Serial Electrophysiologic Testing of Multiple Drugs in Patients with Atrioventricular Nodal Reentrant Paroxysmal Tachycardia

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SUMMARY Serial electrophysiologic testing of multiple drugs was performed in 21 patients with recurrent atrioventricular (AV) nodal reentrant paroxysmal supraventricular tachycardia (PSVT). All patients had reproducible sustained PSVT induced before drug administration. Serial daily PSVT induction was attempted after administration of i.v. ouabain (0.01 mg/kg) (16 patients), i.v. propranolol (0.1 mg/kg (17 patients), i.v. ouabain + propranolol (same dosages) (12 patients), i.v. procainamide (600–1000 mg) (17 patients) and oral quinidine (1600–2400 mg/day) (nine patients). In two of 21 patients (10%), no tested drug prevented induction of sustained PSVT. In 19 of 21 patients (90%), one or more drugs prevented induction of sustained PSVT: ouabain — seven patients, propranolol — seven patients, ouabain + propranolol — seven patients, procainamide — 11 patients, quinidine — seven patients. The site of action of ouabain and/or propranolol was either the antegrade limb or the retrograde limb (RL) of the circus movement. The site of action of procainamide or quinidine was always the RL. These 19 patients were treated with oral drugs, based on results of serial testing. Eighteen patients were successfully followed for 6–50 months. In 13 of these 18 patients PSVT did not recur. Two patients (11%) had > 95% reduction in frequency of PSVT recurrences, and three (17%) did not respond to chosen oral drugs.

Serial electrophysiologic testing of multiple drugs is feasible in patients with AV nodal reentrant paroxysmal tachycardia. Drug responses are variable. In most but not all patients, serial electrophysiologic testing defines effective prophylactic drug therapy. This method of defining prophylactic drug therapy appears most suitable for patients with poorly tolerated tachycardias that occur only sporadically.

REENTRANT paroxysmal tachycardias can be reproducibly initiated and terminated by cardiac pacing.1 This capability has facilitated the evaluation of drug effects, as they relate to the induction of these tachycardias. One can also use electrophysiologic study to serially test multiple drugs in an attempt to define efficacious drug therapy for the patient.2 Laboratory testing of multiple drugs has been applied to a series of patients with preexcitation and reentrant paroxysmal tachycardia3 and to several series of patients with reentrant ventricular tachycardia.4–6

Dual pathway atioventricular (AV) nodal reentrance is the most common mechanism of paroxysmal supraventricular tachycardia in man.7–9 Several investigators have reported the effects of individual drugs on the induction of this tachycardia.10–18 In this study, we report the results of serial laboratory testing of multiple drugs in 21 patients with AV nodal reentrant paroxysmal tachycardia. We also report the results of oral drug therapy based on the results of these laboratory studies.

Methods

Patient Selection

Criteria for inclusion in the present study were: (1) A history of recurrent episodes of sustained paroxysmal tachycardia, with at least one electrocardiographic documentation of paroxysmal supraventricular tachycardia; (2) ability for induction of sustained dual pathway AV nodal reentrant paroxysmal tachycardia using cardiac stimulatory techniques (see below); and (3) serial testing of two or more drugs for ability to prevent induction of sustained AV nodal reentrant paroxysmal tachycardia.

Twenty-one patients, referred to this center between July 1975 and May 1979, met the above criteria. These patients had had recurrences of paroxysmal tachycardia for at least 6 months, and in most cases for many years.

Clinical Evaluation

Patients were carefully questioned regarding frequency of distinct episodes of paroxysmal palpitations during the 6 months before referral. Patients were also questioned regarding drugs that had been taken before referral, in an attempt to prevent recurrences of tachycardia. Heart rates during paroxysmal supraventricular tachycardia were determined from ECGs obtained from referring physicians and hospital emergency rooms. Patients were evaluated noninvasively, and when indicated invasively, for presence or absence of underlying organic heart disease.
Initial Electrophysiologic Study

This study was performed in the postabsorptive, nonsedated state after cardioactive drugs had been discontinued for at least 48 hours. Each patient gave informed written consent. A quadripolar electrode catheter was passed percutaneously into a femoral vein and advanced across the tricuspid valve for His bundle recording. A hexapolar electrode catheter was advanced from an antecubital vein to the right ventricular apex. The distal two electrodes (tip) were used for ventricular pacing, the middle two electrodes (10 cm) for recording high right atrial electrograms, and the proximal two electrodes (13.5 cm) for high right atrial pacing. In 11 patients a third electrode catheter (quadripolar) was advanced from an antecubital vein into the coronary sinus to determine the atrial activation sequence during tachycardia. Surface electrocardiographic leads I, II, III, and V₁, as well as intracardiac electrograms, were recorded simultaneously on a multichannel oscilloscopic recorder (Electronics for Medicine DR-16) at paper speeds of 100 and 200 mm/sec. Pacing stimuli were provided by a programmable digital stimulator (M. Bloom, Narberth, Pennsylvania) with a strength of approximately twice diastolic threshold and a duration of 2 msec.

