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Preferential Effect of Procainamide on the Reentrant Circuit of Ventricular Tachycardia

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Transient entrainment was used to test the hypotheses that 1) procainamide prolongs the cycle length of ventricular tachycardia in patients with coronary artery disease because it has a preferential effect on the reentrant tachycardia circuit, and 2) regions of slow conduction in the reentrant circuit are more susceptible to the effect of procainamide than are other areas of the ventricles. In five patients with prior myocardial infarction, sustained ventricular tachycardia with identical QRS configuration was inducible before and after intravenous infusion of procainamide. Transient entrainment of ventricular tachycardia was demonstrated at two or more cycle lengths by rapid pacing in the baseline state and after procainamide. Rapid pacing was performed from the same site during sinus rhythm at the cycle lengths that demonstrated transient entrainment of ventricular tachycardia. The conduction interval to the transiently entrained site during ventricular tachycardia (orthodromic interval) was compared with the conduction interval to the same site during pacing in sinus rhythm (antidromic interval).

The mean tachycardia cycle length increased by 27% after procainamide administration ($p = 0.002$). The antidromic conduction intervals were prolonged by 9% ($p = 0.06$) compared with a 28% increase in the mean orthodromic conduction interval ($p = 0.002$). The difference between the orthodromic and antidromic conduction intervals increased by 40% ($p = 0.003$). Prolongation of the tachycardia cycle length after procainamide administration correlated positively with increases in the orthodromic conduction intervals ($r = 0.94$, $p = 0.02$) but not with changes in the antidromic intervals ($r = -0.08$, p = NS). The effect of procainamide on the difference between orthodromic and antidromic conduction intervals correlated strongly with changes in the cycle length of ventricular tachycardia ($r = 0.97$, $p = 0.006$).

Thus, procainamide has a preferential effect on the reentrant circuit of ventricular tachycardia compared with other areas of ventricular myocardium. In addition, these results are compatible with the hypothesis that the effect of procainamide is more marked in regions of conduction delay in the reentrant circuit.

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Procainamide and other type 1 antiarrhythmic agents are often effective in prolonging the cycle length of ventricular tachycardia (1). The mechanism responsible for the effectiveness of these drugs to slow down the rate of ventricular tachycardia in humans is incompletely understood. Antiarrhythmic agents have a wide range of potential electrophysiologic effects, including changes in myocardial conduction, refractoriness, excitability and automaticity (2,3). In addition, these drugs may have different effects on normal and abnormal areas of myocardium (2). It is probable that their net effect is a complex interaction of their effects on active and passive membrane properties in normal and abnormal regions (3).

Sustained ventricular tachycardia related to coronary artery disease in humans has been shown (4–13) to be frequently based on a reentrant mechanism. Isochronal endocardial mapping studies of human ventricular tachycardia have demonstrated regions of slow conduction in ventricular myocardium that may form the functional basis for a reentrant circuit (13). Further support for the existence of slow conduction in the reentrant circuit in patients with ventricular tachycardia has been provided by studies of the response to rapid pacing during this arrhythmia (6–10,14–16). The ability to continuously reset (transiently entrain) ventricular tachycardia by rapid pacing has provided a method to determine the functional properties of slowly conducting reentrant circuits (7,14). With this technique, decremental conduction properties and localized

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block in these areas of conduction delay in human ventricular tachycardia have been demonstrated (7,14).

In this study, transient entrainment was used to test the hypothesis that procainamide prolongs the cycle length of ventricular tachycardia in patients with coronary artery disease because of a preferential effect on slow conduction in the reentrant tachycardia circuit compared with other regions of myocardium.

Methods

Electrophysiologic study protocol. Patients with a history of spontaneous sustained monomorphic ventricular tachycardia who were referred for electrophysiologic testing were studied prospectively. Electrophysiologic studies were performed in the fasting state, at least four half-lives after discontinuation of antiarrhythmic medications. In all patients, quadripolar electrode catheters with 0.5 cm interelectrode distance (USCI 6F Josephson) were introduced from the femoral vein and positioned at the right ventricular apex and outflow tract. A custom-designed octapolar catheter (USCI 6F) was advanced from the femoral artery to the left ventricle. Surface electrocardiographic (ECG) leads I, II, III and V_1 and bipolar intracardiac electrograms filtered at a bandpass of 30 to 500 Hz were recorded onto photographic paper with use of a switched-beam oscilloscopic recorder (Electronics for Medicine VR-16) and onto frequency-modulated tape with use of a Honeywell 101 recorder. A standard 12 lead ECG (Hewlett-Packard) was also recorded during tachycardia.

