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Recurrent Sustained Ventricular Tachycardia: Recent Understandings and Therapeutic Implications

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Summary. **This paper reviews the mechanism of recurrent sustained ventricular tachycardia (VT) which have been extensively studied by the electrophysiological means. Initiation and/or termination of VT by electrical stimulation, resetting of VT by ventricular extrastimuli or by overdrive pacings, recording of continuous local electrical activity, and demonstration of slow conduction are all best explained by the re-entrant mechanism of recurrent sustained VT. The localization of the re-entrant circuit has become possible by mapping studies. The selection of antiarrhythmic regimens and non-pharmacological interventions guided by electrophysiologic study has been proved useful.**

Recurrent sustained ventricular tachycardia (VT) lasts for minutes or days and usually requires drugs or DC shock for termination.[1-7] It develops in paroxysmal form and frequency of recurrence varies from one case to another unless the VT was aggravated by antiarrhythmic drugs.[8-11] VT can be a common cause of aborted sudden death.[12-13] Since it can be induced by the electrical stimulation, the management of VT are established on the basis of electrophysologic studies.[1-7,14-16] This paper reviews the recent findings of recurrent sustained VT.

UNDERLYING HEART DISEASES OF VT

The most common cause of the underlying heart disease of recurrent sustained VT in Western countries is coronary atherosclerosis.[1-6]. It is important, however, to note that such fatal arrhythmias, VT, and ventricular fibrillation (VF), are frequently not associated with acute ischemic events, such as myocardial infarction or angina pectoris, but they occur in the heart with scar formation from a previous myocardial infarction.[12-13,17] In Japan, no precise data concerning the underlying heart disease of VT or VF have been obtained, but reports from several centers, including the authors' institution, suggest that, non-ischemic heart disease is now the most common cause of VT.[7-8,18-21] Ischemic heart disease occupies only 22% (16 among 72 patients) of the underlying heart diseases of VT in our series as shown in Table 1. The reason why the underlying heart diseases of patients with VT differ from those of the Western countries is to be determined.

Since 1978, a new clinical entity has been established as the underlying heart disease of VT : right ventricular dysplasia as reported by Fontaine.[22] This disease is characterized by fatty infiltration of the myocardium of the right ventricle though the left

Table 1. Underlying heart diseases of recurrent sustained monophorphic ventricular tachycardia (VT)

Coronary atherosclerosis	acute infarction
	scar related
Cardiomyopathy	primary hypertrophic
	primary dilated
	myocarditis
	secondary cardimyopathy
LV aneurysm or regional wall motion abnormality (non-ischemic)	
Arrhythmogenic right ventricular dysplasia (ARVD)	
Post-cardiac surgery	
Valvular heart disease/prolapse	
No underlying heart disease	verapamil responsive
	verapamil non-responsive

ventricle seems not to be immune to such a lesion. The pathogenesis of this disease is unknown but is not limited to the people of the Western countries. Rather, it would be frequent even in Japan since in our clinics it was found in 12 among 72 patients with VT in our clinics.[23]

Some VT have a characteristic configuration of the QRS complex and responsiveness to verapamil for the termination and the slowing of VT rate.[21,24-26] No underlying heart disease has been reported, but rarely, probably by chance, mitral prolapse was found in a female as the only abnormality of the heart (Aizawa et al published in Japanese).

Among Japanese people and the American-Asian people, a peculiar form of sudden death has been noted. It is characterized by the sudden unexpected death in young adult males at midnight and is called "pokkuri disease";[27-29] a Japanese term, "pokkuri" means "sudden and unexpected death". Minor abnormalities in the coronary vasculature or other organs have been reported from autopsy studies,[27-28] but the precise mechanism of sudden death is still speculative. Two young males died suddenly and unexpectedly at midnight, their terminal event was VF.[29] No warning arrhythmia was recognized in the electrocardiographic monitoring for 10-20 days, but R-on-T type premature ventricular beats occurred sporadically just prior to death, and the VF followed the premature beats as terminal events.[29] These two cases can be diagnosed as "pokkuri disease", but more detailed informations are required to solve the genesis of this disorder and to prevent death from arrhythmia.