The electrophysiologic protocol used in these patients included incremental atrial pacing, atrial extrastimulus testing during sinus rhythm and at one or more shorter (atrial) paced cycle lengths, incremental ventricular pacing, and ventricular extrastimulus testing at one or more ventricular paced cycle lengths. Two atrial extrastimuli were introduced in some patients for induction or termination of paroxysmal tachycardia.

Diagnosis of Mechanism of Tachycardia

All 21 patients fulfilled the following criteria for the diagnosis of dual pathway AV nodal reentrant paroxysmal tachycardia: (1) induction of tachycardia relating to achievement of a critical AV nodal delay (AH interval), with both incremental atrial pacing and atrial extrastimulus testing; (2) demonstration of antegrade dual AV nodal pathways, with induction of tachycardia relating to antegrade block in the fast pathway; and (3) atrial activation occurring before or simultaneously with the onset of ventricular activation during tachycardia. Additional support for the diagnosis of AV nodal reentrant paroxysmal tachycardia was present in most patients: (4) normal retrograde atrial activation sequence (present in all 11 patients in whom coronary sinus electrograms were recorded), and (5) demonstration with ventricular extrastimulus testing that atrial activation (A₂) was temporarily related to, and dependent on, His bundle activation (H₂) (17 patients).

In the control state, 17 patients had reproducible inductions of AV nodal reentrant paroxysmal tachycardia that was sustained, i.e., lasting longer than 2 minutes and requiring conversion with atrial stimula-

tion. The remaining four patients only had reproducible sustained tachycardia after i.v. atropine sulfate, 0.5–1.0 mg.¹⁴

Drug Studies

After the initial electrophysiologic study, a drug was administered intravenously and the electrophysiologic protocol was repeated. At the end of the first day of study, the hexapolar catheter was secured in a position suitable for both atrial and ventricular pacing on subsequent days, while other catheters were removed. On subsequent days, control studies were performed to confirm that sustained tachycardia was inducible before other i.v. drugs were administered. Control studies could not be performed on days when oral drugs were evaluated. In the four patients in whom sustained tachycardia was induced only after atropine, subsequent control and drug studies were performed after atropine administration.

The drugs tested in this study were i.v. ouabain (0.01 mg/kg) (16 patients), i.v. propranolol (0.1 mg/kg) (17 patients), i.v. ouabain plus propranolol (same dosages as above) (12 patients), i.v. procainamide (600–1000 mg, with blood levels obtained in nine patients ranging from 2–12.6 [mean of 5.4 mg/ml]) (17 patients), and oral quinidine (1600–2400 mg/day, with blood levels obtained in six patients ranging from 3.2–4.4 [mean 3.9 mg/ml]) (nine patients). Each patient was tested with two to five drugs (mean 3.4 drugs per patient).

These drugs were evaluated for ability to prevent induction of sustained tachycardia. When a drug prevented sustained tachycardia (successful drug response), its site of action was determined. When induced tachycardias terminated with atrial depolarization not followed by His bundle (or ventricular) depolarization, the site of drug action was considered to be the antegrade limb of the circus (AV nodal slow pathway). When induced tachycardias terminated with His bundle (or ventricular) depolarization not followed by atrial depolarization, the site of drug action was considered to be the retrograde limb of the circus (AV nodal fast pathway). The site of drug action was also considered to be the retrograde limb of the circus when atrial echoes could not be induced, despite AV nodal conduction times sufficient to induce tachycardia before drug administration.¹⁴ In these situations, the increase in retrograde fast pathway refractoriness was confirmed by demonstration of a marked decrease in the ventricular paced rate required for second-degree ventriculoatrial block.¹⁴

Selection of Oral Drug Therapy

Patients who responded to only one drug were placed on an oral form of the same drug to prevent further episodes of paroxysmal tachycardia. Patients who responded to two or more drugs were placed on an oral form of one of the same drugs. The drug selected was usually the agent which, in our opinion, had the least short- and long-term toxicity. Our order of preference (from least to most toxic) was digoxin,
propranolol, digoxin plus propranolol, procainamide and quinidine. Dosages of oral drugs were individualized, based on patient body weight and on blood levels of drugs, when available.