Transient entrainment. Programmed electrical stimulation was performed using a pulse width of 2.0 ms at twice the diastolic current threshold. Sustained monomorphic ventricular tachycardia was induced in all patients with one or two extrastimuli coupled to an eight beat S_1 drive delivered from the right ventricular apex. After a 12 lead ECG was recorded, rapid pacing was performed during ventricular tachycardia from the right ventricular apex at a cycle length 10 to 20 ms less than that of the tachycardia. The pacing train was started synchronously, with the first pacing stimulus delivered at the tachycardia cycle length. Pacing was continued for 15 beats, then abruptly terminated. If ventricular tachycardia continued, rapid pacing at the same cycle length was performed in the same manner sequentially from the right ventricular outflow tract and from two sites in the left ventricle. If ventricular tachycardia continued, the pacing cycle length was decreased in decrements of 10 ms, and the same sequence repeated until the tachycardia was interrupted. With the catheters left in the same position, pacing was also performed during sinus rhythm over the same range of cycle lengths for 15 beats at each pacing site.

Procainamide infusion. Procainamide (12 mg/kg body weight) was infused intravenously over 30 min and programmed stimulation repeated. After induction of sustained ventricular tachycardia, a 12 lead ECG was performed. If the configuration of ventricular tachycardia after procainamide was identical to that induced in the baseline state, the same rapid pacing protocol described earlier was repeated during ventricular tachycardia and during sinus rhythm. Intervals were measured at a paper speed of 100 mm/s.

Definitions. The criteria for transient entrainment have been described previously (17). A recording site was considered to have been activated orthodromically during transient entrainment of ventricular tachycardia if 1) the local electrogram at that site during rapid pacing occurred at the pacing cycle length and maintained a constant configuration during both pacing and spontaneous ventricular tachycardia; and 2) after termination of pacing, the last captured local electrogram occurred at the pacing cycle length and was associated with a nonfused QRS configuration identical to that of the spontaneous ventricular tachycardia.

Experimental model. Figure 1 illustrates diagrammatically the experimental model used in the study. In panel A, a reentrant ventricular tachycardia circuit is shown, with earliest activation of the ventricles occurring in the left ventricle as the wave of depolarization emerges from a region of slow conduction. The tachycardia loop is completed with reactivation of the proximal portion of the region of slow conduction. With rapid ventricular pacing from the right ventricle at a rate faster than ventricular tachycardia (panel B), an excitable gap in the tachycardia circuit is entered with resetting of the ventricular tachycardia. Each paced wave front enters the region of slow conduction at the proximal end and collides with the wave front of activation from the previous beat. The tachycardia is reset continuously to the faster pacing rate without being terminated, and is, therefore, transiently entrained. The left ventricular (LV) recording site distal to the region of slow conduction is activated in the same direction during both transient entrainment and spontaneous tachycardia by an orthodromic wave front emerging from the region of slow conduction. In panel C, pacing from the same right ventricular site during sinus rhythm at the same rates that demonstrated transient entrainment activates the left ventricular recording site with a short conduction time from a different direction by a wave front of depolarization that does not traverse the region of slow conduction. This wave front from the pacing stimulus is designated as antidromic. The interval from the pacing stimulus to the orthodromically activated local electrogram was measured during transient entrainment of ventricular tachycardia and designated the orthodromic conduction interval (panel B). When more than one recording site demonstrated orthodromic activation during transient entrainment, only the site activated earliest in relation to the onset of the surface QRS complex was considered.

With use of the same pacing rates, the interval from the pacing stimulus to the same recording site that had been activated orthodromically during transient entrainment of

