve.¹⁰⁾ By extensive endocardial mapping, we confirmed such revolution of wave fronts but only in 4 (2.6%) among 150 patients (Figure 1). During intraoperative mapping, other workers have demonstrated the reentrant circuit was suggested in up to 25% but they were incomplete ones.¹¹⁻¹⁴⁾

Most MSVT can be mapped as that which spreads radially from a focal point, as shown in Table II. For the majority of MSVT, we have to confirm the reentrant mechanism by indirect means. Of these, a clinically useful tool is to demonstrate the phenomenon of transient entrainment.^{3,4,9)}

As shown in Figure 2, the QRS complexes show intermediate but constant morphology during rapid pacing when MSVT was overdriven and the original

Table I. Underlying Heart Diseases in Patients with Monomorphic Ventricular Tachycardia

	Number of patients	%
All	150	100
Old myocardial infarction	42	28.0
Cardiomyopathy	20	13.3
Right ventricular dysplasia	26	17.3
Non-ischemic LV aneurysm	12	8.0
Post-cardiac surgery	6	4.0
Idiopathic LV origin	20	13.3
RV origin	24	16.0

Figure 1. Reentrant ventricular tachycardia in a postoperative case of Tetralogy of Fallot. As shown in the center, wave fronts were confirmed to revolve around the scar of the myotomy of the right ventricle. Two different morphologies of ventricular tachycardia (VT) were shown to revolve in the reverse direction as shown in the left and the right in which V₁ morphology is showing either QS or qR pattern, respectively. VT was inducible by the electrical stimulation and could be entrained. Slow conduction area was found between the plunomic valve and the presumed upper edge of myotomy. VT was ablated by a linear lesion across the this area. I, II, V₁ = surface lead; RVA = right ventricular outflow tract and apex; HBE = His bundle electrogram recording site; MAP = mapping catheter for the activation sequence. #14-18 = mapping site according to Josephson ME. (Chinushi *et al.* from Ref. 10)

VT resumes immediately after the cessation of rapid pacing. The constant but intermediate morphology of QRS complex is due to the fusion complex: fusion between the wave fronts from the paced site and that from the exit of VT which was accelerated to the pacing rate: constant fusion. As the paced cycle length shortens, the site of fusion of two wave fronts moves towards the exit of VT and the myocardium directly captured from the paced site will increase resulting in the QRS morphology closer to that of fully paced morphology: progressive fusion.

The ability to demonstrate constant fusion is affected by the spatial relationship between the pacing site and the VT origin.^{9,15} The closer to the VT origin, the more difficult in demonstrating fusion complex in the surface ECG since the myocardium activated from the VT origin becomes smaller. However, when the

Table II. Electrophysiologic Findings of Origin of Ventricular Tachycardia during Mapping for Catheter Ablation

Reentrant VT ($n = 28, 40$ VTs)	%VT
Site of earliest activation Ecg-QRS = -38 ± 28 msec	45.0%
Site of diastolic electrogram Ecg-QRS = 86 ± 13 msec	12.5%
Area with fragmented electrogram >2 cm $\times$ 2 cm	27.5%
Revolution of wave fronts (macroreentry)	0.5%
Pace-mapping	12.5%

Figure 2. Transient entrainment of ventricular tachycardia. Idiopathic ventricular tachycardia originating from the left ventricular interventricular septum. Rapid pacing was performed from the outflow tract of the right ventricle (RVO) at 310–280 msec. The VT cycle length was 320 msec. The postpacing return cycle of the exit at the left ventricle (LV) is identical to each paced cycle length. Constant fusion is evident at each paced cycle length and progressive fusion at different paced cycle length. Other abbreviations are same as Figure 1.

electrogram was recorded from the exit from the presumed slow pathway of VT, or within the area of slow conduction, we can confirm that VT was really entrained though the QRS complexes show fully paced morphology.⁴⁾ When VT is entrained, the local electrogram at the VT origin will be accelerated to the