Evaluation of Oral Drug Therapy

Patients were followed in our arrhythmia research clinic (16 patients), or by direct contact with patients and referring physicians (five patients), at intervals of 1–4 months. Only one patient was lost to follow-up.

Results

Clinical and Electrocardiographic Characteristics (table 1)

The study group included nine males and 12 females, ages 20–82 years (mean ± SD 54 ± 16 years). Eight (39%) of these patients had organic heart disease and 13 (61%) did not. Five patients had experienced paroxysmal tachycardia more often than once per week during the 6 months before study. The other 16 patients had experienced paroxysmal tachycardia once per week to once in 6 months (mean frequency 2.7 per month). Rates of spontaneous paroxysmal supraventricular tachycardia ranged from 142–226 beats/min (182 ± 26 beats/min). Before referral, 16 patients had been unsuccessfully treated with one or more drugs alone or in combination: 16 with digoxin (0.125–0.50 mg/day, mean 0.28 mg/day), 12 with propranolol (30–240 mg/day, mean 124 mg/day), 10 with digoxin (0.125–0.50 mg/day, mean 0.27 mg/day) plus propranolol (30–240 mg/day, mean 123 mg/day), five with procainamide (1.5–3.0 g/day, mean 1.9 g/day), and 11 with quinidine (0.4–1.2 g/day, mean 0.82 g/day). With these drug regimens, duration of therapy was often short and patient compliance poor.

Drug Studies (table 2)

Induced AV nodal reentrant paroxysmal tachycardia was sustained in each control study in all patients (four patients receiving atropine, with cycle lengths from 275–400 msec (340 ± 39 msec) (figs. 1–3). Nineteen of the 21 patients (90%) (patients 1–19), responded to one or more of the tested drugs or drug combinations (see below). Patients 20 and 21 did not respond to any of the tested drugs.

Intravenous ouabain prevented induction of sustained tachycardia in seven of 16 patients (44%) (fig. 2). In four of these seven patients the site of action of ouabain was the antegrade limb (slow pathway), while in three patients the site of action was the

### Table 1. Clinical and Electrocardiographic Characteristics

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<th>OHD (type)</th>
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<th>Rate of PSVT (beats/min)</th>
<th>Digoxin</th>
<th>Propranolol</th>
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<th>Procainamide</th>
<th>Quinidine</th>
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Abbreviations: OHD = organic heart disease; PSVT = paroxysmal supraventricular tachycardia; HHD = hypertensive heart disease; CAD = coronary artery disease; HOCM = hypertrophic obstructive cardiomyopathy; MVP = mitral valve prolapse; + = drug given; 0 = drug not given.
Table 2. Laboratory Drug Testing

<table>
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<tr>
<th>Pt</th>
<th>PSVT CL (control study)</th>
<th>Ability to sustain PSVT (and site of action)</th>
<th>Therapy selected (mg/day)</th>
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<td></td>
<td>(ms)</td>
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<tr>
<td>21</td>
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Abbreviations: PSVT CL = cycle length of induced tachycardia; Yes = sustained tachycardia; No = did not sustain tachycardia; NT = not tested; AL = antegrade limb; RL = retrograde limb; RF = radiofrequency pacemaker.

retrograde limb (fast pathway) (fig. 2). Intravenous propranolol prevented induction of sustained tachycardia in seven of 17 patients (41%). In three of these seven patients the site of action of propranolol was the antegrade limb and in four it was the retrograde limb. Intravenous ouabain plus propranolol prevented induction of sustained tachycardia in seven of 12 patients (58%) (fig. 1). In six of these seven patients the site of action of ouabain plus propranolol was the antegrade limb (fig. 1) and in one patient it was the retrograde limb.

Intravenous procainamide prevented induction of sustained tachycardia in 11 of 17 patients (65%) (fig. 1). Oral quinidine prevented induction of sustained tachycardia in seven of nine patients (78%) (fig. 3). For all of these successful responses to procainamide and quinidine, the site of drug action was the retrograde limb (figs. 1 and 3).

