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Randomized Controlled Comparison of Antitachycardia Pacing Algorithms for Termination of Ventricular Tachycardia

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Objectives. **This study compared the efficacy and safety of two antitachycardia pacing algorithms in the treatment of ventricular tachycardia.**

Background. **There is agreement that antitachycardia pacing should be adapted to tachycardia rate and be delivered in a burst, but the ideal pacing pattern is not well understood. Effective antitachycardia pacing burst patterns include those with a between-burst decrement (SCAN) with or without an additional within-burst decrement (RAMP).**

Methods. **Prospective randomized crossover comparison of two antitachycardia pacing algorithms (RAMP vs. SCAN) on identical induced sustained ventricular tachycardias was performed.**

Results. **Sixty-five ventricular tachycardias (mean cycle length 364 ± 74 ms) from 37 invasive studies performed in 29 patients were studied; 86% of patients had coronary artery disease and 72% were receiving antiarrhythmic therapy at the time of study. Of the 65 tachycardias, 40 were identical pairs and 25 were unpaired (including 8 with a >30-ms difference in cycle length of induced ventricular tachycardia pairs). In the paired pacing trials, conversion to sinus rhythm occurred, respectively, in 85% of SCAN versus 90% of RAMP protocols ($p = 0.63$, power = 93%) and within 1.4 ± 0.7 versus 1.7 ± 1.1 attempts ($p = 0.41$). Discordance for pacing success was seen in three pairs. In unpaired trials, conversion to sinus rhythm occurred in 73% and 57%, respectively ($p = 0.68$, power = 88%). Tachycardia acceleration during pacing occurred in 7 (11%) of 65 attempts (5 SCAN, 2 RAMP). Acceleration in unpaired ventricular tachycardia trials was correlated with tachycardia cycle length. Failure to convert ventricular tachycardia was associated with a shorter tachycardia cycle length ($p < 0.05$).**

Conclusions. **In the patients studied, adaptive antitachycardia pacing was safe and effective and, when successful, occurred within three attempts of an 8-beat adaptive burst algorithm. Changes in burst pattern did not affect pacing safety or efficacy. Antitachycardia pacing success was dependent on induced ventricular tachycardia cycle length.**

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It has long been known that overdrive ventricular pacing is often effective in terminating sustained ventricular tachycardia (1). Newer investigational implanted antitachycardia devices (2,3) are capable of both antitachycardia pacing and shock delivery for the treatment of ventricular arrhythmias. The goal of therapy with such systems is the prevention of shock delivery whenever feasible by means of a safe and effective antitachycardia pacing algorithm. Such an algorithm would limit patient discomfort, permit enhanced battery longevity and allow more rapid conversion to normal rhythm with possibly fewer symptoms during tachycardia episodes (4). Although pacing is effective, the possibility of inadvertent pacing-induced acceleration to ventricular fibrillation or failure of pacing termination requires backup defibrillatory capabilities in any implanted automatically activated antitachycardia device.

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The optimal use of implanted antitachycardia devices requires an understanding of the relative safety and efficacy of various modes of antitachycardia pacing. Despite general agreement that the rate of such pacing should be adapted to the prevailing tachycardia rate and be delivered in bursts (5), the optimal antitachycardia pacing algorithm among the many available is not known. The rate of bursts of adaptive antitachycardia pacing can be kept constant both within and between bursts or may change either within a burst or between bursts, or both. Few studies have compared different algorithms in a controlled manner (6) and the best pacing prescription for successful antitachycardia pacing has not been defined. In this report, the sequence of two different antitachycardia pacing algorithms was randomly selected and each algorithm was applied to the same morphologic ventricular tachycardia in the same patient in a crossover fashion. The key end points to this study were efficacy and safety of antitachycardia pacing.

Methods

The two methods of antitachycardia pacing compared were an adaptive burst with an interburst decrement (SCAN)

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and one that also had a decrement within each burst of antitachycardia pacing (RAMP).

Patients with recurrent sustained ventricular tachycardia or fibrillation referred for clinical electrophysiologic study at our institution from February 1991 to February 1992 were eligible for study. Any antitachycardia pacing that was clinically required during the invasive study was initially delivered according to the study protocol. This study was approved by the institution's Human Subjects Review Committee.

