Characterization of Return Cycle Responses Predictive of Successful Pacing-Mediated Termination of Ventricular Tachycardia

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Objectives. The purpose of this study was to characterize response patterns during overdrive pacing that predict successful termination of ventricular tachycardia.

Background. Overdrive pacing during ventricular tachycardia typically results in entrainment at slow pacing rates and in termination or acceleration at faster rates. The factors that determine the critical paced cycle length that results in tachycardia termination have not been extensively studied.

Methods. Ventricular tachycardias in 14 patients with coronary artery disease were studied with overdrive pacing at several cycle lengths. Return cycles were measured after each additional paced beat at each paced cycle length. The return cycle responses during pacing trials that resulted in tachycardia termination and those that resulted in entrainment were compared.

Results. Three return cycle responses were identified: flat, plateau and increasing. Twenty trials of overdrive pacing resulted in tachycardia termination; all were characterized by an increase in the return cycle with the delivery of each successive beat in the pacing drive until the tachycardia terminated (increasing response). Thirty-four pacing trials resulted in entrainment and not termination; these were characterized either by a constant return cycle (flat response) or an initial increase in return cycle followed by a longer, constant return cycle (plateau response) with the delivery of additional paced beats. The longest paced cycle length that resulted in tachycardia termination correlated with the relative refractory period of the circuit, defined as the tachycardia cycle length minus the fully excitable gap ($r^2 = 0.764, p = 0.0001$). Tachycardia termination was not observed unless the paced cycle length was shorter than the relative refractory period of the circuit.

Conclusions. The critical paced cycle length that causes termination of ventricular tachycardia depends on the relative refractory period of the circuit because this factor determines whether the nth + 1 beat of the pacing drive will encounter partially recovered tissue. These data provide insights into the mechanism of pacing-mediated tachycardia termination and entrainment and are applicable to the development of improved antitachycardia pacing algorithms.

(J Am Coll Cardiol 1995;25:47-53)
during overdrive pacing that predict pacing-mediated ventricular tachycardia termination.

Methods

Study patients and tachycardias. Fourteen uniform, sustained ventricular tachycardias from 14 patients with chronic coronary artery disease and healed myocardial infarction were studied. Trials of overdrive pacing during each tachycardia resulted in entrainment during at least one paced cycle length and in termination during at least one different paced cycle length. All episodes of tachycardia were reproducibly inducible and hemodynamically well tolerated. There were 13 men and 1 woman in the group; they ranged in age from 55 to 72 years. The mean left ventricular ejection fraction was 31%. Previous episodes of spontaneous sustained ventricular tachycardia or aborted sudden cardiac death were documented in all patients. Four of the 14 patients were receiving no antiarrhythmic medications at the time of the study; three, two and five patients, respectively, were receiving propafenone, amiodarone and a type IA agent with or without mexiletine (Table 1). Written informed consent was obtained from all patients.

Stimulation protocol. Ventricular tachycardia was induced with our standard stimulation protocol (10). Premature stimuli were introduced during ventricular tachycardia from the right ventricular apex to assess the response to resetting and overdrive pacing (8). Resetting was performed to characterize the excitable gap (11-13), thereby allowing derivation of the relative refractory period of the circuit. This period, which we defined as the tachycardia cycle length minus the duration of the fully excitable gap, is the amount of time in each cycle that the tachycardia wave front conducts through tissue that is not fully recovered. This definition does not imply that conduction and refractoriness are uniform throughout the tachycardia circuit. Instead, the circuit relative refractory period is reached when interval-dependent conduction first occurs in the most vulnerable of the circuit's individual elements.

Overdrive pacing was performed at two to six paced cycle lengths during each tachycardia, depending on the patient's tolerance of the tachycardia and the pacing protocol. At each cycle length, paced beats were delivered in increments (i.e., 1 beat, then 2, then 3, up to 15 beats) with each successive pacing trial, as previously described (8). This protocol allowed both identification of the nth beat, defined as the first beat that influenced the tachycardia (8), and evaluation of the effect of each subsequent paced beat by measurement of the corresponding return cycle. Return cycles were measured as the interval from the pacing stimulus to the onset of the first postpacing beat in the right ventricular apex recording. Entrainment was recognized by the criteria established by Maclean (1) and Waldo (2,14) and their colleagues.