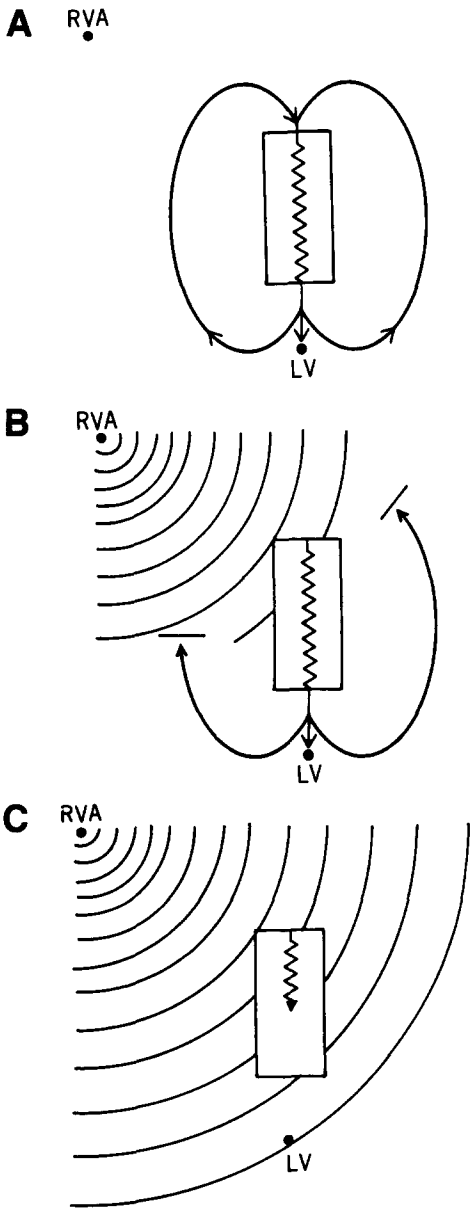

Figure 1. The experimental model is illustrated diagrammatically. **A,** A reentrant circuit sustaining ventricular tachycardia is shown. The orthodromic wave front emerges from a region of slow conduction (**rectangle**), with activation of the left ventricle (LV). The tachycardia circuit is completed as the orthodromic wave front reenters the proximal region of slow conduction. Note that the right ventricular apex (RVA) is not activated as a critical component of the reentrant circuit. **B,** The activation sequence during transient entrainment of ventricular tachycardia by pacing from the right ventricular apex (RVA). **C,** Rapid pacing during sinus rhythm activates the left ventricular (LV) recording site from a different direction with a short conduction time without traversing the region of slow conduction. See text for discussion.

ventricular tachycardia was measured during pacing in sinus rhythm. This interval was designated the antidromic conduction interval (panel C). The orthodromic interval includes the time required for conduction from the pacing site to the tachycardia circuit, through the excitable gap and through the region of slow conduction. The antidromic interval does not include the time required for conduction through the region of slow conduction. Orthodromic and antidromic conduction intervals from the same pacing site to the same recording site were also measured after procainamide infusion in precisely the same manner. The difference between the orthodromic and antidromic intervals at each paced cycle length was also calculated. This interval may provide insights relevant to the region, or regions, of slow conduction in the reentrant circuit.

Inclusion criteria. Patients were included in the study if all of the following criteria were met: 1) patients had documented coronary artery disease by coronary arteriography, segmental wall motion abnormalities by left ventriculography, a documented history of myocardial infarction at least 6 months previously and no known intolerance to procainamide; 2) sustained ventricular tachycardia with the same QRS configuration in all 12 ECG leads was inducible in the baseline state and after procainamide infusion; 3) a recording site was identified that demonstrated orthodromic activation during transient entrainment with rapid pacing at two or more cycle lengths before and after procainamide; and 4) rapid pacing from the same site during sinus rhythm at the cycle lengths that demonstrated transient entrainment during ventricular tachycardia before and after procainamide did not induce ventricular arrhythmias.

Statistical analysis. Conduction intervals before and after procainamide infusion were compared using the nonparametric Mann-Whitney test. Conduction intervals were expressed as mean values ± SD. Correlation was performed using Pearson's correlation coefficient.

Results

Study patients. Five patients with sustained ventricular tachycardia met the entry criteria and were included in the study (Tables 1 and 2). In all patients, hemodynamically well tolerated ventricular tachycardia was induced reproducibly in the baseline state and after intravenous procainamide administration by programmed electrical stimulation using one or two extrastimuli. Both the first and second criteria for transient entrainment were demonstrated for all episodes of ventricular tachycardia. The mean serum procainamide level achieved was 8.4 ± 1.9 mg/liter. The mean cycle length of ventricular tachycardia prolonged from 323 ± 23 ms in the baseline state to 410 ± 42 ms after procainamide, an increase of 27% ($p = 0.002$). The effective refractory period of the right ventricular apex prolonged from a mean of 232.5 ± 15 ms baseline to 250 ± 18 ms after procainamide. The range of pacing cycle lengths demonstrating transient entrainment of ventricular tachycardia was 24 ± 5.5 ms at baseline and 30 ± 17.3 ms after procainamide (p = NS). In all patients, this

Table 1. Effects of Procainamide in Five Patients

Patient No.	QRS	Baseline						Procainamide						
		CL	Orth	Anti	O-A	ERP	Range	CL	Orth	Anti	O-A	ERP	Range	Serum Level
1	RBBB	330	440	155	285	225	20	390	545	185	360	240	20	7.5
2	LBBB	350	475	155	320	215	20	480	653	170	483	225	20	7.0
3	LBBB	330	425	150	275	245	20	400	505	152	353	260	20	10.5
4	RBBB	320	390	130	260	—	30	410	510	150	360	270	60	10.3
5	LBBB	288	340	138	202	245	30	370	455	140	315	255	30	6.5
Mean		324	414	146	268	233	24	410	533	159	374	250	30	8.4
± SD		23	51	11	43	15	6	42	4	18	64	18	17	1.9