MECHANISM OF VT

Before the use of electrical stimulations for initiation and termination of VT, a controversy existed on the mechanism of recurrent sustained VT. By intense studies by Wellens and other workers.[1-7] most cases of recurrent sustained VT has come to ascribed to a re-entrant mechanism. In the earlier era, VT was assumed to be a macro-reentry, and a bundle-branch was thought to be the essential part of the re-entrant circuit.[30-31] However, the absemce of a constant relation between the His bundle electrogram and the QRS complex,[32] or the continuation of VT even after the capture of the major part of the ventricle by the atrial beat or by the prematurely given ventricular depolarization, means that the VT origin is localized and relatively protected.[5,33] Electrophysiological findings which support the re-entrant mechanism are given in Table 2.

Table 2. Electrophysiologic data suggestive of re-entrant tachycardia.

1.	Initiation and/or termination by elecrical stimulation
2.	Inverse relation between VT-initiating coupling interval of extrastimulus and return cycle of VT
3.	Phenomena of transient entrainment by overdrive pacing of VT
4.	Localized continuous electrical activity
5.	Demonstration of slow conduction

Most recurrent sustained VT can be initiated and/or terminated by programmed stimulation (Fig. 1), but the rate and morphology of VT is constant irrespective of the site or the mode of stimulation. From animal experiments it has been known that VT due to triggered activity may be initiated by electrical stimulation, but the rate is believed to be affected by cycle length or by duration of the electrical stimulation and also is abolished by verapamil.[34-36]

An inverse relationship between the VT-initiating coupling intervals of the extrastimuli and the interval to the first VT beat may be observed at the time of the initiation (Fig. 1). From the analogy of the AV nodal re-entrant tachycardia,[37] this inverse relationship implies that re-entry is the causal mechanism of VT. However, absence of such an inverse relationship could not deny the re-entrant mechanism, and, more frequently, VT is initiated by double extrastimuli which make it impossible to see the underlying relationship of these intervals if any.[1,19,22]

The phenomenon of transient entrainment of VT by overdrive pacing would most strongly support the re-entrant mechanism. This phenomenon was first verified in macro re-entry[38] or atrial flutter in men as well as in animals.[39] When VT is paced at a shorter cycle length than that of VT, the entire heart is accelerated to the paced cycle length while we obtain some characteristic electrophysiological findings.[39,40-42]

First, the verification of constant fusion is fact of the evidence that the VT is entrained (Fig 2).[38,40-45] Here, the configuration of the QRS complex during pacing assumes an intermediate configuration between the fully paced one and that of VT. For constant fusion to take place, there should be two wave fronts simultaneously in the heart. One is obviously from the paced site, the other from the exit of the re-entrant circuit. The latter wave front emerging from the exit is caused by the preceding pacing.