Table III. Criteria of Transient Entrainment of Ventricular Tachycardia

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(1)	During tachycardia, while pacing at a constant rate that is faster than the rate of the spontaneous tachycardia and that fails to interrupt it, the demonstration of constant fusion beats in the electrocardiogram, except for the last captured beat, which is not fused.
(2)	During tachycardia, while pacing at two or more constant rates that are faster than the rate of the spontaneous tachycardia but that fail to interrupt the tachycardia, the demonstration of constant fusion beats on the ECG at each rate, but different degrees of constant fusion at each rate (progressive fusion).
(3)	During tachycardia, while pacing at a constant rate faster than the rate of the spontaneous tachycardia that interrupts the tachycardia, the demonstration of localized conduction block to a site(s) for 1 beat followed by activation of that site(s) by the next paced beat from a different direction and with a shorter conduction time.
(4)	During tachycardia, when pacing at two constant rates that are faster than the rate of the spontaneous tachycardia but that fail to interrupt the tachycardia, the demonstration of a change in conduction time to and electrogram morphology at an electrogram recording site.
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(Waldo *et al.*)

pacing rate without a change in the morphology: advancement of the local electrogram without a change in morphology. When VT resumes immediately after cessation of rapid pacing, the first interval of the local electrogram will be equal to the paced cycle length. Such advancement of the local electrogram must be an underlying requirement for other criteria of transient entrainment (Table III) and we are routinely seeking if the local electrogram at the VT origin to confirm that VT is entrained or not. The relationship between the local electrogram at the exit of VT origin and the QRS morphology in the surface electrocardiogram have been well discussed by Almendral *et al.*¹⁶⁾

By endocardial mapping, we might be able to record diastolic potential from the site which is engaged in the active limb of the reentrant circuit. If the site is the active limb, we pace at the site and demonstrate that VT accelerates to the pacing rate without a change in the configuration of the QRS complexes: concealed entrainment. Further criteria are that the stimulus to the QRS complex interval is identical to the diastolic potential to the QRS complex of VT interval and the return cycle of the local potential is equal to the cycle length of VT.¹⁷⁻¹⁹⁾

THE ELECTROPHYSIOLOGIC PROPERTIES OF THE AREA OF SLOW CONDUCTION

For the revolution of wave fronts (reentry), an area of slow conduction is essential. Histologically, surviving myocardial cells separated by interstitial fibrosis with a loose intercellular connection (gap-junction) observed at the site of "VT origin" in VT are associated with old myocardial infarction.^{13,20)} The myocardial cells within such diseased tissue were found to show normal resting membrane potential, though some workers demonstrated depolarized cells.^{13,21-23)}

From these diseased myocardium, fragmented activities or wide local electrogram are recorded and considered to represent depressed regional conduction as a result of a poor intercellular electrical connection.²⁴⁾ Such diseased myocardium must form the area of slow conduction but, the electrophysiologic properties of the area of slow conduction of reentrant VT are limited.

Using extrastimulus, Almendral *et al.*²⁵⁾ reset VT and analyzed the response patterns of the return cycle in the reset beat as the coupling interval of extrastimulus was shortened. Whether VT was reset or not was confirmed by the advancement of the VT in the beat immediately following the stimulus.

The analysis of the return cycle permits the estimation of the conductive property since the return cycle represent conduction time from the stimulus site to the exit. They observed three response patterns as the extrastimulus was given at a progressively shorter interval: flat pattern, increasing pattern and mixed pattern characterized by initially flat but followed by a increasing pattern. The increasing part of the return cycle was considered to be due to a conduction delay within the area of slow conduction which is caused when the stimulated wave front entered the reentrant circuit and met the refractory tissue.²⁵⁾

However, a delay in the intervening tissue between the pacing site and the entrance to the area of slow conduction: outside of the reentrant circuit, could be partly responsible for the increasing part of the return cycle especially when extrastimuli were given at shorter coupling intervals. This delay in the interven-

Figure 3. Schema of transient entrainment of ventricular tachycardia with rapid pacing and the measurement of conduction time through the reentrant circuit. The reentrant circuit was represented by a ring-model. The paced wavefront entered the reentrant circuit and emerged at the exit resulting in a fusion complex. On cessation of rapid pacing, VT resumed and the conduction time (CT) was obtained most easily by measuring the time interval between the stimulus and the entrained local electrogram (**) by the last pacing at the exit. Constant fusion (*) is due to the collision of the two wave fronts: one from the paced site and the other from the exit of slow conduction of entrained VT. ECG: surface electrocardiogram. Dark area represent effective absolute period and dotted area is partially responsive state. As mentioned in the text, the inner border at which 1:1 conduction fails within the area of slow conduction was considered to be due to a failure in intercellular conduction. Using the phenomenon of transient entrainment, the zone of entrainment was obtained and used as an index of the excitable gap. fr = fully responsive state; pr = partially responsive state.