Selection of Oral Drug Therapy (table 2)

An oral drug or drug combination was chosen in the 19 patients who responded to one or more drugs tested in the laboratory (patients 1–19). Based on the results of laboratory drug trials, five patients were treated with oral digoxin (0.25–0.50 mg/day, mean 0.35 mg/day), four with oral propranolol (80–160 mg/day, mean 120 mg/day), four with oral digoxin (0.25–0.50 mg/day, mean 0.35 mg/day) plus oral propranolol (80–160 mg/day, mean 140 mg/day), three with oral procainamide (2.25–4.00 g/day, mean 3.08 g/day), and three with oral quinidine (1.60–2.40 g/day, mean 1.88 g/day). Before hospital discharge, eight of the 16 patients treated with oral drugs other than quinidine were tested on their chosen oral drug regimens. In none of these patients could sustained tachycardia be induced.

Of these 19 patients who were treated with oral drugs based on the results of laboratory drug trials, 11 (patients 2, 3, 7, 8, 11–13 and 16–19) were treated with drugs or drug combinations that had not been tried before referral. Patients 1, 4, 6, 10, 14 and 15 were treated with drugs or drug combinations that had been tried, but in smaller dosages, before referral. Patients 5 and 9 were treated with drug regimens identical to those tried before referral. We felt that these two patients had complied poorly with drug regimens before referral.

Patients 20 and 21, who did not respond to any drugs tested, were treated with radiofrequency atrial pacemakers. In each of these two patients, more
FIGURE 1. Results of serial drug testing in patient 2. Each panel shows electrocardiographic lead II and a high right atrial (HRA) electrogram. Time lines are at 1-second intervals in this and subsequent illustrations. Atrioventricular nodal reentrant paroxysmal tachycardia was induced by atrial pacing (arrows). Induced tachycardias were sustained (A) in control studies, (B) after ouabain, and (C) after propranolol. (D) After ouabain plus propranolol, induced tachycardias were nonsustained because of block in the antegrade limb (the last atrial echo [E] is not followed by a QRS complex). (E) After procainamide, induced tachycardias were also nonsustained, but (in this case) due to block in the retrograde limb. (The last QRS complex is not associated with an atrial echo.)

FIGURE 2. Response to ouabain, with site of action in the retrograde limb in patient 1. Atrioventricular nodal reentrant paroxysmal tachycardia was induced by atrial extrastimulus testing (arrows). (A) Induced tachycardias were sustained in control studies performed after atropine administration. (B) After administration of ouabain, induced tachycardias were nonsustained (despite atropine administration) because of block in the retrograde limb (the last QRS complex is not associated with an atrial echo).
than 50 episodes of tachycardia had been terminated with atrial pacing during the course of laboratory drug trials. Patient 20 was also treated with a small dose of oral digoxin (0.125 mg/day), which potentiated pacing conversions of tachycardia.

**Evaluation of Oral Drug Therapy**

Of the 19 patients treated with oral drugs (based on the results of laboratory studies), only patient 10 failed to return to the clinic and could not be contacted by other means. The other 18 patients were followed for at least 6 months.

Of the 18 patients treated with oral drugs and successfully followed, 13 (72%) (patients 3, 5, 6, 8 and 11–19) had no recurrences of paroxysmal tachycardia during follow-up periods of 6–40 months (mean ± SD 17 ± 12 months). Patient 11 was lost to follow-up after 6 months. Patient 12 stopped taking quinidine...
after 7 months because of drug side effects, and has since had recurrences of paroxysmal tachycardia. Patients 8 and 18 briefly stopped taking propranolol, and each had paroxysmal tachycardia within days.

Patients 1 and 2 have had recurrences of paroxysmal tachycardia, but at less than one-twentieth of their frequencies before laboratory study. Patient 1 has had only three episodes in 50 months of follow-up and patient 2 had only two episodes in 30 months of follow-up (before dying of a stroke). Therefore, oral drug therapy was considered to be successful in 15 of 18 patients (83%) (absolutely successful in 13 patients and relatively successful in two).

In the other three patients (17%) (nos. 4, 7 and 9), oral drug therapy was unsuccessful, despite obtaining therapeutic blood levels of drugs. These patients have had recurrences of paroxysmal tachycardia at frequencies similar to their frequencies before laboratory study. Patient 7 was taken off of oral procainamide and started on oral disopyramide after 25 months of follow-up.