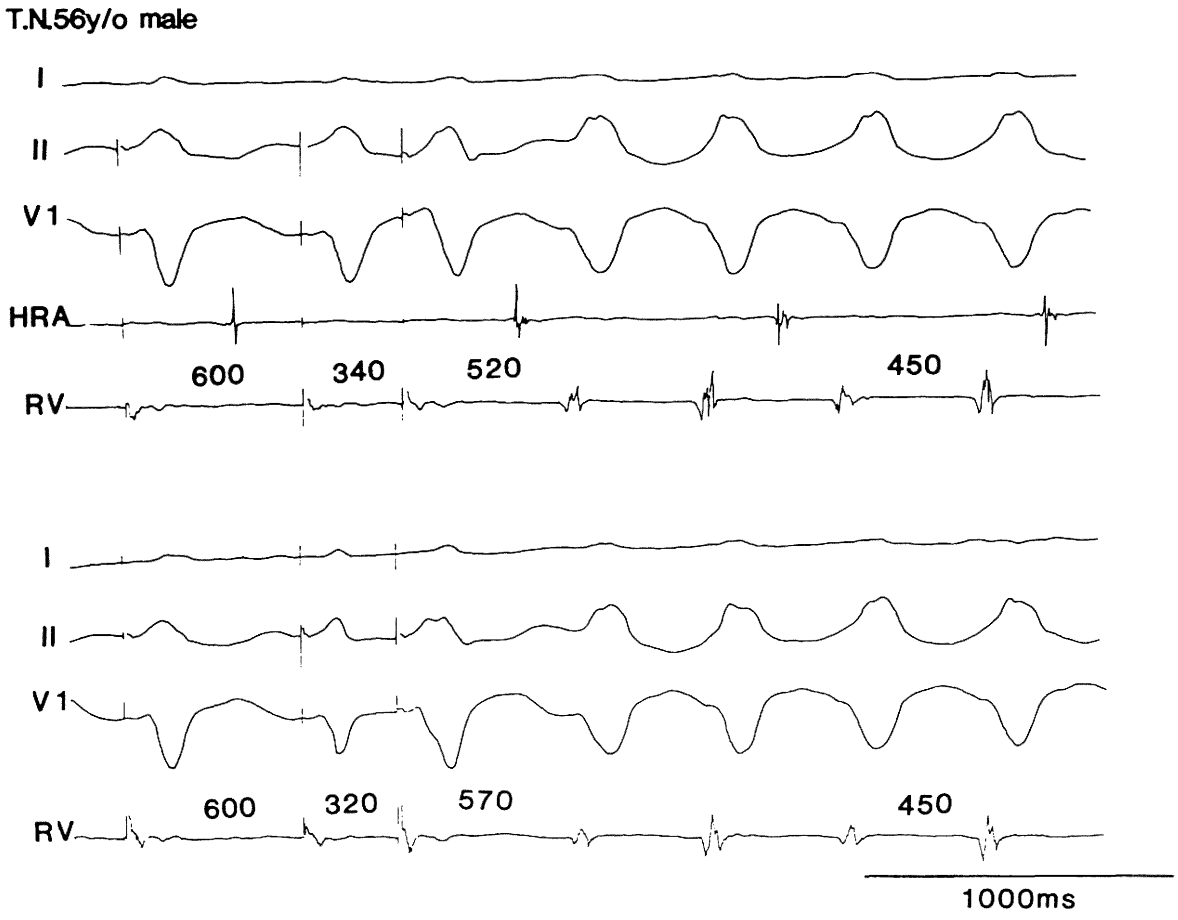

Fig. 1. Initiation of VT by single ventricular extrastimulus.
The patient was a 52-year-old male with right ventricular dysplasia. After 8 basic stimuli at 600 msec of cycle length, single extrastimuli were given with a coupling interval of 340 and 320 msec, and VT was induced. The interval from the last paced beat to the first beat of VT was prolonged from 520 to 570 msec when the coupling interval was shortened from 340 to 320 msec ; they were inversely correlated. I, II, VI : surface electrocardiographic leads. HRA : electrogram from high right atrium. RV : electrogram from the right ventricle.

During pacings with shorter cycle lengths, the configuration of the QRS complex comes closer to the fully paced one because the greater part of the heart is directly activated by the wave front from the site of the pacing, and this paced-rate dependent change in the configuration of the QRS complex is called progressive fusion.[40] For resetting the VT, the proper site of the pacing and the existence of the excitatory gap are essential.[42-46] If we pace VT at the exit or directly at the entrance of the re-entrant circuit,[47-48] no fusion complex will be discernible because of the similarity in the configuration between the QRS complex of VT and that of the fully paced one. Evidence that VT is entrained by the overdrive pacing is obtained, however, by seeing the post-paced return cycle length which becomes identical to the paced cycle length as shown in Fig. 3.[40,42-45] The interval from the stimulus to the entrained beat or local electrogram is long enough and considered as evidence of slow conduction.[48-49] Not infrequently, the post-paced return cycle may be longer than the VT cycle length as well as the paced cycle length.[45]

In a limited number of cases, it has been reported that the slow pathway can be directly paced.[47,48] In this situation, the configuration of the QRS complex will show little or no change during the overdrive pacing, but the rate becomes identical to the paced one as shown in Fig. 3. The post-paced return cycles were identical to the paced cycle lengths, and this finding means that the first non-paced beat is