*Procainamide serum levels expressed in mg/liter and conduction intervals expressed in milliseconds. Anti = antidromic conduction interval; CL = ventricular tachycardia cycle length; ERP = effective refractory period; LBBB = left bundle branch block; QRS = QRS configuration during ventricular tachycardia; O-A = orthodromic minus antidromic interval; Orth = orthodromic conduction interval; Range = range of pacing cycle lengths demonstrating transient entrainment; RBBB = right bundle branch block; SD = standard deviation.

range was the same or greater after procainamide than in the baseline state.

Effects of procainamide on ventricular tachycardia conduction intervals (Fig. 2 to 5). In patient 1 (Fig. 2A), ventricular tachycardia with a right bundle branch block configuration is entrained transiently by rapid pacing at a cycle length of 300 ms from the right ventricular apex. Note that the last captured electrogram at the left ventricular (LV)1-2 recording site (asterisk) is activated at the pacing cycle length with a constant configuration and is associated with a nonfused surface QRS complex and the same intracardiac activation sequence noted during spontaneous ventricular tachycardia. The orthodromic conduction interval measured 440 ms. In panel 2B, rapid pacing from the right ventricular apex at a cycle length of 300 ms activates the LV1-2 recording site with an antidromic conduction time of 155 ms. Transient entrainment of ventricular tachycardia after procainamide administration (panel 2C) activates the LV1-2 recording site with an orthodromic conduction time of 545 ms. The antidromic conduction time at the same pacing cycle length (360 ms) after procainamide prolonged to 185 ms (panel 2D). The results for Patient 1 at each paced cycle length are illustrated in Figure 3.

Orthodromic and antidromic conduction intervals before and after procainamide are shown for the entire group in Figures 4 and 5. The mean antidromic conduction interval prolonged by 9%, from 146 ± 11 ms before, to 159 ± 18 ms after procainamide ($p = 0.06$). The mean orthodromic conduction interval increased by 28%, from 414 ± 51 ms in the baseline state to 533 ± 74 ms after procainamide ($p = 0.002$). The difference between the orthodromic and antidromic conduction intervals increased by 40% after procainamide from a mean of 268 ± 43 to 373 ± 64 ms ($p = 0.003$).

Relation of changes in ventricular tachycardia cycle length to changes in orthodromic and antidromic conduction intervals produced by procainamide (Fig. 6). Increases in the ventricular tachycardia cycle length correlated with changes in the orthodromic conduction intervals ($r = 0.94$, $p = 0.02$), but not with changes in the antidromic conduction interval ($r = -0.08$, p = NS). The difference between orthodromic and antidromic conduction intervals also demonstrated a strong correlation with changes in the cycle length of ventricular tachycardia ($r = 0.97$, $p = 0.006$).

Table 2. Effects of Procainamide on Conduction Intervals in Five Patients

VT Cycle Length	Antidromic	Orthodromic	Ortho–Anti Interval
(+) 27 ± 7%	(+) 9 ± 8%	(+) 28 ± 8%	(+) 40 ± 13%
$p = 0.002$	$p = 0.06$	$p = 0.002$	$p = 0.003$

Values expressed as mean percentage change after procainamide compared to baseline ± standard deviation. Ortho–Anti = orthodromic minus antidromic interval; VT = ventricular tachycardia.

Discussion

Region of slow conduction in ventricular tachycardia. The mechanism of sustained monomorphic ventricular tachycardia related to previous myocardial infarction has been shown to be based on reentry with a gap of excitability in many patients (4). The presence of a region of slow conduction as a critical component of the reentrant ventricular tachycardia circuit in humans has also been demonstrated previously (7,13,14). With the use of transient entrainment techniques, decremental conduction properties and localized block in a region of slow conduction have also been demonstrated (7,14). The results of our study suggest that procainamide prolongs the cycle length of ventricular tachycardia related to previous myocardial infarction by a preferential effect on slow conduction in the reentrant tachycardia circuit.