Figure 4. Frequency-dependent change of the conduction time through the reentrant circuit. A: Rapid ventricular pacing was performed at progressively shorter cycle lengths and the conduction time showed a so-called decremental property in 16 patients. B: A flat pattern was observed in the other 12 patients when rapid pacing was attempted at progressively shorter cycle lengths. During rapid pacing, criteria of transient entrainment was confirmed in all VT (Aizawa *et al.* from Ref. 28).

ing tissue outside of the reentrant circuit seems to be minimized by giving one premature stimulus which did not reset VT. By giving the one conditioning premature stimulus, the flat portion was found to be wider.²⁵⁾

Another approach to evaluate the conductive property of the area of slow conduction is to entrain VT with rapid pacing. We will be able to determine the conduction time through the area of slow conduction by measuring the time interval between the pacing stimulus and the entrained local electrogram at the exit from the slow conduction zone as shown in Figure 3.^{4,26,27)} The conduction time through the area of slow conduction was analyzed while the paced cycle length was decreased in increments of 10 msec and rapid pacing was continued for 5–10 seconds starting at a cycle length which was 10–20 msec shorter than the cycle length of VT. For this study, it was essential to confirm that VT was entrained with rapid pacing.

As the paced cycle length was shortened, the conduction time from the pacing site to the exit showed two response patterns: a frequency-dependent prolongation or a constant conduction time, and the former was more frequent: 57% vs 36% as shown in Figure 4.²⁸⁾ When a decremental conduction is observed, the conduction time reached a plateau within 6 beats at each cycle length. For the frequency-dependent prolongation of orthodromic conduction time, we speculate a delay in the intercellular conduction may be involved. This issue will be discussed later.

The results of the resetting study by extrastimulus²⁵⁾ or transient entrainment^{26,28)} showed that the conductive property through the area of slow conduction is not uniform.

As an implication of the response pattern, Gottlieb *et al.*²⁹⁾ showed that the steepness of the increasing part of the response pattern of the return cycle was associated with terminability of VT with extrastimulus. They suggested that the increasing part is due to partial refractory tissue within the area of slow conduction and termination was considered to be caused by the refractory tissue which the paced wave fronts encountered at a critical interval.

In our study,²⁸⁾ VT showed a so-called decremental property in 16 patients and a constant conduction in another 12 patients (Figure 4). VT with decremental conduction was terminated more often than VT without such a property: 93.8% vs 50% ($p < 0.05$). The cycle length of VT was not different between the two groups: 327 ± 50 msec vs 310 ± 27 msec. Pacing-induced acceleration of the VT rate was found in only one of the 16 patients (6.3%) with VT with decremental conduction but was found in 6/12 patients (50%) in VT without decremental conduction. The higher incidence of the pacing-induced termination in VT with a decremental property seems to be consistent with that of Gottlieb *et al.*²⁹⁾ This finding should be considered when anti-tachycardia pacing is contemplated. Whether the different conductive properties of the area of slow conduction result in different responses to antiarrhythmic agents is still to be determined.

PACING-INDUCED TERMINATION OF VT

It is thought that if a premature stimulus given at a critical coupling interval had entered the area of slow conduction and encountered the refractory tissue, the wave front will be blocked resulting in a termination of VT.^{2,29)} By this technique, we will be able to measure the width of the excitable gap. However, the incidence that VT is terminated with extrastimulus is limited. This must be due to the fact that extrastimulus given at a site distant from the reentrant circuit is unable to arrive early enough to result in a block because of a delay in the intervening tissue or local refractoriness at the pacing site.

As rapid pacing was repeated at progressively shorter cycle lengths, VT was more often interrupted when a critical cycle length was reached^{4,26,27)} and we can obtain the critical paced cycle length which interrupts VT and is acknowledged as the block cycle length.

