Predicting Ventricular Tachycardia Cycle Length After Procainamide by Assessing Cycle Length–Dependent Changes in Paced QRS Duration

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To determine if paced cycle length–dependent changes in the QRS duration correlate with the change in ventricular tachycardia (VT) cycle length after procainamide, we measured the QRS duration during sinus rhythm and during right ventricular pacing before and after procainamide (mean concentration, 9.9 µg/ml) in 18 patients with morphologically identical VT induced at both study periods. Pacing was performed at 600 msec or the longest cycle length that allowed for uninterrupted capture and at a cycle length that was within 50 msec of the VT cycle length observed during the control study (mean, 313±51 msec). After procainamide, the VT cycle length increased from 285±62 to 368±70 msec (percent change, 30±13%). The QRS duration during sinus rhythm increased from 125±25 to 145±29 msec (percent change, 16%). The QRS duration at both paced cycle lengths was the same in the baseline state (191±26 msec). However, the change in QRS duration after procainamide at the shorter paced cycle length compared to a 39±13 msec (18%) increase at the longer paced cycle, \( p < 0.001 \). There was a significant correlation between the percent change in QRS duration at the shorter paced cycle length and the percent change in VT cycle length (\( r = 0.84, p < 0.001 \)) with the relation expressed by the regression equation: percent change in VT cycle length = \(-2.8 + 1.16 \times \) percent change in QRS duration. These findings support the hypothesis that the mechanism for the change in VT cycle length after procainamide is due to a rate-dependent change in conduction. (Circulation 1989;79:39–46)

Many antiarrhythmic agents, including procainamide, slow myocardial conduction in a cycle length–dependent fashion.\(^1\)–\(^3\) Morady et al\(^4\) have demonstrated in humans a greater increase in QRS duration with increased rates of ventricular pacing after procainamide. Furthermore, analysis of the resetting response of ventricular tachycardia to ventricular extrastimuli has demonstrated that the slowing of most tachycardias after procainamide administration is probably due to slowing of ventricular conduction and not due to an increase in refractoriness.\(^5\)–\(^6\) We, therefore, reasoned that after procainamide, the change in the paced QRS duration at a cycle length that approximated the ventricular tachycardia cycle length might reflect the change in conduction at that rate due to procainamide. We anticipated that the degree of change in QRS duration at that cycle length may approximate the degree of change in conduction in the tachycardia circuit and, therefore, the same degree of change in the ventricular tachycardia cycle length. The purpose of this study was to determine if paced cycle length–dependent changes in the QRS duration after procainamide correlate with the increase in ventricular tachycardia cycle length.

Patients and Methods

Patient Population

There were 16 men and two women in the study population, who ranged in age from 53 to 78 years (mean, 67±7 years). All 18 patients had coronary
artery disease with previous myocardial infarction and a history of sustained ventricular tachycardia or cardiac arrest or both. All patients included in the study had the same morphologically distinct (based on 12-lead electrocardiogram) ventricular tachycardia induced in the baseline state and after intravenously administered procainamide (see below). In addition, all patients had a stable catheter position for right ventricular apical pacing at both study periods confirmed by multiplane fluoroscopy.

**Study Protocol**

Baseline electrophysiologic studies were performed in the nonsedated postabsorptive state after all antiarrhythmics were discontinued for at least five half-lives in 17 patients. Amiodarone was discontinued 3 months before study in one patient. For the purpose of the study protocol, a 6F quadripolar electrode catheter was introduced percutaneously into the venous system and positioned under fluoroscopic guidance at the right ventricular apex. Additional multipolar electrode catheters were introduced percutaneously and positioned as necessary for completion of the electrophysiologic evaluation of the patients clinical arrhythmia.

Stimulation was performed with a custom-designed, programmable stimulator (Bloom Associates) using a constant current source. Rectangular impulses of 1-msec duration were delivered at twice-diastolic threshold. Recordings were made with a sixteen-channel physiologic recorder (VR 16, Electronics for Medicine), and real-time records were obtained with an ink jet recorder (Siemen’s Elema Mingograph).