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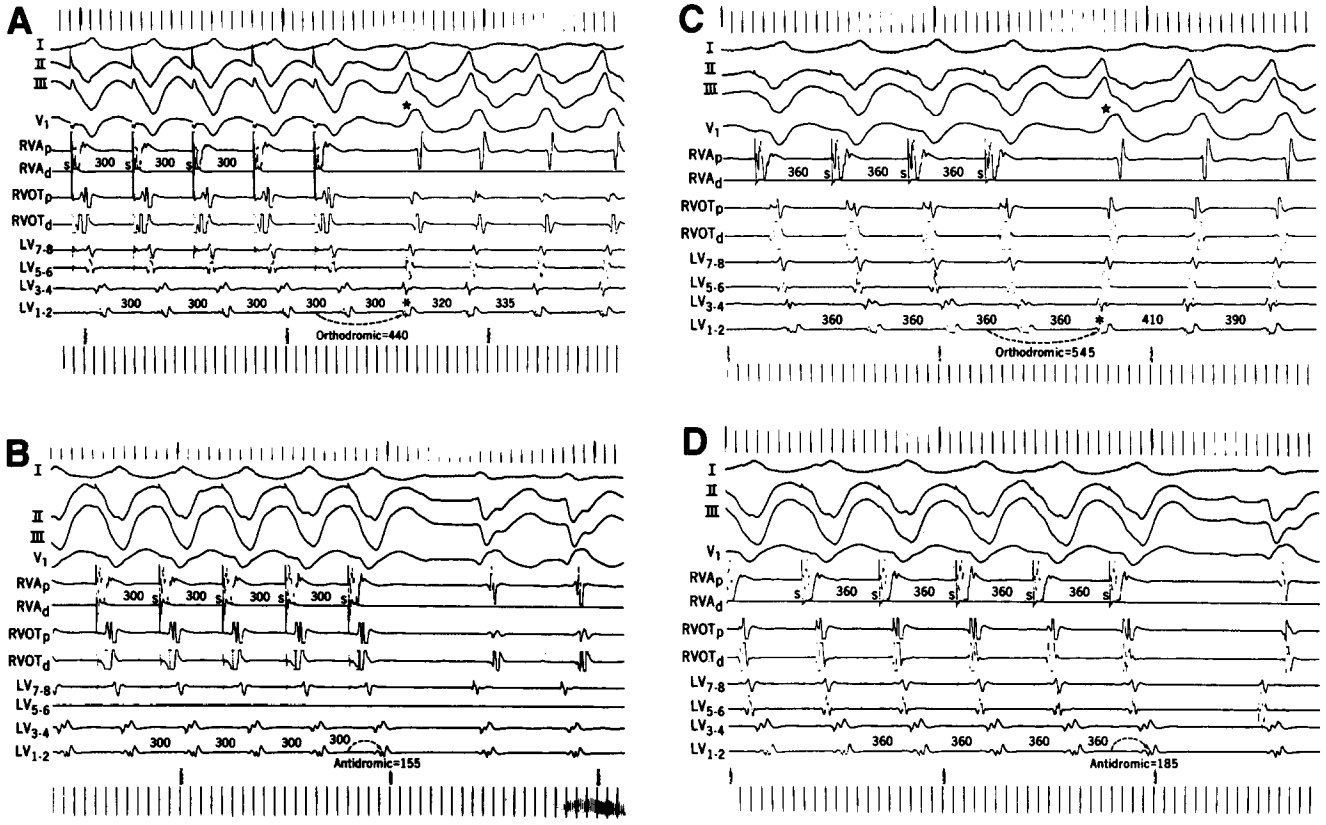

Figure 2. Patient 1. Determination of orthodromic and antidromic conduction intervals in the absence of antiarrhythmic drugs (**A and B**) and after intravenous procainamide infusion (**C and D**). Surface electrocardiographic (ECG) leads I, II, III and V_1 are recorded simultaneously with intracardiac electrograms from the right ventricular apex proximal (RVAp) and distal (RVAd), right ventricular outflow tract proximal (RVOTp) and distal (RVOTd) and left ventricular electrode pairs 7 to 8 (LV_{7-8}), 5 to 6 (LV_{5-6}), 3 to 4 (LV_{3-4}) and 1 to 2 (LV_{1-2}). **A,** Rapid pacing at a cycle length of 300 ms from the right ventricular apex distal (RVAd) electrode pair during ventricular tachycardia activates all recording sites at the paced cycle length. After termination of pacing, ventricular tachycardia continues with the last captured beat in the most distal left ventricular electrode pair (LV_{1-2}) occurring at the paced cycle length (**asterisk**). The QRS configuration in the surface ECG leads of the last captured beat (**star**) is not fused but is identical to that during ventricular tachycardia. **B,** Rapid pacing from the right ventricular apex distal (RVAd) electrode pair at a cycle length of 300 ms during sinus rhythm. After termination of pacing, sinus rhythm resumes. The configuration of the LV_{1-2} electrogram during pacing at the same cycle length in ventricular tachycardia (**A**) is different from that during pacing in sinus rhythm (**B**). The interval from the last pacing stimulus (**S**) to the LV_{1-2} recording site measures 155 ms and is termed the antidromic conduction interval. **C,** Rapid pacing at a cycle length of 360 ms during ventricular tachycardia is performed after intravenous administration of procainamide. The QRS configuration and intracardiac activation sequence during ventricular tachycardia after procainamide are the same as in **A** in the absence of antiarrhythmic drugs. After termination of pacing, ventricular tachycardia continues with the last captured beat in the LV_{1-2} recording site occurring at the paced cycle length (**asterisk**). The QRS configuration of the last captured beat is identical to that during spontaneous ventricular tachycardia (**star**). The orthodromic interval from the pacing stimulus (**S**) to the last entrained electrogram (**asterisk**) measures 545 ms after procainamide. **D,** Rapid pacing from the right ventricular apex distal (RVAd) electrode pair at a cycle length of 360 ms during sinus rhythm after procainamide. The antidromic interval measures 185 ms. See text for discussion.