The following measurements were made during overdrive pacing at each paced cycle length: 1) the difference in the return cycle from the nth to the nth + 1 beat, 2) the total change in return cycle from the nth to the last paced beat, and 3) the slope of the relation between the return cycle and the number of paced beats delivered, determined by linear regression analysis. When overdrive pacing resulted in an initial increase in the return cycle followed by a new, longer equilibrium return cycle, the reported slope refers to the increasing portion of the relation. Examples of these measurements are schematically depicted in Figure 1.

In the event that pacing resulted in termination of ventricular tachycardia before completion of the protocol, programmed stimulation was repeated. The pacing protocols were

## Table 1. Return Cycle Responses in Individual Patients

<table>
<thead>
<tr>
<th>Pt No.</th>
<th>VT CL (ms)</th>
<th>Antiarrhythmic Agent</th>
<th>Antiventricular Pacing Cycle Length (% of VT CL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Flat</td>
</tr>
<tr>
<td>1/M</td>
<td>410</td>
<td>Quinidine</td>
<td>88, 93</td>
</tr>
<tr>
<td>2/M</td>
<td>360</td>
<td>Amiodarone</td>
<td>89</td>
</tr>
<tr>
<td>3/M</td>
<td>470</td>
<td>Propafenone</td>
<td>—</td>
</tr>
<tr>
<td>4/M</td>
<td>390</td>
<td>None</td>
<td>—</td>
</tr>
<tr>
<td>5/M</td>
<td>340</td>
<td>Procainamide</td>
<td>—</td>
</tr>
<tr>
<td>6/M</td>
<td>460</td>
<td>Propafenone</td>
<td>—</td>
</tr>
<tr>
<td>7/M</td>
<td>380</td>
<td>None</td>
<td>87</td>
</tr>
<tr>
<td>8/M</td>
<td>390</td>
<td>Propafenone</td>
<td>—</td>
</tr>
<tr>
<td>9/M</td>
<td>450</td>
<td>Quin/Mex</td>
<td>96, 91</td>
</tr>
<tr>
<td>10/M</td>
<td>370</td>
<td>Amiodarone</td>
<td>89, 87, 84, 78</td>
</tr>
<tr>
<td>11/M</td>
<td>450</td>
<td>Procainamide</td>
<td>—</td>
</tr>
<tr>
<td>12/M</td>
<td>350</td>
<td>Procainamide</td>
<td>91, 86</td>
</tr>
<tr>
<td>13/F</td>
<td>300</td>
<td>None</td>
<td>93, 86</td>
</tr>
<tr>
<td>14/M</td>
<td>260</td>
<td>None</td>
<td>—</td>
</tr>
</tbody>
</table>

Each trial of overdrive pacing is listed under the column of the return cycle pattern it produced (flat, plateau or increasing); the rate of pacing in each trial is expressed as a percent of the tachycardia cycle length in that individual patient. F = female; M = male; PCL = paced cycle length during overdrive pacing; Pt = patient; Quin/Mex = quinidine and mexiletine; VT CL = ventricular tachycardia cycle length.
Figure 1. Schematic representation of return cycle responses. The relation between the return cycle and the number of paced beats delivered in the pacing drive is displayed at several paced cycle lengths in a hypothetical example. At the first paced cycle length during overdrive pacing (PCL = X), the return cycle remains constant at 400 ms. The total return cycle increase is zero, and the slope of the return cycle response is zero. At a faster paced cycle length (PCL = X - 20 ms), the return cycle increases from beat 3 to beat 7 but then remains constant at 440 ms. The total return cycle increase is 40 ms, and the slope of the response is 10 ms/paced beat. Pacing at a faster cycle length (PCL = X - 40 ms), the tachycardia terminates (TERM) after beat 8 is delivered. The total increase in return cycle before tachycardia termination is 80 ms, and the return cycle response slope is 20 ms/paced beat.

then continued after verifying that the same tachycardia was induced (by 12-lead surface electrocardiogram), and that the cycle length had not changed (±10 ms) from previous episodes of tachycardia.

