PATHOPHYSIOLOGY AND NATURAL HISTORY
VENTRICULAR TACHYCARDIA

Resetting response patterns during sustained ventricular tachycardia: relationship to the excitable gap

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ABSTRACT We analyzed the resetting response (a noncompensatory pause after electrical stimulation) during 37 hemodynamically tolerated ventricular tachycardias (VTs) induced by programmed electrical stimulation in 32 patients with chronic coronary artery disease. The mean cycle length of VT was 369 ± 59 msec. Single extrastimuli were delivered at the right ventricular apex during all 37 VTs, and double extrastimuli were delivered at the same site during 23 VTs. The resetting response pattern was considered increasing, decreasing, or flat if the return cycle increased, decreased, or remained constant in response to progressively shorter coupling intervals of the extrastimuli. Ten VTs had an increasing pattern and nine a flat pattern. In 11 VTs the pattern was mixed (flat at longer coupling intervals and increasing at shorter ones), and in the remaining seven the pattern could not be defined. No VT had a decreasing pattern. The mean duration of the resetting interval (range of coupling intervals resulting in resetting) was 66 ± 45 msec, or 17% of the cycle length of VT. VT with a mixed pattern had longer resetting intervals than VT with an increasing pattern (102 ± 34 vs 64 ± 40 msec; p < .035); however, cycle lengths of VT were similar (370 ± 58 vs 386 ± 86, p = NS). An excellent correlation was observed between the shortest return cycles in response to single and double extrastimuli (r = .99), with a mean difference of 5 msec. The cycle length of VT exceeded the return cycle (measured to the QRS onset) during 15 VTs (41%). The findings of flat and mixed resetting response patterns and relatively long resetting intervals favor a reentrant circuit, which is at least in part anatomically defined, for the majority of these tachycardias.


SEVERAL lines of evidence suggest that sustained uniform ventricular tachycardia (VT) in the setting of chronic coronary artery disease is caused by a reentrant mechanism.1 Timed premature stimuli delivered during a sustained rhythm may interact with it, causing a pause that is not fully compensatory; this phenomenon is referred to as resetting.2 In reentrant rhythms, this response is presumably determined by the characteristics of both the intervening tissue and the reentrant circuit.

Two recent reports have focused on the resetting response in isolated cases of VT.3, 4 Recently the incidence and “requirements” of resetting of VT have been described.5, 6 The phenomenon of continuous resetting (i.e., entrainment) has also been described.5, 7-11 However, no systematic analysis of the pattern of the resetting response (i.e., the relationship of the timing of the first tachycardia beat following resetting stimuli and coupling intervals of the premature stimuli producing resetting) during a large number of VTs is available.

The resetting phenomenon in sustained, electrically induced, and well-tolerated VT was prospectively studied in order to (1) describe the patterns of response to resetting during VT, and (2) analyze the implications these observations have for models of reentry in VT.

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Materials and methods

**Patients and characteristics of tachycardia.** Criteria for entry into this study included: (1) sustained uniform VT reproducibly initiated by programmed electrical stimulation (PES) in patients with chronic coronary artery disease and prior myocardial infarction, (2) stability of the cycle length of VT (i.e., \( \pm 20 \) msec difference in the cycle length of 20 consecutive beats), (3) hemodynamic tolerance of VT, and (4) demonstration of resetting of the VT in response to PES. Resetting was observed during 37 morphologically distinct VTs in 32 patients undergoing PES. The resetting responses of these arrhythmias constitutes the basis of this report. Characteristics of the patient population and their tachycardias are given in table 1. VT with a right bundle branch block morphology was as common as VT with a left bundle branch block morphology. Intracardiac electrophysiologic studies were performed as previously described.\(^{15,16}\) Initiation of tachycardia was accomplished by single ventricular extrastimuli (SVE) for seven VTs, double ventricular extrastimuli (DVE) for 17 VTs, and triple ventricular extrastimuli for 13 VTs.