Our stimulation protocol for evaluation of suspected or documented ventricular tachycardia has been previously described in detail.² In all patients, ventricular tachycardia having a uniform morphology was induced with from one to three programmed extrastimuli introduced during pacing cycle lengths of 600, 550, or 400 msec from either the right ventricular apex or right ventricular outflow tract or both. In all patients, the morphology based on analysis of the 12-lead electrocardiogram recorded on arrhythmia induction was noted. The cycle length of the ventricular tachycardia was documented from recordings made at a paper speed of 200–250 mm/sec. After arrhythmia termination, the QRS complex (Table 1) in leads 1, aV₆, and V₁ or leads 1, 2, 3, and V₁ (0.5–1.0 cm/mV calibration) were recorded during sinus rhythm, right ventricular apical pacing at a cycle length of 600 msec (n = 14 patients) or at a cycle length 50–100 msec less than the sinus cycle length if the sinus cycle length was shorter than 600 msec (right ventricular pacing slow: mean cycle length, 583±42 msec), and right ventricular apical pacing at a cycle length within 50 msec (one patient, 55 msec) of the baseline induced ventricular tachycardia cycle length (right ventricular pacing fast: mean cycle length, 317±55 msec). All pacing was bipolar (5-mm interelectrode distance) using a current strength equal to twice-diastolic threshold and a pulse width of 1 msec. Pacing at each cycle length was performed for 15 beats with recordings made at paper speeds of 200–250 mm/sec.

After the baseline recordings, procainamide was infused as a loading dose of 15 mg/kg at a rate of 50 mg/min followed by continuous infusion of 0.11 mg/kg/min. Between 5 and 10 minutes after the onset of the continuous infusion, the QRS complexes were again recorded during normal sinus rhythm and during the same paced cycle lengths (right ventricular pacing slow and fast) as used in the baseline state. A serum sample was obtained for a procainamide concentration just before the post-procainamide pacing protocol (mean concentration, 9.9±2.7 μg/ml). Ventricular tachycardia was then reinitiated with the standard stimulation protocol as previously described. The morphology (based on the recorded 12-lead electrocardiogram) and the cycle length of the induced ventricular tachycardia were again noted. Analysis was performed only on the ventricular tachycardia, which matched the morphology of the ventricular tachycardia induced during the baseline study. In 15 of the 18 patients, a second serum sample was obtained after ventricular tachycardia induction at the end of the stimulation protocol to document stability of serum procainamide concentrations. The mean difference in the procainamide concentration was −1.0±1.8 (p = NS) with only three patients demonstrating a procainamide concentration difference of more than 2 μg/ml (−2.9, +4.0, and −4.8 μg/ml, respectively).

**Measurement of Intervals and Statistical Analysis**

The QRS duration was measured from the onset to the end of the QRS complex recorded in leads 1, aV₆, and V₁ or leads 1, 2, 3, and V₁. To facilitate accuracy in the measurement of QRS duration, the onset of the QRS duration was timed to the pacing spike during right ventricular pacing. The QRS duration of the last beat of the 15 beats of pacing was used for data analysis. To further ensure that the timing of the offset was the same, measurements of QRS duration before and after procainamide were made at the same setting from recordings obtained at paper speeds of 200–250 msec with recordings made at a slower paper speed used to help define the end of the QRS complex. Measurement reproducibility was within 15 msec for the QRS duration with pacing and within 5 msec for the ventricular tachycardia cycle length as measured by two observers. Measurement reproducibility for the

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<th>Table 1. Cycle Lengths at Which QRS Width Was Determined</th>
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<td>Sinus rhythm CL (msec)</td>
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<td>RV pacing slow CL (msec)</td>
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<td>RV pacing fast CL (msec)</td>
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CL, cycle length; RV, right ventricular.
QRS duration was equal to or less than 5 msec when measured in a blinded fashion by the same observer at two different settings.