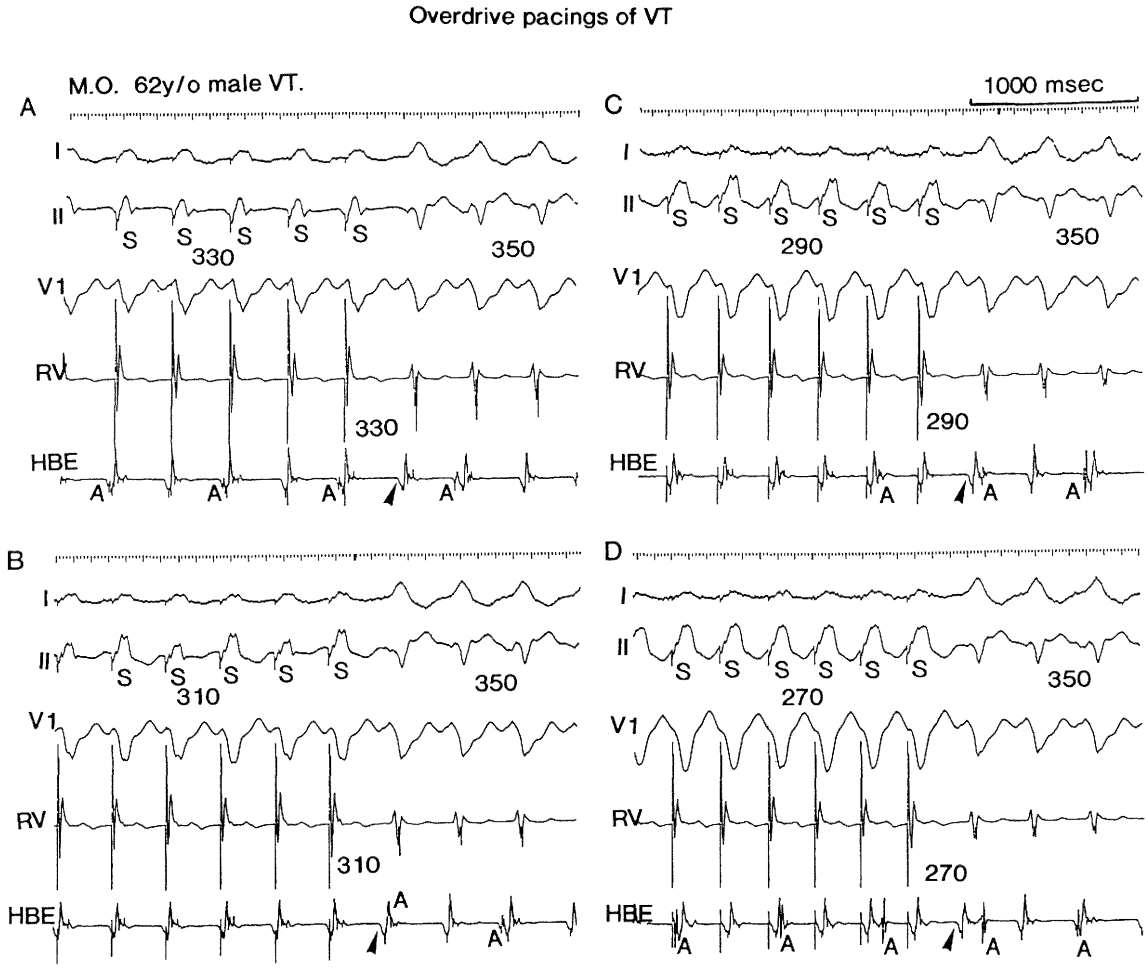

Fig. 2. Entrainment of VT by overdrive pacing.
The patient was 62-year-old male who had recurrent sustained non-ischemic VT. VT was able to be initiated by double extrastimuli, and the rate was 350 msec. VT was overdriven at 330, 310, 290, and 270 msec in cycle length. During the pacing, the rate was accelerated to the paced rate, and the configuration of the QRS complex was constant (constant fusion). At higher rates, the QRS morphologies came closer to the fully paced one (progressive fusion). Furthermore, the post-paced return cycle (the interval from the last paced beat to the first beat as shown by arrow head) was identical to each paced cycle length. I, II, V1 : surface electrocardiographic leads. RV : electrogrogram from the right ventricle. HBE : electrogram from the His-bundle recording site.

entrained by the last pacing. It may be said that the wave from the pacing site is conducted unidirectionally to the exit through the re-entrant circuit but not in the other direction ; hence, a unidirectional block seems to be operating here.

When VT is terminated by pacing, we may be able to observe a local conduction block, which is the other criterion of transient entrainment as proposed by Waldo.[40] These phenomena of transient entrainment are best explained by re-entry as a causal mechanism of VT.