**Pacing protocol during ventricular tachycardia.** All stimulation during VT was performed at the right ventricular apex. SVE were delivered during VT in 10 msec decrements, beginning 20 msec less than the cycle length of VT, until local ventricular refractoriness was reached, VT was terminated, or a sustained change in the morphology of VT or cycle length took place. DVE were delivered during VT in the following fashion: The coupling interval of the first extrastimulus was fixed for each VT and exceeded the longest coupling interval that produced resetting of the VT with SVE by 20 msec. If SVE did not result in resetting of the VT, the coupling interval of the first extrastimulus was maintained 20 msec above ventricular refractoriness. Thus, regardless of whether there was resetting with SVE, only the second extrastimulus with DVE interacted with the reentrant circuit. The second extrastimulus was delivered with increasing prematurity, beginning at a coupling interval equal to the cycle length of VT and decreasing its coupling interval by 10 msec decrements until ventricular refractoriness was reached, termination of VT occurred, or a sustained change in the tachycardia took place. SVE were delivered during all 37 VTs, and DVE were delivered during 23 VTs. The pacing protocol was not completed in all patients. Reasons for this included termination of the VT, a sustained change in morphology of VT, or consideration by the electrophysiologist that immediate termination of the VT should be undertaken.

**Definitions and statistical analysis.** Resetting of the VT was said to have occurred if (1) the interval from the last VT beat before each particular mode of stimulation to the first nonpaced VT beat after stimulation (measured both at the pacing site and at the surface QRS) was less than 20 msec less than the cycle length of VT for SVE and less than 20 msec less than three cycle lengths of VT for DVE; i.e., the pause following stimulation was less than fully compensatory, and (2) the same VT (identical cycle length and morphology) resumed after pacing (figure 1). The return cycle was defined as the interval from the last paced electrogram to the next electrogram measured at the pacing site. Each coupled SVE or DVE was repeated two to four times to ensure reproducibility of the responses. Measurements were made from the rapid deflection of the local electrograms recorded from the proximal pair of the quadrupolar pacing catheter.

The local activation time at the pacing site was defined as the interval from the onset of the QRS to the local electrogram at that site during VT. This was considered an estimate of time from the exit point of the VT circuit to the pacing site.

Response patterns during resetting were characterized by plotting the return cycle versus the coupling intervals of the extrastimuli (figure 2). The responses observed could be grouped into three patterns. A flat pattern was defined as the presence of 10 msec or 100% difference in return cycle occurring over a 30 msec or greater range of coupling intervals. An increasing pattern was defined as an increase in the return cycle as the coupling interval was increased in the extrastimulus. If the opposite had occurred, it would have been defined as decreasing. There were tachycardias meeting criteria for a flat response at long coupling intervals, followed by an increasing response at shorter coupling intervals, and such a pattern was defined as mixed or "flat plus increasing." Finally, in some cases a specific

### Table 1

**Clinical, electrocardiographic, and electrophysiologic characteristics of the 37 VTs studied**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of VTs</th>
</tr>
</thead>
<tbody>
<tr>
<td>VT QRS morphology (RBBB/LBBB)</td>
<td>20/17</td>
</tr>
<tr>
<td>Antiarrhythmic drugs(^a) (yes/no)</td>
<td>24/13</td>
</tr>
<tr>
<td>Mode of initiation (1/2/3 extrastimuli)</td>
<td>7/17/13</td>
</tr>
<tr>
<td>Mean ± SD VT cycle length (msec)</td>
<td>369 ± 59</td>
</tr>
</tbody>
</table>

\(^a\)RBBB = left bundle branch block; LBBB = right bundle branch block.