Results are reported as mean±SD. Student’s t test for paired data was used to compare measurements before and after procainamide. Linear regression analysis was used to determine the degree of correlation between the percent change in ventricular tachycardia cycle length and the percent change in QRS duration during sinus rhythm, right ventricular apical pacing at a cycle length of 600 (500–550 msec) (right ventricular pacing slow), and at paced cycle length that was within 50 msec of the VT cycle length (right ventricular pacing fast). Analysis of variance was used to compare the effects of procainamide on the percent change in QRS duration in sinus rhythm and during the two paced rates. p<0.05 was considered statistically significant.

**Results**

In the baseline state, the mean sinus cycle length was 707±80 msec (range, 520–860 msec), and the mean ventricular tachycardia cycle length was 285±62 msec (Figure 1A) with a range of 205–380 msec. There was no difference during the baseline study between the QRS durations (191±26 compared with 191±26 msec) during right ventricular pacing at the two different pacing cycle lengths, 583±42 and 313±51 msec (Figure 1B).

Procainamide had no significant effect on the sinus cycle length (Table 1). After procainamide, the mean ventricular tachycardia cycle length (Figure 1A) increased by 83 msec from 285±62 to 368±69 msec (p<0.001), and the mean QRS duration during sinus rhythm (Figure 1B) increased by 20 msec from 125±25 to 145±29 msec (p<0.001). After procainamide, the QRS duration during right ventricular pacing at both cycle lengths also increased significantly (p<0.001) with an increase of 34 msec from 191±26 to 225±30 msec at the slower paced cycle length and by 53 msec from 191±26 to 244±51 msec at the faster paced cycle length (Figure 1B). The increase in QRS duration at the faster paced cycle length after procainamide was more than the increase at the slower paced cycle length (p<0.001) (Figures 2 and 3). Of note, the mean percent change in the

![Bar charts showing effect of procainamide on the ventricular tachycardia length (Panel A), the QRS duration during sinus rhythm and during right ventricular pacing at a long (583±42 msec) cycle length (panel B), and the percent change in ventricular tachycardia cycle length.](image)
ventricular tachycardia cycle length after procainamide approximated the degree of change in the QRS duration during pacing at the faster paced cycle lengths (Figure 1C).

The percent change in QRS duration during sinus rhythm after procainamide did not correlate with the percent change in ventricular tachycardia cycle length (Figure 4A). In contrast, there was a significant correlation between the percent change in QRS duration when pacing at the shorter paced cycle length and the percent change in VT cycle length (Figures 2, 3, and 4C) with \( r=0.84 \) (\( p<0.001 \)) and \( \text{SEE}=6.9\% \). The percent change in QRS duration when pacing at the longer paced cycle length also correlated with the change in ventricular tachycardia cycle length, although to a lesser extent \( (r=0.65, p<0.01) \).

Of note, the serum procainamide concentration also correlated with the change in ventricular tachycardia cycle length \( (r=0.53, p=0.028) \) and with the percent change in QRS duration during rapid pacing \( (r=0.46, p=0.056) \), although the relations were much weaker. Of note, the uniform dosing regimen and, thus, the relatively narrow range of serum procainamide concentrations (17 of the 18 concentration
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Figure 3. A second electrocardiographic example with a format similar to that of Figure 2 showing the changes in the ventricular tachycardia cycle length and QRS durations after procainamide. The percent change in QRS duration when pacing at the more rapid rate (26%) approximates the percent change in ventricular tachycardia cycle length (26%). The panels are arranged with surface electrocardiographic leads 1, 2, 3, and V₁; intracardiac recordings from the right ventricular apex (RVA); and 10-msec time lines (TL).
values between 6.0 and 13.0 μg/ml) may have precluded the ability to define a better relation between the serum procainamide concentration and the change in the measured electrocardiographic intervals.

In 14 of the patients, the ventricular tachycardia had a left bundle branch block morphology, and in four patients, the ventricular tachycardia had a right bundle branch block morphology. The correlation coefficient between the percent change in QRS duration at the faster pacing rate and percent change in the ventricular tachycardia cycle length was 0.86 (p<0.001) for tachycardias with a left bundle branch block morphology and 0.76 (p=NS) for tachycardias with a right bundle branch block morphology. For the subgroup of nine tachycardias with a left bundle branch block morphology and left-axis deviation, the correlation coefficient was 0.87.