Patients 20 and 21, in whom no drugs tested prevented laboratory induction of sustained tachycardia, have continued to have paroxysmal tachycardia at an undiminished frequency. These patients have, however, terminated episodes of paroxysmal tachycardia with their radiofrequency pacemakers.

Discussion

AV nodal reentrance is the most common cause of paroxysmal supraventricular tachycardia in man.4 In patients with AV nodal reentrant paroxysmal tachycardia, atrial extrastimulus testing usually demonstrates discontinuous A1A2, H1H2 conduction curves, suggesting dual AV nodal pathways (fast and slow).8,10,11 In these patients, reentrant tachycardia can usually be induced by atrial impulses that block in the fast pathway but conduct antegradely over the slow pathway. The reentrant pathway consists of a proximal common pathway (probably located within the AV node), a slow AV nodal pathway (antegrade limb), a distal common pathway (also probably located within the AV node), and a fast AV nodal pathway (retrograde limb).14,26 Tachycardia continues as long as the propagating circus impulse does not encounter refractory tissue. If block occurs in a component of the circus movement, the tachycardia terminates. Whether or not AV nodal reentrance is sustained depends on the ability of the components of the reentrant pathway to conduct repetitively at the cycle length of the tachycardia.27

Drugs may be administered to a patient with sustained AV nodal reentrant paroxysmal tachycardia in an attempt to increase refractoriness of a component of the reentrant pathway, and thus cause tachycardia to terminate. Drugs may also be administered prophylactically to a patient with recurrent sustained tachycardia to increase refractoriness of a limb of the reentrant pathway and prevent further recurrences of sustained tachycardia. Cardiac stimulation provides a tool for assessing drug effectiveness in preventing induction of sustained tachycardia.

Several studies have elucidated the effects of drugs as they relate to laboratory induction of sustained AV nodal reentrant paroxysmal tachycardia. Wu and co-workers found that propranolol increases antegrade slow pathway refractoriness and prevents induction of sustained AV nodal reentrant paroxysmal tachycardia in some patients.10 Subsequent studies have shown similar effects after administration of cardiac glycosides or verapamil.11-13 More recently Wu et al. demonstrated that procainamide also prevents induction of sustained AV nodal reentrant paroxysmal tachycardia in some patients.14 The site of action of this drug, however, is the retrograde fast pathway. In this same study, Wu et al. also demonstrated that procainamide could have a detrimental effect in some patients, making previously nonsustained tachycardia sustained by decreasing antegrade slow pathway refractoriness (a vagolytic effect). In another study, Wu et al. demonstrated that atropine could make previously nonsustained tachycardia sustained by facilitating conduction in either the retrograde fast pathway or the antegrade slow pathway.15

The effects of propranolol, digitalis, and procainamide described in these previous reports were observed in the present series of patients. An unexpected finding in the present study was that propranolol and digitalis (alone or in combination) could sometimes prevent induction of sustained tachycardia by increasing refractoriness of the retrograde limb (fast pathway), suggesting that the retrograde fast pathway manifests AV nodal-like properties.16,18,28 The present study also demonstrated that quinidine, like procainamide, could prevent induction of sustained AV nodal reentrant paroxysmal tachycardia, always by increasing retrograde fast pathway refractoriness. The effects of quinidine on induction of AV nodal reentrant paroxysmal tachycardia have not been previously reported.

This study is the first in which the effects of different drugs could be compared in the same group of patients. However, some aspects of the present study limit conclusions regarding patterns of drug responses. First, the present series of patients is a referred population sample. Therefore, our results are applicable only to patients with relatively troublesome tachycardias that are relatively drug-resistant. Second, more patients had been previously refractory to digoxin (16 patients), propranolol (12 patients), digoxin plus propranolol (10 patients), and quinidine (11 patients), than had been refractory to procainamide (five patients), before referral. Although the dosages used before referral were smaller, it is reasonable to assume, for example, that a patient who has not responded to a small dose of digoxin is less likely to respond to a large dose than a patient who has never been treated with digoxin.