*FIGURE 1.* Analog tracing demonstrating resetting of a VT by a single premature stimulus. The tachycardia cycle length is 375 msec; the premature stimulus is delivered from the right ventricle (RV) at a coupling interval of 180 msec. The return cycle, the cycle of the first tachycardia beat following the extrastimulus, measured at the pacing site, is 440 msec. Resetting is recognized because the same VT immediately resumes and because the return cycle is 130 msec less than fully compensatory. The 1, 2, and \( V_1 \) represent surface electrocardiographic leads. \( T = \) time.
pattern could not be characterized, either because resetting occurred over too narrow a range of coupling intervals, or because of variability in the return cycle. If a response pattern was obtained during the same VT with SVE and DVE, the pattern observed in response to the stimulation modality that reset over a longer range of coupling intervals was taken as the response pattern for that VT. For each VT, the difference between the longest and shortest coupling interval resulting in resetting was defined as the resetting interval. If both SVE and DVE reset a VT, the longest resetting interval obtained was considered to be the resetting interval for that VT. The excitable gap was defined as that portion of tissue within the VT circuit that was capable of a propagated response. This gap may be either fully recovered (fully excitable) or partially recovered.

Statistical analysis was performed by the t test for unpaired observations, one-way analysis of variance, the chi-square test, the Fisher’s exact text, or a linear regression analysis when appropriate. A p < .05 was considered to indicate a significant difference.

Results

Response patterns. No pattern could be identified for seven of 37 VTs, for six of these because resetting occurred over too narrow a range of coupling intervals to meet our criteria for characterizing the specific pattern and for one because of variability in the return cycle. The response pattern was flat in nine VTs (figure 3, A to C, and figure 3D), increasing in 10 VTs (figure 4, A to C, and figure 4D), and mixed (flat plus increasing) in 11 VTs. In no VT was a decreasing pattern observed.

No relationship was found when the response pattern was compared with the cycle length of VT, the incidence of termination of VT, or the local activation time at the pacing site relative to the onset of the QRS. However, a significantly longer resetting interval was found in patients with VTs having a mixed response (flat plus increasing) compared with that in those with VTs with an increasing pattern (table 2).

Resetting interval. The mean resetting interval for the entire group was 66 ± 45 msec. There was a significant although weak correlation between resetting interval and the cycle length of VT (r = .37, p = .03). The mean resetting interval considered as a percentage of cycle length was 17% (range 0 to 40%), with 23 VT (62%) having a resetting interval longer than 10% of cycle length.

Return cycle. Resetting was demonstrated in response to both SVE and DVE during 11 VTs. An excellent correlation (r = .99) was demonstrated between the shortest return cycles with resetting in response to SVE and DVE (figure 5). The mean difference in return cycle (SVE vs DVE) was 5 msec.

The return cycle, measured at the pacing site, included conduction time to and from the circuit and exceeded the cycle length in all but one VT. When the return cycle was measured to the onset of the surface QRS complex (instead of to the local electrogram at the pacing site), the return cycle was less than the cycle length in 15 VTs (41%). Among these, the cycle length exceeded the return cycle in response to resetting with the longest coupling interval by a mean of 53 msec. If conduction time to the circuit were considered

<table>
<thead>
<tr>
<th>Response pattern</th>
<th>No. VT</th>
<th>Mean ± SD VT CL (msec)</th>
<th>No. VT termin</th>
<th>Mean ± SD LAT-PS (msec)</th>
<th>Mean ± SD R interval (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flat</td>
<td>9</td>
<td>376 ± 38</td>
<td>2</td>
<td>72 ± 57</td>
<td>71 ± 35</td>
</tr>
<tr>
<td>Mixed</td>
<td>11</td>
<td>370 ± 58</td>
<td>6</td>
<td>73 ± 31</td>
<td>102 ± 34</td>
</tr>
<tr>
<td>Increasing</td>
<td>10</td>
<td>386 ± 86</td>
<td>3</td>
<td>77 ± 83</td>
<td>64 ± 40*</td>
</tr>
</tbody>
</table>

Statistical analysis was performed searching for differences among the three response patterns, as well as comparing each of them with the other two. No statistical differences, except as noted.

CL = cycle length; R = resetting; termin = terminated with SVE or DVE; LAT-PS = timing of the local electrogram at the pacing site relative to the QRS onset during VT.

*p < .035.
equal to conduction time from the circuit to the local electrogram the actual return cycle would be less than the cycle length of VT for 28 VTs (76%) by a mean of 90 msec.