Discussion

We found a cycle length–dependent increase in the paced QRS duration after procainamide administration (Figure 1A) similar to that described by Morady et al.4 Although we did not perform our pacing at exactly the same cycle lengths as Morady et al., it is of interest that the changes described were similar. During a paced cycle length of 300 msec, they noted a mean increase in QRS width of 55 msec compared with a mean increase of 53 msec during pacing at a mean cycle length of 317 msec (right ventricular pacing fast) in this study. Similarly, they noted a mean increase of 30 msec at a paced cycle length of 600 msec compared with a mean increase of 34 msec noted during pacing at a mean cycle length of 583 msec (right ventricular pacing slow). The effect of procainamide on the ventricular tachycardia cycle length is comparable to our previously reported results.8,9

The results of the present study suggest that there is a good relation (r=0.84, p<0.001) between the degree of change in the paced QRS duration and the percent change in the ventricular tachycardia cycle length after procainamide administration when pacing is performed at a cycle length that approximates that of the tachycardia induced in the baseline state. This relation is described by the regression equation: percent change in ventricular tachycardia cycle length =1.16×percent change in QRS duration during right ventricular pacing (right ventricular pacing fast) −2.8%. This equation suggests that the percent change in QRS duration during right ventricular pacing (at a cycle length that approximates that of the ventricular tachycardia) tends to modestly underestimate the percent change in ventricular tachycardia cycle length. It is of note that there was no relation between the change in QRS duration during sinus rhythm and the change in ventricular tachycardia cycle length after procainamide. Furthermore, although a significant relation did exist between the change in tachycardia cycle length and the change in QRS duration during pacing at the slower cycle length, the relation was not as strong (r=0.65, p<0.01) as that noted with pacing at the faster cycle length. The results of our study emphasize the importance of assessing the electrophysiologic effects of a drug over a wide range of cycle lengths.

It is appropriate to speculate on the basis for the significant relation between the change in ventricular tachycardia cycle length and the change in paced QRS duration at the more rapid paced rates. In preliminary studies, Stamato et al 5,6 have shown that after procainamide, most ventricular tachycardias that are hemodynamically tolerated can be reset with premature extrastimuli. Furthermore, the return cycle was usually constant over a variable range of coupling intervals (i.e., a “flat” response), suggesting the presence of a fully excitable gap in the presumed reentrant circuit.10,11 The presence of this excitable gap indicates that the rate of the tachycardia is determined by the conduction velocity and not by impingement on refractoriness in the circuit. These data also suggest that the ability to index change in the conduction velocity of the tachycardia circuit should also index the change in the tachycardia cycle length. Our results indicate that the change in the global ventricular activation time (QRS duration) may reflect the change in conduction velocity in the reentrant circuit as long as attention is paid to the cycle length at which the measurements are made.

Although there is a reasonably strong relation between the percent change in ventricular tachycardia cycle length and the percent change in QRS duration during pacing at a cycle length that approximates that of the tachycardia, it is not a perfect one-to-one relation (1.16:1), and SEE=6.9%. This is not surprising given many factors. First, the wavefront of activation during right ventricular pacing may differ from that during ventricular tachycardia. Moreover, even in normal uniform anisotropic tissue, procainamide suppresses conduction velocity in the longitudinal axis of fiber orientation to a greater extent than in the transverse direction.12 Thus, differences in wavefronts of activation with a differential effect of procainamide dependent on the wavefront of activation make it unlikely that changes in any index of conduction would be exactly the same under both conditions after procainamide.12 In addition, there is no reason to believe that the effect of procainamide on conduction velocity is similar in diseased and normal tissue. Although we found no difference in the increase in normal and abnormal electrogram duration recorded during sinus rhythm after procainamide administration, it appears that the degree of change in conduction, as indexed by electrogram duration, is greater in chronically infarcted tissue at shorter paced cycle lengths.13,14 It is not known whether the QRS duration measured on the surface electrocardiogram at the described gain settings may adequately reflect activation in infarcted tissue. If activation of infarcted tissue is not adequately represented, one might anticipate that the change in QRS duration during pacing may

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underestimate the change in the ventricular tachycardia cycle length.