The electrophysiologic study was performed in a conventional fashion, with multipolar electrodes positioned in the right ventricle for recording and stimulating. Patients were randomly assigned to receive one of the antitachycardia pacing algorithms and induction of ventricular tachycardia was attempted. Eligibility for this study required induction of sustained monomorphic ventricular tachycardia that did not require prompt cardioversion and for which antitachycardia pacing could be used. After termination of ventricular tachycardia, the arrhythmia was reinduced and the alternative antitachycardia pacing algorithm delivered. To be eligible for the main study end point, tachycardia pairs had to be of identical morphology and within 30 ms in cycle length. Those tachycardias that on reinduction were of different cycle length and morphology, patients in whom any tachycardia could not be reinitiated after first tachycardia termination and those who required cardioversion after the first tachycardia induction were analyzed separately as unpaired tachycardias; that is, in that group only one type of antitachycardia pacing algorithm was delivered per tachycardia.

Antitachycardia pacing algorithms. All antitachycardia pacing was delivered through a customized investigational antitachycardia device (Telectronics model 4211). Once stable ventricular tachycardia was initiated, the device was activated and therapy delivered. If ventricular tachycardia was still present after five pacing attempts, the alternative therapy was delivered. The order of therapies was reversed at the second ventricular tachycardia induction. If direct current shock was required at any point, the study was stopped. Throughout the study, the minimal tachycardia cycle length for which antitachycardia pacing could be delivered was set at 250 ms and the minimal pacing interval was set at 240 ms. The therapies used were as follows.

RAMP protocol (Fig. 1A). This consisted of an 8-beat burst with the first beat to beat interval of the first attempt adapted to 90% of the tachycardia cycle length. Within the 8 beats of the burst, there was a 3% decrement between each of the successive intervals from the beginning to the end of the burst. The interval from the last tachycardia beat to the first paced beat and from the first paced beat to the subsequent paced beat interval was progressively decreased in 5% steps from 90% to 75% of the tachycardia cycle length for the first four attempts, after which the first sequence was repeated.

SCAN protocol (Fig. 1B). This method also used an 8-beat antitachycardia pacing drive with the first beat to beat interval initially at 90% of the tachycardia cycle length but with a constant interbeat interval throughout the burst. As for the RAMP algorithm, the first beat to beat interval for the first four attempts was progressively decreased from 90% to 75% of the tachycardia cycle length, after which the first sequence was repeated.

A pacing success was prospectively defined as termination of the ventricular tachycardia on the cessation of the antitachycardia pacing pulse train delivery or spontaneous termination within 5 beats after pacing was delivered. Antitachycardia pacing-induced tachycardia acceleration was defined as a decrease in ventricular tachycardia cycle length by >50 ms after a pacing attempt. Safety of antitachycardia pacing was prospectively defined as absence of either pacing-induced tachycardia acceleration or degeneration into ventricular fibrillation. Ineffective antitachycardia pacing was defined as persistence of induced tachycardia after all five pacing attempts of the given algorithm had been delivered.

Statistical analysis. The goal of this study was to assess two forms of adaptive antitachycardia pacing on ventricular tachycardia induced at the time of invasive study. The study end points were therefore assessed per ventricular tachycardia induced. The Student t test was used to compare means between groups. The McNemar test was used to compare differences in the proportion of successful therapy between identical ventricular tachycardia pairs. The Fisher exact test was used to compare differences in the proportion of successful therapy between nonidentical groups. Where results were not significant, the beta error and statistical power ($1 - \beta$) were calculated. This was defined as the certainty with which one can exclude the presence of a significant difference (at $\alpha = 0.05$) given the differences observed and the number of patients studied. Unless otherwise indicated, all data are presented as mean value ± SD.

Results

In the time period of this study, 139 invasive studies for ventricular arrhythmias were performed in 104 patients. Eighty-three (60%) of these studies were not amenable to antitachycardia pacing therapy because of rapid or polymorphic ventricular tachycardia, ventricular fibrillation or noninducible ventricular tachycardia. Of the remaining 57 studies, 37 were included in this study and 20 were excluded for technical reasons (protocol violation in 5, equipment malfunction or absence in 15). A total of 65 ventricular tachycardias were available for analysis from those 37 separate invasive electrophysiologic studies carried out in 29 patients. Mean rest nuclear left ventricular ejection fraction was 29 ± 11%; the mean age of the patients was 62.5 ± 12.5 years. Twenty-five patients had coronary artery disease as their underlying condition; of the remaining four, three had dilated cardiomyopathy and one had mitral valve prolapse.