Despite these limitations, we may draw several conclusions related to patterns of drug responses: (1) Drug responses vary markedly from patient to patient. Some patients responded to all drugs tested, while
other patients did not respond to any drug. Response patterns also varied among patients who responded to some, but not all, drugs. For example, one patient responded to procainamide but not to ouabain plus propranolol, while another patient responded to ouabain plus propranolol but not to procainamide. (2) The combination of ouabain plus propranolol appears to be more effective than ouabain or propranolol alone. All patients who responded to ouabain or propranolol alone also responded to ouabain plus propranolol. On the other hand, several patients who failed to respond to ouabain or propranolol alone did respond to ouabain plus propranolol. (3) Procainamide and quinidine appear to be at least as effective as even the combination of ouabain plus propranolol. Eleven of 17 patients responded to procainamide. The results after administration of quinidine were even more impressive, with seven of nine patients responding. Several patients who failed to respond to all other drugs responded to quinidine. Furthermore, neither patient who failed to respond to quinidine responded to any other drug tested. The relative efficacies of procainamide and quinidine demonstrated in this study suggest that these might be drugs of choice in managing recurrent AV nodal reentrant paroxysmal tachycardia. However, short- and long-term toxicities of these agents should be considered in determining their use.

The present study demonstrates that laboratory drug trials quite successfully define effective prophylactic oral drug therapy in patients with AV nodal reentrant paroxysmal tachycardia. Oral drug therapy based on laboratory studies resulted in absolute or relative prevention of recurrences of tachycardia in 15 of 18 patients (83%), but did not prevent recurrences of tachycardia in only three patients (17%). These results are comparable to those reported by Wu et al. for patients with AV reentrant paroxysmal tachycardia and by Horowitz et al., Mason and Winkle and Denes et al. for patients with ventricular tachycardia.

Effective drug therapy for AV nodal reentrant paroxysmal tachycardia is often delineated non-invasively, during a period of trial and error with various drug regimens. This method is satisfactory for patients with tachycardias that recur often, allowing the efficacy of drug regimens to be evaluated quickly, and for patients whose tachycardias are well tolerated. However, the method is far from ideal for patients with poorly tolerated tachycardias which recur only sporadically. These patients may be better served by performing laboratory drug studies. For the majority of these patients, laboratory drug studies quickly delineate drug therapy, which is very likely to give successful prophylaxis against recurring tachycardia. For patients in whom no promising drug responses are found, alternative treatments, such as radiofrequency pacemakers, should be considered.

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FRAGMENTATION OF THE VENTRICULAR ELECTROGRAM HAS BEEN OBSERVED DURING EXPERIMENTAL MYOCARDIAL INFARCTION IN THE CANINE HEART USING EPICARDIAL, INTRAMURAL AND ENDOCARDIAL ELECTRODE RECORDINGS.\(^1\)-\(^{10}\)


FRAGMENTED VENTRICULAR ELECTROGRAMS/Waxman and Sung

Significance of Fragmented Ventricular Electrograms Observed Using Intracardiac Recording Techniques in Man

HARVEY L. WAXMAN, M.D., AND RUEY J. SUNG, M.D.

SUMMARY Recent studies using intracardiac recordings (ICR) have demonstrated that fragmentation of the ventricular electrogram (VE) can be detected in patients with chronic ventricular tachycardia (VT) associated with cardiomyopathy or arteriosclerotic heart disease with ventricular aneurysm. This study suggests that fragmented VE reflects desynchronized local electrical activity related to conduction delay in the ventricular myocardium and may be necessary for the genesis of reentrant VT in man, a finding similar to that observed during experimental myocardial infarction in the canine heart. We studied 17 patients using ICR, five with and 12 without a documented history of VT. Of these 17 patients, two had cardiomyopathy, five arteriosclerotic heart disease (three of five had ventricular aneurysm), five rheumatic heart disease and two congenital heart disease; the remaining three had no apparent heart disease. The left and right VEs were recorded at multiple sites with variable interelectrode distances and filter frequency settings. Fragmented VE could be recorded in the right VE in four patients (23.5%) (one with and three without VT) and in the left VE in all 17 patients (100%) using interelectrode distances of 12 mm or greater and filter frequency settings of 40–500 Hz or less. Furthermore, we observed that (1) incremental atrial pacing could induce progressive prolongation of VE fragmentation without the induction of VT; (2) when VT was induced, it bore no relationship to VE fragmentation; and (3) during VT, interruption of VE fragmentation with ventricular extrastimuli did not terminate VT. These findings suggest that (1) recordings of fragmented VE depend on the ICR location, interelectrode distance and filter frequency setting; (2) fragmentation of the VE can be observed in patients with and without VT; and (3) fragmentation of the VE may reflect fractionated myocardial potentials, but it may also represent artifacts associated with intracardiac catheter electrode movement during cardiac systole and diastole. Therefore, VE recorded as such should be interpreted with caution in defining the mechanism of VT in man.

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