Another important finding which supports the re-entrant mechanism of VT is obtained by recording the electrical activity from the re-entrant circuit.[50] In animal experiments, the extension of the fractionated electrogram into the diastole was observed when VT was initiated.[51,52] Using endocardial catheter mapping, Josephson et al.[50] domonstrated such a progressive fractionation in an area of healed infarction. On initiation of VT, the local electrical activity spanned the whole cardiac cycle. The site in which a continuous local activity is recorded will be quite circumscribed and cannot be recorded in the adjacent area. A distortion of the activities was associated

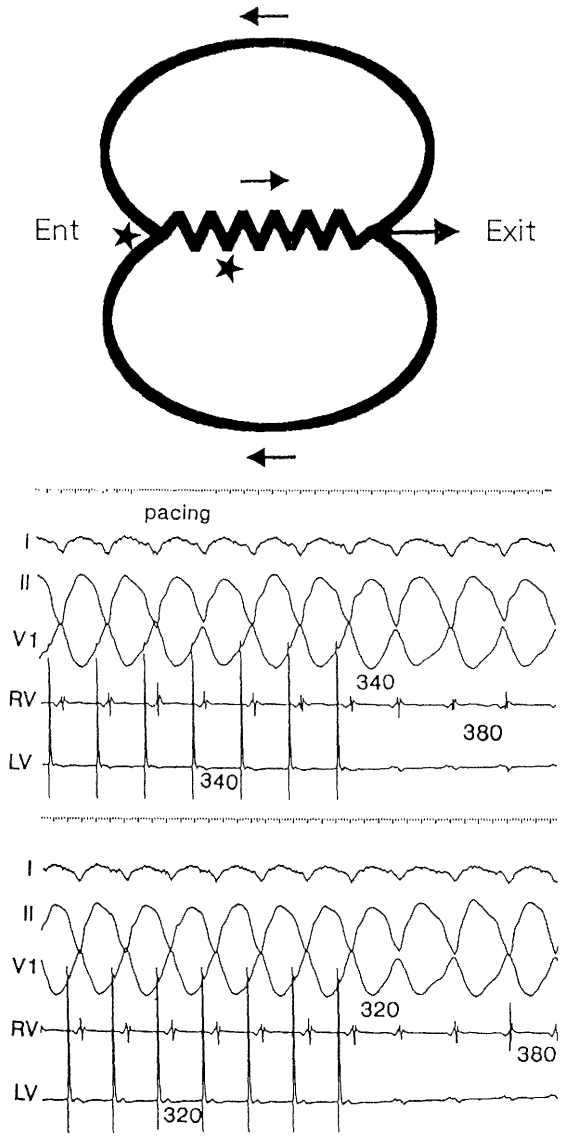

Fig. 3. Pacing of the slow pathway.

The patient was a 58-yera-old male with dilated cardiomypathy. The scheme shows an 8-figure model of re-entrant circuit. If we pace VT at the entrance of the circuit (Ent) or directly along the slow pathway as shown by asterisks, the rate would become identical to the paced rate without change in the configuration of the QRS complex. The lower panel shows the actual recordings. VT cycle length was 380 msec which was paced with a cycle length of 340 and 320 msec. During the pacing from the circumscribed area of the left ventricle little change in the QRS morphology was evident, which was confirmed by 12-lead electrocardiographic recordings. The post-paced return cycle length was identical to the paced one. RV and LV : electrogram of the right and left ventricle. Other abbreviations are same as Fig. 1 and 2.

with the termination of VT when VT was paced.[50] More direct proof that the continuous activity represents activity from the re-entrant circuit can be obtained by intraoperative mapping.[50] It is possible that continuous activity cannot be related to VT but merely represents local slow conduction. So, we have to be cautious before concluding that the site at which continuous activity is recorded is the site of the re-entrant circuit. To diagnose that the continuous activity is recorded from a re-entrant circuit, it is required that the criteria proposed by Josephson should be satisfied[50] Rarely, we might be able to demonstrate simultaneously both transient entrainment and continuous local electrical activity.[53]

Localization of VT origin and the re-entrant circuit

The site of origin of VT can be determined in several ways as schematically shown in Fig 4. If we record from an entire re-entrant circuit, a continuous activity can be seen during VT[50,53] but this is not the usual case, and one needs alternative methods for the localization of the VT origin.