During pacing at the block cycle length, we could observe constant fusion and such initial constant fusion was replaced abruptly by a fully-paced QRS morphology as shown in Figure 5.^{26,27)} At the same time, the local electrogram at the exit from the zone of slow conduction showed a change in morphology and

Figure 5. Interruption of VT with rapid pacing. The cycle length of VT was 290 msec and interrupted at the paced cycle length of 250 msec (A). On the right, fusion complexes were evident but followed by the fully paced QRS morphology. At the same time, the local electrogram at the exit in the right ventricular outflow tract (RVO) showed a change in the timing of activation and the morphological change as magnified in B. I, II, V₁ = surface ECG leads; HBE = His bundle area; RVA = right ventricular apex.

the timing of activation. These findings are best explained by orthodromic block within the area of slow conduction. The determinant of the block cycle length or the mechanism of orthodromic block is, however, not known and we addressed this problem by pharmacological intervention.

In patients with reentrant VT ($n = 16$), 18 morphologically distinct VTs were studied before and after procainamide administration.³⁰⁾ MSVT was inducible and terminable with rapid pacing while the criteria of transient entrainment were confirmed in all VTs. After procainamide, the block cycle length was shown to be prolonged to a similar degree as that of the cycle length of VT: $33 \pm 18\%$ vs $31 \pm 17\%$, while the effective refractory period was prolonged to a smaller degree than the change in the block cycle length: $6 \pm 3\%$ (Table IV). Though there is no rationale to compare the block cycle length with the effective refractory period, this discrepancy suggests that the determinant of the block cycle length is not the action potential duration.

Since procainamide acts to prolong the duration of the action potential,³¹⁾

Table IV. Drug-induced Changes in Electrophysiologic Parameters

	VTCL	Block CL	Paced QRS	CT	ERP
% Changes	31 ± 17%	33 ± 18%	14 ± 17%*	11 ± 5*	6 ± 3%**

*: $p < 0.02$ vs. VTCL and $p < 0.02$ vs. Block CL. **: $p < 0.001$ vs. VTCL and Block CL. VTCL = VT cycle length; Block CL = the block cycle length; Paced QRS = the paced QRS duration; CT = the local conduction time. (Aizawa *et al.* Ref. 30)

the study was repeated using mexiletine³²⁾ and the block cycle length was again found to be prolonged significantly after mexiletine. Because mexiletine shortens the duration of the action potential,³¹⁾ the change in the block cycle length must be determined by a factor other than the duration of the action potential. Actually, the effective refractory period remained unchanged at the pacing site (normal myocardium) and at the VT origin (diseased myocardium).

We considered that postrepolarization refractoriness is the major determinant of the block cycle and the orthodromic block occurs as a result of uncoupling of intercellular conduction at a critical cycle length.

THE EXCITABLE GAP VS. THE ZONE OF ENTRAINMENT

From the studies mentioned above, we may be able to define the width of the excitable gap as the difference between the cycle length of VT and the shortest coupling interval of extrastimulus which terminated VT.^{2,25)} However, the VT-terminating critical coupling interval is achieved only in limited cases. Furthermore, when an extrastimulus is given far from the reentrant circuit, the excitable gap might be overestimated because of a delay between the pacing site and the entrance to the reentrant circuit at increasing prematurity.

With rapid pacing, VT can be highly terminated and the difference between the cycle length of VT and the block cycle length at which 1:1 intercellular conduction fails will constitute the excitable gap. We defined the width of zone of entrainment as the difference between the cycle length of VT and the block cycle length and used this as the index of the width of the excitable gap, and we attempted to characterize VT and to use it in evaluating the action of antiarrhythmic agents.^{16,17,32)} However, it is noted that the major determinant of the block cycle length is not defined by the duration of action potential, but by a failure in 1:1 cell to cell conduction.

PHARMACOLOGICAL INTERVENTIONS OF MSVT

In reentrant VT inducible with programmed stimulation, the ability to prevent the induction of VT has been used as a hallmark of drug efficacy,⁵⁻⁸⁾ but

the precise mechanism by which MSVT is rendered non-inducible is not known.