Preferential effect of procainamide on reentrant circuit. The observation that procainamide prolonged the cycle length and orthodromic conduction intervals of ventricular tachycardia to a proportionately greater extent than the antidromic conduction intervals is evidence of a preferential effect on the reentrant circuit of ventricular tachycardia. Because the difference between orthodromic and antidromic intervals was prolonged to a greater degree than either the antidromic or orthodromic intervals, it is likely that this effect of procainamide occurred in a region of slow conduction. However, because the orthodromic interval includes conduction from the pacing site, and through both an excitable gap and a region (or regions) of slow conduction, our data do not prove that the preferential effect of procainamide occurred only in a region of conduction delay. For example, a partially excitable gap in the reentrant circuit potentially may respond to antiarrhythmic drugs in a similar manner. However, because the range of pacing cycle lengths that demonstrated transient entrainment of ventricular tachycardia was either the same or greater after procainamide than in

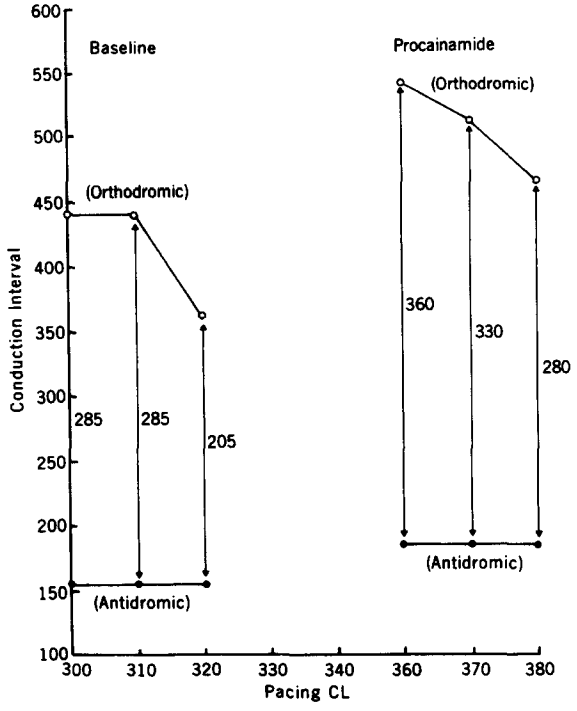

Figure 3. The orthodromic (**open circles**) and antidromic (**closed circles**) conduction intervals at baseline and after procainamide for Patient 1 (Fig. 2) are illustrated over the range of pacing cycle lengths (CL) demonstrating transient entrainment. The gradual prolongation of the orthodromic conduction intervals at shorter paced cycle lengths before and after procainamide is evidence of progressive conduction delay in the tachycardia circuit. There is no change in the antidromic intervals at shorter pacing cycle lengths. **Vertical arrows** and adjacent numbers indicate the difference between orthodromic and antidromic conduction intervals at each pacing cycle length.