Data analysis. Results are presented as the mean value ± SD unless otherwise stated. Analysis of variance with Scheffé subgroup testing was used to compare return cycle responses between groups. The relation between the longest paced cycle length that resulted in ventricular tachycardia termination, ventricular tachycardia cycle length and the duration of the fully excitable gap was determined by using least squares linear regression. A p value < 0.05 was considered significant.

Results

Tachycardia characteristics. The mean ± SD ventricular tachycardia cycle length was 389.3 ± 50.1 ms (range 260 to 470 ms). Eight tachycardias had a right bundle branch block configuration and six had a left bundle branch block configuration. All but one tachycardia had a fully excitable gap (mean gap duration 47.9 ± 25.8 ms [range 0% to 23.8% of the tachycardia cycle length]).

Figure 2. Flat return cycle response to overdrive pacing. Figures 2 to 4 are analog recordings of the same right bundle, right inferior axis ventricular tachycardia (cycle length 450 ms) during overdrive pacing at different cycle lengths. All show surface electrocardiographic leads I, II and V1 along with an intracardiac recording from the right ventricular apex (RVA) and time lines (T). During pacing at 410 ms, the nth beat was beat 3 of the pacing drive. The nth beat resulted in a return cycle of 520 ms (A). The nth + 1 beat, or beat 4, also resulted in a return cycle of 520 ms (B). The return cycle remained constant with the delivery of additional paced beats at this cycle length, as shown after the paced beat 10 (C). The tachycardia was entrained after the delivery of the nth + 1 beat, as identified by the presence of fixed fusion and the transient acceleration of the tachycardia to the paced cycle length. S = pacing stimulus.
A paced cycle length of 370 ms, the nth beat is beat 2, which results in a return cycle of 520 ms (not shown), identical to the return cycle after the nth beat during pacing at 410 ms (Fig. 2). The return cycle increases to 530 ms with the nth + 1 beat (A); it increases to 540 ms with the delivery of beat 4 (B) and continues to increase until beat 6 results in a return cycle of 560 ms. With the addition of paced beats after beat 6, the return cycle remains constant at 560 ms, and the tachycardia is entrained, as shown after paced beat 10 (C). Format and abbreviations as in Figure 2.

Response to overdrive pacing during ventricular tachycardia. There were 54 separate trials of overdrive pacing during ventricular tachycardia. Tachycardia termination was observed in 20 trials; the remaining 34 produced entrainment without termination. The mean paced cycle length resulting in tachycardia termination was 300.5 ± 53.6 ms or 77.5 ± 4.1% (range 72.2% to 87.0%) of the tachycardia cycle length. The cycle length of trials that produced entrainment was significantly longer: 342.4 ± 55.6 ms or 86.4 ± 4.6% (range 77.8% to 95.6%) of the tachycardia cycle length. The median number of paced beats required for termination was 9 (range 3 to 15). In five patients, tachycardia termination was observed at more than one paced cycle length; the number of paced beats required for termination consistently decreased as the pacing cycle length decreased. No episodes of tachycardia acceleration occurred with this pacing method.

Return cycle response patterns—relation to tachycardia termination. Three types of return response patterns were observed with the delivery of an incremental number of paced beats at a given paced cycle length (Table 1). In the flat response (Fig. 2), there was no change in the return cycle from the nth beat, the first beat that influences the tachycardia, to the nth + 1 beat (<10 ms difference). This relation predicted further stability in the return cycle and entrainment rather than termination with the delivery of additional paced beats at that cycle length. A flat response was observed in 14 trials of overdrive pacing at a mean cycle length of 87.7 ± 4.4% (range 78.4% to 95.6%) of the tachycardia cycle length.

In the plateau response (Fig. 3), the return cycle increased from the nth to the nth + 1 beat (≥10 ms) and continued to increase until a new, longer equilibrium return cycle was achieved. The slope of the return cycle response, determined by the increasing portion of the relation, was initially positive but changed abruptly and became flat with additional beats. At this point, the criteria for entrainment were met and the return cycle remained stable; the tachycardia did not terminate with the delivery of additional beats (up to 15) at that paced cycle length. A plateau response was seen in 20 trials at a mean paced cycle length of 85.5 ± 4.6% (range 77.8% to 93.6%) of the tachycardia cycle length (p = NS vs. the flat response). The equilibrium return cycle was established after a range of 4 to 14 beats (median 7) in the pacing trials that resulted in a plateau response.