So far, some electrocardiographic or electrophysiologic parameters have been shown in association with drug-efficacy in reentrant VT. They include the baseline refractory period and the QT interval,³³⁾ the HV interval,³⁴⁾ drug-induced changes in the effective refractory period, the duration of the paced QRS complex³⁵⁻³⁸⁾ and the change in the signal average surface electrocardiogram.³⁹⁾ However, these parameters were obtained from the normal myocardium⁴⁰⁾ and not from the area of slow conduction which must be composed of diseased myocardium. Different responses will be obtained between the normal and diseased myocardium as discussed below.

Though the classification of antiarrhythmic agents by Vaughan Williams³¹⁾ is most commonly used, it offers no assistance when selecting effective agents⁴¹⁾ and the selection of the optimal agent has to be undertaken in a trial-and-error manner. Furthermore, efficacy of the antiarrhythmic agents is limited and the overall efficacy rate is <50%⁵⁻⁸⁾ and no predictor of drug-efficacy has been established so far.

The Sicilian Gambit⁴²⁾ provided a new formulation in classifying antiarrhythmic agents depending on the mechanism of arrhythmia and the characteristics of the target of the drug: ion channels or receptors. For reentrant VT, they proposed a hypothesis that if VT has a narrow excitable gap, the gap might be obliterated by class III drugs by which the revolution of the wave fronts is rendered impossible.⁴³⁾ On the other hand, if VT has a wider excitable gap, class I drugs are preferred to depress the conductivity of the reentrant pathway.⁴³⁾ This hypothesis has not yet been addressed and our recent studies have provided some new data.

We address two issues of antiarrhythmic drug therapy: (1) if an antiarrhythmic agent acts preferentially on the diseased myocardium and (2) what is the possible mechanism by which induction of MSVT is suppressed.

PREFERENTIAL ACTION OF ANTIARRHYTHMIC AGENTS

Kay *et al.*⁴⁴⁾ compared the change in the orthodromic conduction time: the time interval from the paced stimulus to the entrained local electrogram at the site of VT origin with that of the antidromic conduction time which was measured when the heart was paced during sinus rhythm. The change in the cycle length of VT was highly correlated with the change in the orthodromic conduction time but not with that of the antidromic conduction time. This result was considered to represent a preferential action of procainamide on the area of slow conduction. They treated VT associated with old myocardial infarction but a similar finding was confirmed in reentrant VT unrelated to coronary artery dis-

Figure 6. The effects of mexiletine on the ventricular tachycardia and the local electrogram. The cycle length of VT was prolonged from 270 msec to 310 msec by mexiletine and the orthodromic conduction time defined as the time interval between the pacing spike to the local electrogram at the exit in the outflow tract of the right ventricle showed a concomitant prolongation: from 220 msec to 290 msec. The abnormal local electrogram at the right ventricular outflow tract was prolonged from 115 msec to 135 msec but, that of the pacing site (the normal myocardium): RVA or His bundle area (not shown) showed no change. (Aizawa *et al.* from Ref. 48).

eases.⁴⁵⁾

Alternatively, a preferential action of antiarrhythmic agents on the diseased myocardium might be demonstrated by observing the drug-induced change of the local electrical activity.⁴⁶⁻⁴⁸⁾ The electrogram from diseased myocardium, within the area of slow conduction at the exit, often showed fragmentation (>70 msec) with low amplitude (<0.5 mV in peak to peak amplitude).²⁴⁾

Procainamide was shown to prolong the duration of fragmented activity much more than the duration of the local electrogram from the normal myocardium during sinus rhythm.^{46,47)} At relatively lower rates, mexiletine may show no effect on the diseased myocardium because of its rapid dissociation from Na-channels but a preferential action of mexiletine can be revealed at higher heart rates or during VT as shown in Figure 6.⁴⁸⁾

Bigger changes either in the cycle length of VT or of block cycle length defined above compared to that of the width of the QRS complex or local conduction time: from exit to a remote site, can be easily confirmed in an electrophysiologic study and from these findings, a preferential action on the diseased myocardium is confirmed in humans (Figure 6).