Discussion

Resetting in reentrant circuits. Sustained uniform VT in the setting of chronic coronary artery disease and a previous myocardial infarction is believed to be due to reentry.1 The phenomenon of resetting was originally described for the sinus node and automatic rhythms.2, 15, 16 However, it is well known that in the best human model of reentry, circus-movement tachycardia incorporating an atrioventricular bypass tract, premature extrastimuli can result in resetting of the tachycardia.17 In the present discussion we will assume that the same mechanism, i.e., premature penetration of the circuit advancing the activation within the circuit.
The flat response pattern of this VT is coupling interval (CI) of the extrastimulus along the return cycle (RC) along the ordinate. (figure 6), is responsible for resetting in our patients with presumably reentrant VTs. This was recently shown to be the case in the dog preparation of reentrant VT.18

Significance of resetting patterns: functional properties of the excitable gap

Flat pattern. A flat resetting pattern produced during a reentrant rhythm is best explained by fixed sites of entrance to and exit from the circuit, with a gap of fully excitable tissue in the reentrant circuit. This would fix the conduction time along the reentrant pathway (figure 6). Our definition of resetting required that the QRS morphology of the first VT beat after the paced impulse(s) be identical to the QRS morphology of the VT. We believe that this suggests a fixed exit site from the VT circuit in this population. Therefore, if the conduction time along the reentrant pathway does not vary, either the entrance site and conduction velocity within the circuit must vary in a complex compensatory fashion or the entrance site is also fixed. The lack of any delay of conduction in the circuit suggests an excitable gap composed of fully recovered tissues, and the fact that flat curves are seen with DVE at longer coupling intervals than with SVE during the same VT suggests that a fixed entrance site is present as well.19

Increasing and mixed patterns. Three mechanisms could

FIGURE 4, A to C. An increasing response pattern during a delivery of double extrastimuli. The second extrastimulus fails to reset a tachycardia at a coupling interval of 295 msec (A). At a coupling interval of 270 msec resetting of the tachycardia is seen with a return cycle of 355 msec (B). As the coupling interval of the second extrastimulus is decreased to 240 msec the return cycle increases to 380 msec (C). Surface leads 1, aVF, and V1 are displayed along with an electrogram from the right ventricular apex (RVA). T = time lines.
explain an increasing response pattern or an increasing zone in a mixed response pattern (figure 7): (1) Conduction delay of the paced impulse between the pacing site and the circuit. Although this could be the case in individual instances, the virtually identical return cycles in response to SVE and DVE (figure 5) make this possibility unlikely. Since resetting with DVE is achieved with longer coupling intervals than with SVE, conduction delays to the circuit should have resulted in less delay and shorter return cycles than would be expected with DVE. (2) A variable site of entrance determined by the tail of refractoriness in the reentrant circuit (figure 7, A), or by a functional conduction block in the tissue surrounding the circuit (figure 7, B). In these cases, late coupled impulses (left-hand sides of figure 7, A and B) would enter the reentrant pathway more distally than early coupled ones (right-hand sides of figure 7, A and B). Thus, more premature impulses would have to proceed over a longer pathway within the reentrant circuit, resulting in a longer return cycle and an increasing response. (3) An excitable gap composed entirely of partially refractory tissue (figure 7, C). In this case premature stimuli would encounter increasingly refractory tissue with decreasing conduction delays and longer return cycles at shorter coupling intervals. If a zone of fully excitable tissue preceded that of partially refractory tissue, a mixed (flat plus increasing) response would ensue. The finding that resetting intervals with an increasing pattern are shorter than those with mixed patterns (table 2) is consistent with the hypothesis that excitable gaps totally composed of partially refractory tissue are likely to be shorter than those composed of fully excitable and partially refractory tissue.

**Significance of the resetting interval.** For a flat response (as shown in figure 6), the duration of the excitable gap should at least equal the range of coupling intervals of premature extrastimuli resulting in resetting, i.e., the resetting interval. The same would apply to increasing responses if, as is likely, they were due to the mechanism depicted in figure 7, C. However, the excitable gap may exceed the resetting interval since the degree of prematurity achieved by the extrastimuli is limited by local refractoriness at the pacing site or in the intervening tissue.