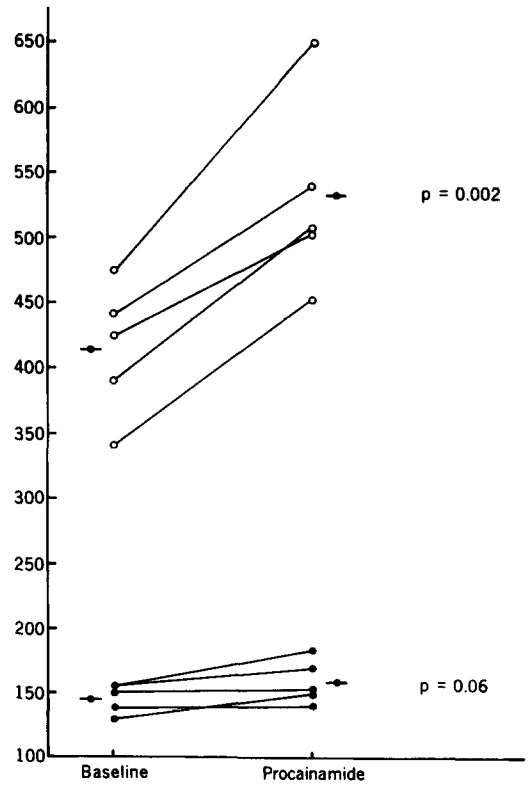

Figure 4. Orthodromic (**open circles**) and antidromic (**closed circles**) conduction intervals at the minimal pacing cycle length demonstrating transient entrainment before and after procainamide are illustrated for all five patients. The **vertical axis** indicates the conduction interval from the last pacing stimulus to the last captured electrogram at a site that was activated orthodromically during transient entrainment of ventricular tachycardia. The **horizontal axis** indicates the baseline state and after procainamide. The effect of procainamide was greater for orthodromic than for antidromic conduction. See text for discussion.

the baseline state, localization of drug effect to a partially excitable gap seems unlikely. Therefore, although the available data do not allow precise localization of the effect of procainamide between the functional components of the reentrant circuit, the results are compatible with the hypothesis that it is a region of slow conduction in the tachycardia circuit that is most susceptible to the effects of this agent.

Potential mechanisms for a preferential effect of procainamide on the ventricular tachycardia circuit. There are several potential mechanisms by which procainamide may preferentially affect the reentrant circuit. Previous studies (18) of ventricular myocardium resected at the time of surgery for refractory ventricular arrhythmias have demonstrated reduced resting membrane potentials and diminished action potential amplitude and duration in infarcted regions. Conduction block and decremental properties have also been demonstrated in these areas (18). The anatomic and functional substrate for the development of reentry in infarcted human ventricular myocardium may be related to islands of viable myocardium within or at the border of scar tissue that are linked to normal myocardium by strands of slowly conducting but viable myocardium (2,19). If slow conduction is present in a functional isthmus between damaged and normal areas of the ventricle, this area may be more susceptible to the effects of procainamide than are more normal areas (2). For example, previous canine studies (20) have shown that surgical creation of a narrow isthmus of atrial muscle joining two broader sheets of normal myocardium results in a region that is vulnerable to conduction block during pacing from either side of the isthmus. The site of block in these preparations is at the distal end of the isthmus near the junction with the broader mass of myocardium.

In more recent studies using this experimental model, Inoue and Zipes (21) showed that procainamide lengthens the effective refractory period of the isthmus to a far greater extent than it does in regions proximal or distal to this site. Similar findings of a low safety margin for conduction have been demonstrated at the junction of Purkinje fibers and

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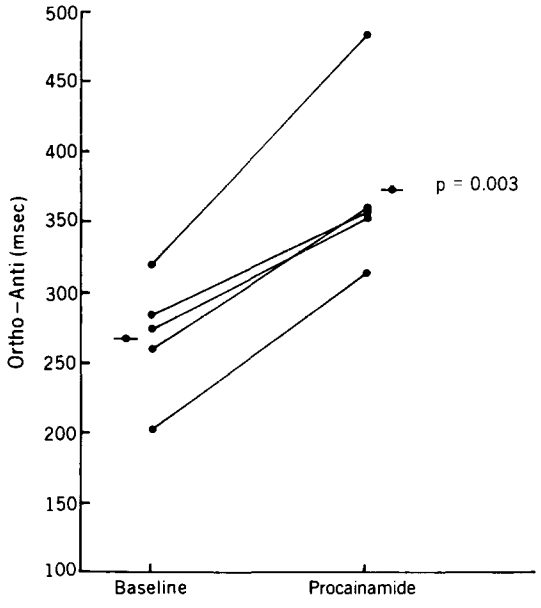

Figure 5. Effect of procainamide on the calculated difference between orthodromic and antidromic (Ortho–Anti) conduction intervals (**vertical axis**) is plotted against the change in ventricular tachycardia cycle length (CL) induced by procainamide (**horizontal axis**). The change in this value is strongly associated with the change in ventricular tachycardia cycle length produced by procainamide. See text for discussion.