DRUG-EFFICACY

We can characterize MSVT (reentrant VT) by a new parameter: block cycle length and the zone of entrainment. VT with a mean cycle length of 285 ± 43 msec was induced in the control state and interrupted at 231 ± 31 msec. The width of the zone of entrainment was 54 ± 23 msec. The patients underwent 18 drug-tests and in 8 tests, VT was not inducible (procainamide in 4, cibenzoline in 1 and mexiletine in 3), but VT remained inducible in the other 10 tests. The final doses were comparable to the tests with effective and non-effective drugs.⁴⁹⁾ There has been, however, no basal electrophysiologic parameter which has been able to predict non-inducibility by class I antiarrhythmic agents.

Next, we studied the effects of amiodarone and dl-sotalol: class III drugs. The responders and non-responders had VT with a mean cycle length of 286 ± 67 msec and 281 ± 27 msec, respectively. The block cycle length and the width of the zone of entrainment were not different between the two groups: 240 ± 70 msec vs. 230 ± 28 msec and 48 ± 24 msec vs. 51 ± 15 msec, respectively. The basal characteristics of VT were again unable to predict drug-efficacy (Our data, in preparation). Therefore, the width of the excitable gap (Figure 7) was not the parameter by which the selection of an antiarrhythmic agent is guided as hypothesized by the Sicilian Gambit.^{42,43)}

A limitation of the study is that we did not measure the excitable gap within the area of slow conduction by an extrastimulus technique but used the zone of entrainment as an index of the excitable gap.

Finally, we attempted to characterize the drug-induced changes in electrophysiologic parameters: the cycle length of VT, the block cycle length and

Figure 7. The width of the excitable gap and selection of antiarrhythmic agents. When the width of the excitable gap is relatively narrow, class III drugs might be indicated to obliterate the gap. On the other hand, if the width of the excitable gap is wider, class III drug might be unable to bury the gap and class I drug might be indicated. This is a hypothesis for the selection of antiarrhythmic agent, although it has not yet been tested.

Figure 8. Comparisons of the width of the zone of entrainment between non-responders and responders to class I antiarrhythmic agents. **Upper:** Class I agents were tested at two doses but the width of the zone of entrainment showed no significant change. This may be due to the finding that the cycle length of VT and the block cycle length were prolonged to a similar degree and VT remained inducible. **Lower:** In 8 tests with efficacious agents, the width of the zone of entrainment was significantly narrowed: from 68 ± 30 msec to 20 ± 15 msec ($p < 0.01$) and VT was rendered noninducible after an additional dose of the same agent (Aizawa *et al.* from Ref. 51).

the width of the zone of entrainment at intermediate dosages of the drugs and compared then with the drug-efficacy at the final dosages.

Using procainamide, disopyramide, mexiletine or cibenzoline, 18 drug tests were performed and VT was rendered noninducible in 8 tests of 8 patients. None of the basal electrophysiologic characteristics was a predictor of drug-efficacy. In this study, we evaluated the parameters of VT at the intermediate dosage. The cycle length of VT and the block cycle length were prolonged to a similar degree in the tests with efficacious drug and those with the non-efficacious drugs. However, when the width of the zone of entrainment was compared, a significant narrowing was observed only when tested with efficacious drugs and the absolute value of the width of the zone of entrainment was significantly narrower compared to the non-responders or the tests with non-efficacious drugs (Figure 8). The drug-induced obliteration of the width of the excitable gap was suggested to be associated with the subsequent non-inducibility when the same drug was increased at the final dose.⁵⁰⁾

Unfortunately, we are again unable to predict the drug-efficacy prior to its trial from the baseline parameters; the cycle length of VT, the block cycle length

or the zone of entrainment. The clinical implication of the last study is that if the zone of entrainment was narrowed after a specific drug, there is reason to add the same drug and repeat the induction study. On the other hand, if the zone of entrainment is not altered or widened by a drug, further testing after addition of the same drug may be of no use. If this hypothesis is true or not, more data needs to be accumulated in a large number of patients.

We need to know the precise site of unidirectional block, the mode of formation of functional block, the electrophysiologic characteristics of the area of slow conduction or the site of orthodromic block caused by electrical stimulation to characterize MSVT, and to predict the drug efficacy, so further studies are needed.

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