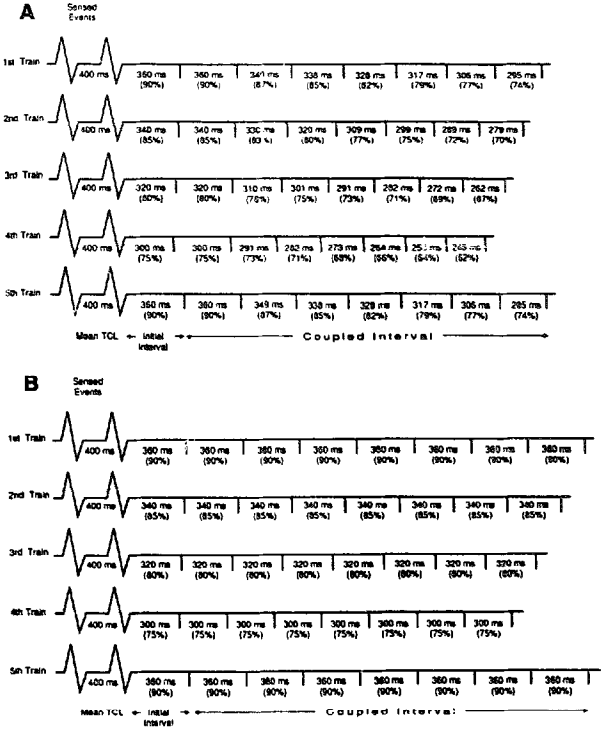

Figure 1. Diagram of pacing intervals that would be delivered for a tachycardia at a cycle length of 400 ms in either antitachycardia pacing mode. In both, 8 pulses of antitachycardia pacing were delivered. All antitachycardia pacing was adapted to the tachycardia cycle length (TCL) with both the first initial interval and the second first coupled interval starting at 90% of tachycardia cycle length. The minimal pacing interval for antitachycardia pacing attempts was 240 ms. In both cases, up to five antitachycardia pacing attempts were performed, with the fifth train being the same as the first train. **A**, The RAMP mode, with a decrement within each burst. Each successive beat of the 8-beat train decreased by 3% of the initial antitachycardia pacing interval. **B**, The SCAN mode in which all tachycardia intervals within a burst were identical but, as in the RAMP mode, the initial interval between successive bursts decreased from 90% to 75% of the tachycardia cycle length.

Mean ventricular tachycardia cycle length was 364 ± 74 ms (164 ± 8 beats/min) among all study patients; 72% of patients were receiving antiarrhythmic therapy at the time of study.

Paired ventricular tachycardias (Fig. 2A). Among the 65 tachycardias available for study, 20 pairs (40 ventricular tachycardias) met the primary study entry criteria with identical and reproducibly initiated ventricular tachycardia cycle length and morphology. These 20 ventricular tachycardia pairs were induced in 20 different patients. Among these 20 patients, 5 (included in the unpaired ventricular tachycardia group) had a different ventricular tachycardia induced that either was not reproducible or was unstable at a previous ventricular tachycardia induction trial and 13 were

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taking antiarrhythmic medications at the time ventricular tachycardia was initiated. All but one of these medication regimens comprised a combination of type IA and type III antiarrhythmic medications. The mean ventricular tachycardia cycle length in this group was 388 ± 74 ms. The ventricular tachycardia was terminated in 18 of 20 attempts with RAMP and in 17 of 20 attempts with SCAN ($p = 0.63$). The statistical power of the comparison was 93% at $\alpha = 0.05$.

Results were discordant in three pairs. In two of these pairs, success occurred with RAMP only but not with SCAN, and in one pair success occurred with SCAN only but not with RAMP. In the one RAMP antitachycardia pacing attempt that failed, the secondary SCAN method was successful on the first attempt. In the two SCAN attempts that failed, the secondary RAMP method was successful on the third attempt in one and required manual pacing conversion in the second.

Among the successful RAMP procedures, ventricular tachycardia termination required 1.7 ± 1.1 attempts compared with 1.4 ± 0.7 with the SCAN antitachycardia pacing algorithm ($p = 0.41$). There were no episodes of tachycardia acceleration among the paired ventricular tachycardias as defined prospectively. One ventricular tachycardia was not successfully terminated after five attempts of pacing termination with either RAMP or SCAN. The ventricular tachycardia cycle length was 370 ms (162 beats/min) in a patient being treated with a combination of sotalol and quinidine. Ventricular tachycardia was terminated with direct current cardioversion.