The most popular method is to map such the earliest activation site (EAS) of VT which is assumed to represent the site of the exit of a re-entrant circuit.[14,16] The local electrogram of EAS (i.e. the exit), should appear before the onset of the QRS complex. The time interval from the local electrogram at the EAS to the onset of the QRS of VT may vary from one case to another. In ischemic VT, VT originates from the tissue at the border of the infarction scar located in the subendocardium,[5,6,54] and the endocardial mapping is ideal for localizing the origin of such VT.[6,55]

Pacings at EAS will result in the same configuration of the QRS complex, and this pace-mapping technique can be used as an additional tool to localize the site of the VT origin.[55]

In VT of non-ischemic heart diseases, the site of the VT origin may vary from one case to another. No site at which the local electrogram precedes the onset of the QRS complex may be obtained by endocardial mapping if the site of origin is located on the epicardial side or deep in the wall (Fig 4). In this situation, the endocardial mapping detect a rather wide area in which the local electrograms may be earlier than that of other parts but never precedes the onset of the QRS complex of VT. However, the slow pathway may be able to be paced from certain circumscribed area.[47,48] In ischemic VT of Morady et al., slow pathways were paced by a intense electric current

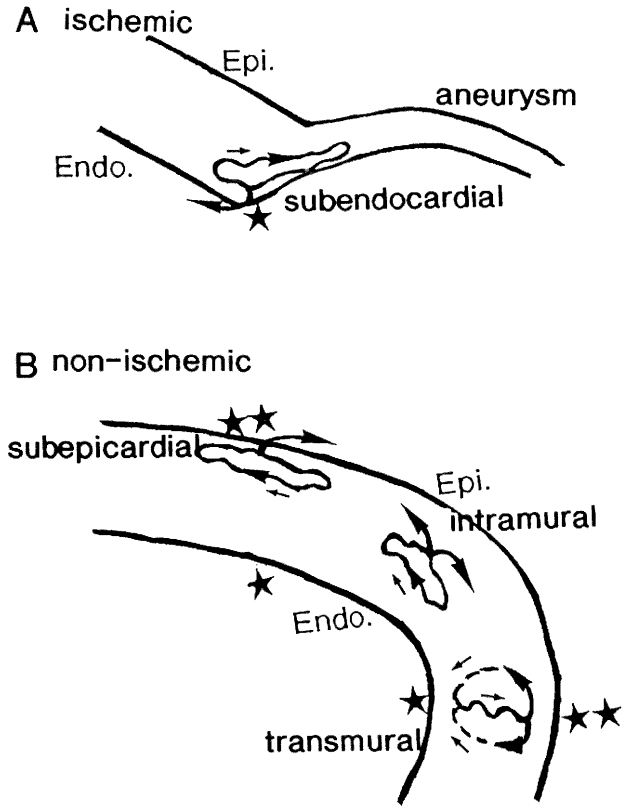

Fig. 4. Possible localization of the re-entrant circuit.
A means the subendocardial localization of the re-entrant circuit as found in ischemic VT. Here, the earliest activation site, continuous electrical activity or the pace-mapping would be used for the localization of the re-entrant circuit by endocardial mapping studies (as one asterisk). However, when the circuit is located on the epicardial side (B), in the intramural layer, or transmurally, the endocardial mapping alone my be inadequate. Rarely may the endocardial pacing be able to localize the site of slow conduction as shown in Fig 3. Abbreviations are the same as in Fig. 3. The epicardial mapping (as shown by two asterisks) or even the intramural mapping is essential in non-ischemic VT. Endo. : endocardial surface. Epi. : epicardial surface.

because of interposing non-excitable tissue.[47] In our non-ischemic case, the slow pathway was able to be paced from the circumscribed endocardial side with its usual strength of electrical stimulation (Fig. 3). In this case, the EAS was detected on the epicardial side in the intraoperative mapping study.

It is to be noted that there may be some discrepancies between the EAS and the site of continuous local activity or the site at which the pace-mapping resulted in the same configuration of the QRS complex as VT (Fig. 5). Therefore, the electrophysiological data must be interpreted very carfully by trained persons, especially when one attempts to eradicate the arrhythmogenic substrate by surgery or catheter techniques.

In future, the method to determine the site of intramural origin of VT in the free wall of the left ventricle or the interventricular septum is desired to ablate the arrhythmogenic substrate without unnecessary injury to the normal surrounding tissue.