In all 20 trials of overdrive pacing that resulted in tachycardia termination, an increasing response was observed (Fig. 4). After an initial increase in the return cycle from the nth to the nth + 1 beat, the return cycle continued to increase with the delivery of each successive beat in the pacing drive until the tachycardia terminated. The mean paced cycle length of the 20 trials in this group was 77.5 ± 4.1% (range 72.2% to 87.0%) of the tachycardia cycle length (p < 0.05 vs. both the flat and the plateau response).

Quantitative comparison of return cycle response groups. In addition to the change in return cycle response from the nth to the nth + 1 beat, two other quantitative measurements of the return cycle response differed significantly among groups (Table 2). The total increase in return cycle in the groups with a flat, plateau and increasing response was 11.8 ± 11.9, 64.3 ± 46.6 and 65.0 ± 37.4 ms, respectively (flat vs. plateau and increasing responses, p < 0.05; plateau vs. increasing response, p = NS). The slope of the return cycle response was 1.2 ± 1.2, 11.4 ± 10.6 and 15.6 ± 12.6 ms/paced beat in the three groups, respectively (flat vs. plateau and increasing responses, p < 0.05; plateau vs. increasing response, p = NS). However, in the nine tachycardias that exhibited both plateau and increasing responses at different paced cycle lengths, the slope of the
Table 2. Quantitative Comparison of Return Cycle Responses

<table>
<thead>
<tr>
<th>Return Cycle Response</th>
<th>Flat</th>
<th>Plateau</th>
<th>Increasing</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCL (% of VT cycle length)</td>
<td>87.7 ± 4.4</td>
<td>85.5 ± 4.6</td>
<td>77.5 ± 4.1*</td>
</tr>
<tr>
<td>Change in RC, n to n + 1 (ms)</td>
<td>0.0 ± 0.0</td>
<td>24.5 ± 18.8</td>
<td>32.1 ± 18.5*</td>
</tr>
<tr>
<td>Total RC increase (ms)</td>
<td>11.8 ± 11.9</td>
<td>64.2 ± 46.6</td>
<td>65.0 ± 37.44</td>
</tr>
<tr>
<td>RC response slope (ms/beat)</td>
<td>1.2 ± 1.2</td>
<td>11.4 ± 10.6</td>
<td>15.6 ± 12.6</td>
</tr>
</tbody>
</table>

*p < 0.05, flat and plateau responses versus increasing response; p = NS flat versus plateau response. 1p < 0.05, flat versus plateau and increasing responses; p = NS plateau versus increasing response. Data presented are mean value ± SD. PCL = paced cycle length during overdrive pacing trials; RC = return cycle.

Discussion

We believe that this is the first study to characterize the return cycle patterns during overdrive pacing that predict successful ventricular tachycardia termination. The method of overdrive pacing using an incremental number of paced beats evaluates the effect of each individual beat in the drive (8). This protocol allowed the demonstration of several relations that were not apparent in previous studies of overdrive pacing (1-6,14-16), which typically measured a single return cycle after a fixed duration of pacing at each cycle length.

Increase in return cycle from the nth to the nth + 1 beat—relation to return cycle response with subsequent paced beats. An increase in the return cycle (≥10 ms) from the nth to the nth + 1 beat predicted progressive increase in the return cycle with the delivery of subsequent paced beats until either a longer equilibrium return cycle was achieved (plateau response) or the tachycardia terminated in response to pacing. Conversely, if the return cycle did not increase from the nth to the nth + 1 beat, the return cycle remained constant and termination of the tachycardia did not occur with the delivery of additional paced beats (up to 15) at that cycle length. The slope of the return cycle response was greater during pacing trials that resulted in tachycardia termination than in those that resulted in a plateau response (p = NS, probably because of inadequate sample size). The plateau response was easily identified by a sudden change in the return cycle response slope from increasing to flat. Once the return cycle stopped increasing with each additional paced beat, the tachycardia was entrained and further pacing did not result in additional return cycle increase or tachycardia termination.