**Evidence for a reentrant mechanism.** Our entry criteria for this study were chosen to select patients with VT in which reentry was the likely mechanism. Since the tachycardias in our patients were reproducibly induced by PES, automaticity is an unlikely mechanism. Two
A single extrastimuli increasing partially fibers the during triggered 3).

Bypass atrioventricular fibers which the the extra-ordinary long insensitive, resulting in triggered rhythms, ectopic

In digitalis-induced VT, the return cycle exceeds the cycle length of VT. In contrast, for 41% of VTs in this study, the return cycle was less than the cycle length of VT.

These findings are readily explained on the basis of reentry. The paced impulse may penetrate the circuit at a site different than the exit site, and therefore reach the site of exit before completing a full revolution in the reentrant pathway. In such a situation, the conduction time in the circuit will be less than the cycle length of VT and the return cycle will be shorter than the cycle length of VT. It should be realized that the conduction time between pacing site and reentrant circuit always adds to the return cycle in the intact heart. Thus, the 41% incidence of a return cycle shorter than the cycle length of VT probably underestimates the true incidence of this phenomenon. If conduction time between the pacing site and the circuit was considered equal to conduction time from the circuit, then the return cycle was less than the cycle length of VT in 76% of VTs observed in this study.

Implications for the nature of the reentrant circuit. Several models of reentry have been described. That proposed by Mines suggests an anatomically defined
reentrant pathway. Allessie et al. proposed the so-called "leading circle" model in which the reentrant pathway is the shortest possible pathway, determined on an instantaneous basis by refractoriness ahead of the activation wavefront. Mehra et al. found, in a dog preparation of VT, that reentry could occur with a "figure of 8 model" around two functional areas of block. Since in the leading circle model the reentrant pathway is determined by refractoriness ahead of the activation wavefront, the excitable gap has to be composed of partially refractory tissue. The reset response curve of such a circuit would not be expected to contain a flat zone. Two-thirds of all of those VTs that could be analyzed in our study demonstrated reset response curves with at least some flat zone, therefore militating against the leading circle model as the mechanism of these VTs. This same contention is also supported by the relatively long resetting intervals observed (particularly during VT with mixed patterns; table 2), which exceeded 10% of the cycle length of VT in 62% of the VTs. We believe that this finding is also evidence against a leading circle type of reentry, in which the excitable gap is expected to be absent or of minimal duration. In contrast, in the other two models of reentry, since the circuit is determined by areas of anatomic or functional block, a fully excitable gap of significant duration is conceivable. We found a significant although weak correlation between resetting interval and the cycle length of VT. In an anatomic or defined reentrant circuit, the slower the conduction velocity, the longer the cycle length and the excitable gap (refractoriness being constant). In a leading circle model, however, the cycle length is determined only by refractoriness, and the gap is as short as possible, independent of the cycle length.

Limitations. Our analysis was limited to that of VTs that were hemodynamically tolerated. Therefore, our conclusions may only apply to this selected population of patients with relatively slow VTs, and slower tachycardias may be more likely to have longer excitable gaps.

The significance of the response pattern as an intrinsic characteristic of each VT is limited by the potential contribution of the intervening myocardium to changes in the return cycle, particularly for those VTs having an increasing response pattern. As discussed above, in the VTs in which this could be analyzed by a second mode of stimulation that eliminated the effect of intervening tissue, it did not alter the expected response pattern. However, in some of the remaining tachycardias, the role of the intervening myocardium might have been significant.

Final considerations. We suggest that the resetting pattern and interval are related to functional properties and duration of the excitable gap in the VT reentrant circuit. To the extent that this is the case, two of the identified patterns (a flat or mixed response) and the presence of a long resetting interval are evidence against a leading circle model of reentry and favor a VT circuit that is, at least in part, anatomically determined.

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