Inductions of unpaired ventricular tachycardias (Fig. 2B). Twenty-five ventricular tachycardias in 17 studies from 13 patients could not be studied as identical pairs and were treated with either the RAMP or SCAN antitachycardia pacing protocol. All but two of these studies were conducted with the patient taking no antiarrhythmic medications. Among the 17 studies, 8 ventricular tachycardia pairs (16 tachycardias) were >30-ms different in cycle length in 8 studies, 2 ventricular tachycardias could not be reinitiated in 2 studies and 2 ventricular tachycardias accelerated during an antitachycardia pacing algorithm requiring direct current cardioversion in 7 studies. Multiple inductions of different cycle length ventricular tachycardia were induced in five patients in this group, who demonstrated 13 ventricular tachycardias over nine invasive studies. In the remaining eight patients, 12 ventricular tachycardias were induced in eight invasive studies.

Among these 25 ventricular tachycardias, 11 were treated with RAMP, with success occurring in eight attempts. Successful conversion required 1.4 ± 0.7 attempts. Among the three RAMP failures, two ventricular tachycardias accelerated and one tachycardia was manually terminated.

Among the 14 of the 25 unpaired ventricular tachycardias treated with the SCAN mode, treatment was successful in 8 ($p = 0.68$ compared with RAMP). The statistical power of the comparison was 88% at $\alpha = 0.05$. Acceleration occurred in 7 of 25 unpaired tachycardias during antitachycardia pacing attempts (2 RAMP, 5 SCAN $p = 0.41$), 1 of which was accompanied by pacing termination.

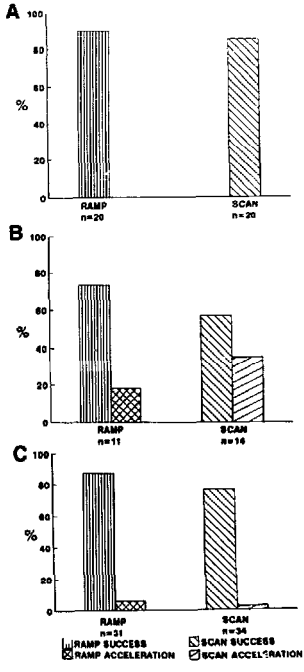

Figure 2. Results of antitachycardia pacing. **A,** Among the 20 paired ventricular tachycardias, no acceleration was seen with either mode; RAMP and SCAN success occurred in 90% and 85%, respectively ($p = 0.63$, power = 93%). **B,** Of the 25 unpaired ventricular tachycardias, 11 were terminated using the RAMP protocol (success rate 73%), with tachycardia acceleration in 18%. Fourteen tachycardias were studied with the SCAN protocol, with a 57% success and a 36% acceleration rate ($p = 0.68$ RAMP vs. SCAN success, power = 88%, $p = 0.41$ for acceleration in RAMP vs. SCAN). **C,** In all ventricular tachycardias studied, 31 were assessed with the RAMP protocol (success rate 84%) with acceleration in 6%, and 34 were studied with the SCAN protocol (success rate 75%) with acceleration in 15% ($p = 0.31$ RAMP vs. SCAN success, power = 81%, $p = 0.43$ for acceleration in RAMP vs. SCAN). See text for discussion.

Among all 65 ventricular tachycardia episodes available for analysis, pacing termination occurred in 37 (78%) and tachycardia acceleration occurred in 7 (11%) (Fig. 2C). Mean

tachycardia cycle length of pacing terminated ventricular tachycardia was 378 ± 69 ms compared with 324 ± 58 among those not terminated by pacing ($p = 0.035$). With one exception, the faster tachycardias that were not terminated by pacing were also those in which pacing induced acceleration. There was no difference in ejection fraction between patients with tachycardias that were or were not terminated by pacing.

Discussion

The chief finding of this study is that two different algorithms for pacing termination of induced ventricular tachycardia have similar efficacy and safety.

Prior studies. The choice of optimal antitachycardia pacing algorithms has had limited study in a prospective controlled fashion. In supraventricular tachycardias, it has been suggested that an antiiachycardia pacing algorithm that consists of scanning without an intraburst decrement is superior to one that has this decrement (7). In ventricular tachycardia, one study (6) found a within-burst adaptive decrement to be superior to one with a fixed burst adapted to cycle length at the initial attempt and then repeated. Other studies (8,9) of nonidentical ventricular tachycardias found no difference in efficacy between two adaptive protocols with or without an intraburst decrement.