Of note, factors other than a uniform increase in conduction velocity throughout the tachycardia circuit may also be responsible for the observed increase in ventricular tachycardia cycle length. This is suggested by the fact that outliers were observed in the data analysis in which the change in ventricular tachycardia cycle length was correlated with the change in QRS duration during rapid pacing (Figure 4C). For example, it is possible that antiarrhythmic agents, due to additional effects on refractoriness or junctional resistance between myocytes, might increase the tachycardia cycle length by creating an increased arc of block around which the impulse must circulate. The tachycardia circuit size may be increased without altering its exit site and resultant QRS morphology. This effect might result in a dramatic increase in ventricular tachycardia cycle length with a less marked change in the QRS duration.

**Limitations**

The faster pacing cycle length at which the QRS duration was assessed approximated (<50-msec difference) the ventricular tachycardia cycle length in the baseline state. Pacing was not performed at the ventricular tachycardia cycle length when that cycle length was short (<250 msec) because of the concern that the known effects of procainamide on refractoriness would preclude the ability to pace and capture at such short cycle lengths. Thus, the selection of the rate of "rapid" pacing was arbitrary and may limit the accuracy of our assessment of the relation between the percent change in the ventricular tachycardia cycle length and the percent change in the QRS duration.
In addition, although Stamato et al\textsuperscript{5,6} demonstrated an excitable gap when introducing ventricular extra-stimuli during ventricular tachycardias that were hemodynamically tolerated and, therefore, associated with a longer cycle length, a fully excitable gap may not be present for faster tachycardias. Such tachycardias may have their rate determined by refractoriness within the circuit. This study did not assess changes in refractoriness at comparable cycle lengths to determine whether such changes were also proportional to the change in ventricular tachycardia cycle length. Of note, in a previous study,\textsuperscript{15} we were not able to demonstrate a cycle length–dependent effect on refractoriness after procainamide that was similar to the cycle length–dependent effect on QRS duration noted in the present study. Nevertheless, this does not preclude a cycle length–independent relation between the change in refractoriness and the change in ventricular tachycardia cycle length.

It is also important to note that this study assessed the effects of acute intravenous procainamide administration. It cannot be assumed that the same response can be anticipated after oral procainamide and, thus, the clinical usefulness of our findings remains to be determined.

Finally, determining the offset (onset was taken as the pacing stimulus artifact) of the paced QRS complex at rapid rates can be difficult (Figures 2 and 3). Differences of up to 15 msec in the measured paced QRS duration between observers were noted. However, although differences were found in identifying the end of the QRS, each observer could identify the same point as the end of the QRS for control and procainamide study periods. This was facilitated by making both measurements at the same setting and superimposing recorded tracings as needed. As a result of this measurement technique, variability in the measured percent increase in QRS duration due to procainamide was less than 5%. Thus, the measurement technique reduced the amplification of the error normally anticipated for the difference measurements and validated the comparisons made.

**Summary**

Procainamide produces a paced cycle length–dependent increase in the QRS duration with a greater increase observed at shorter paced cycle lengths. Furthermore, it appears that the degree of increase in QRS duration at a paced cycle length that approximates the ventricular tachycardia cycle length may reflect the degree of slowing in the cycle length of morphologically identical ventricular tachycardia. The relation can be expressed by the regression equation: percent increase in ventricular tachycardia cycle length = \(-2.8 + 1.16 \times \) percent increase in QRS duration during pacing at a cycle length that approximates that of the baseline tachycardia (\(r = 0.84, p < 0.001\)). This relation may allow for prediction of the cycle length of morphologically identical ventricular tachycardia after intravenously administered procainamide and suggests that the mechanism for the change in ventricular tachycardia cycle length after procainamide is due to a rate-dependent change in conduction.

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**References**


**KEY WORDS**  • ventricular tachycardia • procainamide • ventricular conduction
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