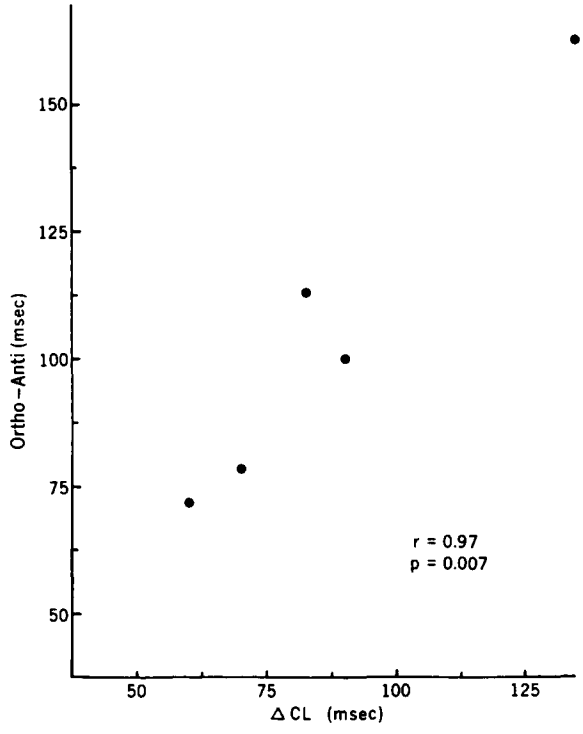

Figure 6. The difference between orthodromic and antidromic (Ortho–Anti) conduction intervals at the minimal pacing cycle length (CL) demonstrating transient entrainment before and after procainamide. This difference may provide information relevant to a region, or regions, of slow conduction in the reentrant ventricular tachycardia circuit. See text for discussion.

ordinary ventricular muscle cells (22). The vulnerability of such sites to failure of impulse propagation has been postulated to be due to a mismatch of impedance at the junction of the narrow bridge of tissue and the broader mass of myocardium (22,23). This might result in failure of the depolarizing wave front traversing the smaller connecting bridge (source) to produce a regenerative response in the larger ventricular mass (sink) because of dilution of electrotonic effect by the many low resistance connections between these regions (21,22). If the safety margin for impulse propagation (the excess of source over sink required to produce a regenerative response) at the junction of a region of slow conduction to less damaged areas of ventricular myocardium is low, procainamide could potentially slow conduction at this site to a greater degree than in other areas of the ventricle (21).

Potential role of anisotropy. The relative selectivity of procainamide on the reentrant circuit could also be related to anisotropy in these zones (24,25). The geometry of fiber orientation has been shown to influence conduction velocity at branch sites from smaller to larger fiber diameter (26). Spach et al. (24) demonstrated the importance of fiber orientation on both the rate of impulse propagation and the upstroke velocity of the action potential in normal canine myocardium. In addition, Kadish et al. (25) demonstrated that procainamide retards conduction in the longitudinal axis of myocardial fibers to a proportionally greater degree than it does in the transverse axis.

Potential role of partially depolarized myocardium. Conduction velocity can also be expected to decrease in the presence of decreased sodium conductance (27,28). Because blockade of sodium channels by antiarrhythmic drugs may depend on the proportion of time that the channels are open, relatively depolarized cells in slowly conducting portions of the tachycardia circuit may be more likely to bind sodium channel blocking agents (29–35). In addition, altered kinetics of activation and inactivation gating may be present in the reentrant circuit and could result in enhancement of the sodium channel blocking effect of procainamide.

Previous studies of procainamide. Previous studies (36) of procainamide in patients with ventricular tachycardia related to coronary artery disease have suggested a uniform prolongation of electrogram duration in normal and abnormal areas of ventricular myocardium during sinus rhythm. However, regions of conduction delay in the reentrant tachycardia circuit may not be evident during pacing in sinus rhythm (7). The results of the present study suggest that the properties of the reentrant circuit can be accurately assessed only by recording during reentry.

Limitations of study. Several important limitations should be emphasized. Various factors suggest that the study population was highly selected. First, procainamide failed to suppress induction of ventricular tachycardia in all patients. Only the five patients in whom the same configuration of ventricular tachycardia could be induced in both the baseline state and after procainamide infusion were included. Second, transient entrainment could be demonstrated for all five patients, indicating that reentry with an excitable gap was the likely mechanism. Third, all five patients had coronary artery disease and prior myocardial infarction as the underlying anatomic substrate. Lastly, ventricular tachycardia was well tolerated by all patients, allowing completion of the study protocol. Whether patients with other forms of structural heart disease, shorter cycle lengths of ventricular tachycardia or other mechanisms of tachycardia would have similar responses to procainamide is uncertain. In addition, whether procainamide suppresses the induction of ventricular tachycardia by a similar action on the region of slow conduction is unknown.

Conclusions. Our results have implications for understanding the mechanism of action of antiarrhythmic drugs on the functional components of human ventricular tachycardia. These data suggest that procainamide slows the rate of ventricular tachycardia related to prior myocardial infarction by a preferential effect on the reentrant tachycardia circuit in comparison with other regions of ventricular myocardium.

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