For EAS determined by endocardial mapping in the free wall of the right ventricle, it will be close to EAS determined by epicardial mapping. This is because the wall is thin in the right ventricle. Cases of a macro re-entrant circuit may be observed in VT with arrhythmogenic right ventricular dysplasia in the intraoperative mapping.[56]

Quite frequently, patients with VT may have morphologically distinct VT ; 2 to 6 QRS morphologies in our series, and multiple VT morphologies is called pleomorphism.[22,57] For pleomorphism, there are two possibilities : one is that different re-entrant circuits are responsible for the different morphologies of VT, and the other is that multiple exits from a single re-entrant circuit are responsible. If we record continuous activity of a re-entrant circuit which is constant during changes in VT morphology, it is likely that the same re-entrant circuit with a changing exit is responsible for different morphologies. If the site with local continuous activity shifts to the other site with change of VT morphology, a different re-entrant circuit may be responsible. From clinical viewpoint, the EAS should be mapped for every morphologically distinct VT, especially when we contemplate surgical intervention or electrical ablation.[15-16,58-62] There is no doubt that the EAS represents a part of the re-entrant circuit.[6,55,62]

THERAPEUTIC IMPLICATIONS

We are still unable to predict when and how recurrent sustained VT reccurs. However, VT can be reproduced by electrical stimulation in electrophysiologic study. This is because the underlying mechanism of recurrent sustained VT is re-entry.[1-6] Most reliable selections of antiarrhythmic drugs are now performed by serial electrophysiologic studies. When VT becomes no more inducible after administration of antiarrhythmic regimen or regimens, recurrence of VT and/or sudden cardiac death has been effectively prevented.[23,63] However, effective prevention of recurrence of VT is achieved only in 30-50% of cases.[63] Furthermore, the most effective drug may