Relation of the relative refractory period of the circuit, paced cycle length and response to overdrive pacing. Termination of ventricular tachycardia occurred only when the paced cycle length was less than or equal to the relative refractory period of the circuit.
period of the circuit (Fig. 5). Stated in another way, when the paced cycle length is significantly longer than the relative refractory period of the circuit, paced beats will continually encounter fully excitable tissue and pacing will not result in termination. When the paced cycle length is sufficiently rapid to encroach on the relative refractory period of the circuit, pacing will cause progressive conduction delay within the circuit, resulting in ventricular tachycardia termination with the delivery of additional paced beats. This observation is analogous to the findings of Gottlieb et al. (9), who demonstrated that tachycardias that terminate in response to a single extrastimulus interacting with the circuit have a steeper resetting response slope than do those that do not terminate. It is not clear from either their study or ours whether the site or sites of conduction slowing and eventual orthodromic block are identical. Detailed multisite mapping studies would be required to answer this issue.

Clinical implications. This method of overdrive pacing using an incremental number of paced beats may have practical application in the development of antitachycardia pacing algorithms. After delivery of the nth beat, if the return cycle ever fails to increase with the delivery of each successive paced beat, further pacing at that cycle length is unlikely to terminate the tachycardia. Return cycle response patterns could be used by antitachycardia devices to predict the success of paced cycle lengths and to minimize the time spent on unsuccessful attempts. There were no episodes of pacing-mediated tachycardia acceleration in our small series. Previous studies (17-21) describing the use of burst or autodecremental burst pacing have noted a significant incidence of acceleration, particularly during rapid tachycardias, ranging from 4% to 35%. Our study was not designed to test the efficacy of this method for antitachycardia pacing or to compare it with other pacing algorithms.

Limitations of the study. All episodes of ventricular tachycardia evaluated in this study were hemodynamically well tolerated; however, many of the studies were performed only after patients were receiving antiarrhythmic medications for treatment of tachycardias that were not well tolerated in the baseline state. This was obviously less optimal than conducting all studies in the drug-free state, especially in light of the known effects of antiarrhythmic agents on conduction within the circuit (22-24). Although we did not identify any confounding effects introduced by inclusion of patients using any specific drug, such effects may exist; in addition, our data may not apply to more rapid ventricular tachycardias than those we studied.

Pacing and recording were performed in this study at the right ventricular apex rather than at the site of tachycardia origin. Although the intervening tissue between the pacing and recording site and the tachycardia circuit could conceivably introduce confounding effects, such effects may have not been observed in previous studies of resetting and overdrive pacing (8,11-13). In addition, use of the right ventricular apex for pacing and recording is more pertinent if this technique is to be adapted for antitachycardia devices.

Conclusions. The critical paced cycle length that results in tachycardia termination during overdrive pacing is directly related to the relative refractory period of the circuit, that is, the ventricular tachycardia cycle length minus the duration of the fully excitable gap. When the paced cycle length is significantly longer than the circuit relative refractory period, the tachycardia will be entrained. When it is significantly shorter, overdrive pacing will eventually result in termination of the tachycardia. The return cycle response pattern, and particularly the change in return cycle from the nth to the nth + 1 beat, is predictive of the effects of additional paced beats at the same cycle length. An increase in return cycle from the nth to the nth + 1 beat was always associated with progressive increases in the return cycle with the delivery of additional paced beats until either a longer equilibrium return cycle was achieved or the tachycardia terminated in response to pacing. These data provide important information about the mecha-

Figure 5. Relations among the relative refractory period of the circuit (Circuit RRP), pacing cycle length (CL) and return cycle response. The difference between the circuit relative refractory period and the paced cycle length for each trial of overdrive pacing (y axis) is plotted against the resultant return cycle response (x axis). This difference was significant in trials that resulted in flat, plateau and increasing return cycle responses (-10.7 ± 22.0, 12.0 ± 25.5 and 40.0 ± 23.4 ms, respectively; p < 0.05 for flat vs. plateau response, flat vs. increasing response and plateau vs. increasing response). Pacing resulted in tachycardia termination only when the paced cycle length was less than or equal to the relative refractory period of the circuit (circuit relative refractory period - paced cycle length >0). Mean values ± SD are shown to the right of each data set.
nism of entrainment and pacing-mediated termination of ventricular tachycardia. In addition, this technique may have practical implications for the development of improved anti-tachycardia pacing algorithms.

References