The efficacy of antitachycardia pacing has traditionally been explained by its effect on the reentrant circuit that supports most ventricular tachycardias. Pacing termination is presumed to occur whenever a critical component of the reentrant circuit is made refractory to successive depolarization by the propagating tachycardia wave front (10). Changes in tachycardia cycle length may occur during the rhythm episode (11); therefore, antitachycardia pacing that is adapted to the sensed tachycardia cycle length is thought to be superior to pacing modes with predetermined and fixed coupling intervals or cycle length. The principle that the excitable gap for termination of a tachycardia may change has led to the advocacy of progressively longer trains of paced beats with a within-burst decrement (12). However, once trains of extrastimuli are adapted to the prevailing cycle length, there is no clear evidence for the superiority of one type of antitachycardia pacing burst to another, and we observed no significant difference between the two algorithms examined in this study.

Present study. Adapted antitachycardia pacing can vary in burst duration and pattern. In this study, we compared only the latter and chose an 8-beat burst duration. Although this produced a safe and effective antitachycardia pacing algorithm, the optimal duration of the drive train is not known. Longer bursts may be related to pacing-induced acceleration, especially if coexisting with an intraburst decrement (13). The optimal rate of bursts relative to ventricular tachycardia cycle length has not been extensively investigated. Our results suggest that antitachycardia pacing is usually effective at 80% to 90% of tachycardia cycle length. In view of the theoretic risk that faster pacing increases the risk of acceleration, limiting the pacing rate to 75% of ventricular tachycardia cycle length seems an acceptable compromise between efficacy and safety.

Although the cycle length of induced ventricular tachycardia was strongly correlated with a successful antitachycardia pacing outcome, there was a considerable overlap between cycle lengths of successful and unsuccessful antitachycardia pacing. Our findings underscore the requirement that antitachycardia pacing must always be performed with backup defibrillatory capabilities. Pacing-induced tachycardia acceleration occurred in 11% of all antitachycardia pacing attempts, always in faster tachycardias. Because antitachycardia pacing efficacy is cycle length dependent, our study tended to focus on ventricular tachycardias with generally slower cycle lengths induced during medical therapy. Our results suggest that antiarrhythmic drugs may be useful adjuncts to treatment with antitachycardia pacing devices, decreasing the need for shock delivery.

Our results also suggest that antitachycardia pacing efficacy is not dependent on burst pattern and may be a statistical probability function related most critically to tachycardia rate. The importance of tachycardia rate in establishing effective antitachycardia pacing has been noted previously (14,15). In this study, effective antitachycardia pacing occurred within three attempts in all cases. These results imply that if rapid establishment of normal rhythm is not achieved within a few attempts of delivery of any adaptive antitachycardia pacing algorithm, prompt progression to alternative therapy should be considered.

Study limitations. This study was a short-term study in sedated patients. Such studies may not predict long-term efficacy of any type of antitachycardia pacing (16,17). An attempt was made to obviate some of the factors that can affect ventricular tachycardia and its termination by examining identical rate and morphologic tachycardias in a prospective fashion. Nonetheless, 25 of 65 episodes of ventricular tachycardia could not be assessed as identical pairs. However, the results in this group were the same as those in the matched pairs, except for a lower success rate that was associated with faster ventricular tachycardia rates in unpaired tachycardias. The study was limited by design to patients with organized and reasonably well tolerated ventricular tachycardia. Although this allows a direct comparison between two different antitachycardia pacing methods, our design may limit the ability to generalize our results to all patients with ventricular tachycardia. All cases of pacing-induced tachycardia acceleration and most failures of antitachycardia pacing occurred in patients in the unpaired ventricular tachycardia group, who generally were not taking antiarrhythmic drugs and tended to have faster ventricular tachycardias than those of patients in the paired ventricular tachycardia group. Overall, 72% of induced ventricular tachycardias occurred in patients taking antiarrhythmic medications. Although this finding may limit the utility of our results, it may indicate the type of patients who

may be candidates for antitachycardia pacing as part of a tiered approach to device therapy. In one study (4), 35% of patients receiving an investigational tiered system were on antiarrhythmic medication that presumably slowed ventricular tachycardia or allowed antitachycardia pacing to occur. In that study, use of antitachycardia pacing allowed a decrease in the requirement for shock delivery.

Conclusions. When antitachycardia pacing was delivered in an adaptive fashion to detected tachycardia cycle length, antitachycardia pacing was effective in 78% of induced ventricular tachycardias. Successful antitachycardia pacing was determined by the induced tachycardia cycle length and was not influenced by whether the antitachycardia pacing bursts had a decrement within each burst.

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