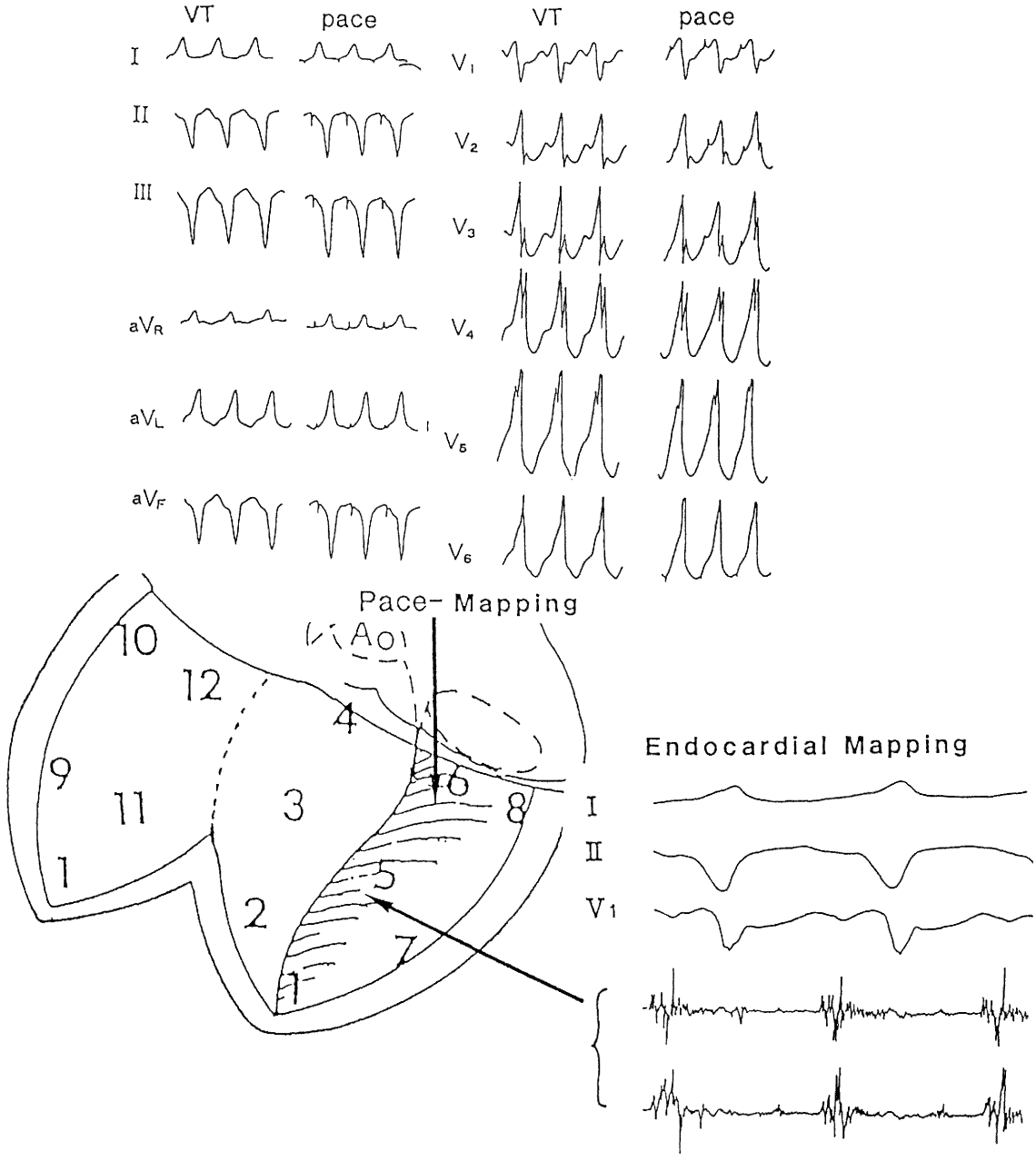

Fig. 5. Discrepant results of mapping studies.

The patient was a 72-year-old male with previous myocardial infarction. VT was inducible by programmed stimulation in a reproducible manner. Pace-mapping from the postero-basal area of the interventricular septum resulted in the same configuration as VT as shown in the upper panel (pace-mapping). However, a continuous electrical activity was recored from the posterobasal area at the more apical side of the septum as shown in the lower panel. They differed by 2.0 cm in distance from each other. The number shown in the scheme of the endocardial surface of the left ventricle was that proposed Josephson (2).

be abandoned because of major side-effects. This limitation of pharmacologic therapy requires non-pharmacological interventions in many patients with VT. Fortunately, we are able to determine the site of VT origin by mapping studies, and the arrhyth mogenic substrate is now effectively ablated.[15-16, 18,23,58-62] Before the establishment of electrophysiologic studies, patients with refractory VT were treated by a resection of the accompanying aneurysm which is frequently obeserved as complications of myocardial infarction, but the success rate for curing VT without knowledge of the VT origin has been very low,[15-16,23,64-65] and now such blind surgical therapies should be considered as contraindicated. The importance of the precise determination of the VT origin is also essential for catheter ablation.[58-61]

Non-pharmacologic intervention means to ablate the arrhythmogenic substrate in which the re-entrant circuit is established,[6,7,15-19,23,65] and mapping studies are employed to determine "the sites of VT origin" and ablation of those sites has been cured the VT in non-pharmacologic therapies.[15-16,18,23,58-61] Endocardial resection with or without cryothermal ablative procedures has now been established as the most reliable surgical therapy of recurrent sustained VT in patients with previous myocardial infarction.[15-16] Since the conditions of most of these patients have been complicated by aneurysm, the resection of the dilated aneurysmal left ventricle results in no problem. However, patients with VT of non-ischemic causes may have normal chamber size, and the site of VT origin may be located in the intramural layer. In these cases, the myotomy results in a post-operative problem, such as low cardiac output with elevation of the end-diastolic pressure because of reduction of size of the left ventricular chamber (Aizawa et al. Unpublished data).

Catheter ablation normally using large electric currents has been gaining success, but it is now still experimental therapy and its application limited to those patients who have low cardiac function, abnormalities in other organs, high age, or contraindications of operative therapy.[23] The minimal effective energy is to be given to avoid unnecessary damage to the normal tissue. Other non-pharmacologcal interventions are now under experimentation, using laser,[66] radiofrequency[67] or sclerosing materials.[68] VT which is refractory to all interventions has indicationd for the automatic implantable cardioverter defibrillator.[69] The use of any therapeutic modalities requires a knowledge of electrophysiologic studies, skill in mapping, and ability to interpret the acquired data correctly.

CONCLUSION

Most recurrent sustained VT is caused by a re-entrant mechanism, and data which can be explained by re-entry have been accumulating. The electrophysiological or pharmacological characteristics of the re-entrant circuit are now under active investigation. The re-entrant circuit can be modified by antiarrhythmic drugs or ablated directly by non-pharmacological intervention which should be done under the guidance of electrophysiologic studies.

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