Shock Reduction Using Antitachycardia Pacing for Spontaneous Rapid Ventricular Tachycardia in Patients With Coronary Artery Disease

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Background—Implantable cardioverter-defibrillators (ICDs) can terminate some ventricular tachycardias (VTs) painlessly with antitachycardia pacing (ATP). ATP has not routinely been applied for VT >188 bpm because of concerns about efficacy, risk of acceleration, and delay of definitive shock therapy. This prospective, multicenter study evaluated the efficacy of empirical ATP to terminate fast VT (FVT; >188 bpm).

Methods and Results—Two hundred twenty coronary artery disease patients received ICDs for standard indications. Empirical, standardized therapy was programmed so that all FVT episodes (average cycle length [CL] 240 to 320 ms, 250 to 188 bpm) were treated with 2 ATP sequences (8-pulse burst pacing train at 88% of the FVT CL) before shock delivery. A total of 1100 episodes of spontaneous ventricular tachyarrhythmias occurred during a mean of 6.9±3.6 months of follow-up. Fifty-seven percent were classified as slow VT (CL≥320 ms), 40% as FVT (240 ms<CL<320 ms), and 3% as ventricular fibrillation (CL<240 ms). A total of 446 FVT episodes, mean CL=301±24 ms, occurred in 52 patients (median 2 episodes per patient). ATP terminated 396 FVT episodes (89%), with an adjusted efficacy of 77% (95% CI 68% to 83%). VT acceleration caused by ATP occurred in 10 FVT episodes (4%). FVT arrhythmic syncope occurred on 9 occasions (2%) in 4 patients.

Conclusions—FVT (CL<320 ms) is common in ICD patients. ATP can terminate 3 of 4 of these episodes with a low incidence of acceleration and syncope. ATP for FVT may safely reduce the morbidity of painful shocks. (Circulation. 2001;104:796-801.)

Key Words: tachycardia • cardioversion • defibrillation • pacing

Implantable cardioverter-defibrillators (ICDs) can be programmed to deliver tiered therapy for spontaneous ventricular tachyarrhythmias. Conventionally, slower, hemodynamically stable ventricular tachycardias (VT) are treated with antitachycardia pacing (ATP) and low-energy cardioversion, whereas faster, hemodynamically unstable VT and ventricular fibrillation (VF) are treated with immediate high-energy shock.1 Cardioversion shocks are very effective in terminating slow and fast VT (FVT) but are painful and impose considerable battery drain, whereas ATP is painless and has negligible battery drain. ATP has been shown to be effective in terminating 90% to 96% of episodes of spontaneous VT with cycle length (CL) >300 ms.2–8 Many episodes labeled as VF by ICDs actually are rapid monomorphic VT.9,10 Although evidence exists that ATP can effectively terminate some of these faster VTs,2,3,5,8 these arrhythmias are usually treated with shocks because of concerns about efficacy, risk of acceleration, and syncope due to delay of definitive shock therapy. The objective of this study was to determine whether spontaneous FVT (CL 240 to 320 ms, 188 to 250 bpm) in patients with coronary artery disease (CAD) can be reliably and safely terminated by ATP, thus reducing painful shocks.

Methods

Patient Selection

Two hundred twenty patients with CAD and standard indications for ICD therapy were enrolled at 25 centers from April 1998 through November 1999. All patients underwent implantation of pectoral ICD systems with a transvenous endocardial lead positioned at the right ventricular apex.

On hospital discharge, patients were given a diary in which they were instructed to list the time and date of symptoms possibly related to spontaneous ventricular arrhythmia, such as near-syncope or syncope. Each patient was followed up for 6 to 12 months, with clinic visits, diary submission, and ICD interrogation every 3

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months. Stored device data regarding spontaneous detections and therapies were retrieved and transferred to a central database for evaluation. Syncope was defined as complete loss of consciousness with loss of postural tone, and near-syncpe was defined as dizziness or lightheadedness.

An independent data and safety monitoring board composed of nonparticipating physicians regularly reviewed all adverse events, including deaths.

**Device Description and Programming**

All patients had Medtronic ICD systems capable of delivering ATP for FVT within the VF detection zone (MicroJewel model 7221, MicroJewel II model 7223, Gem VR model 7227, Gem DR model 7271, Gem II VR model 7229, and Gem II DR model 7273).

FVT detection and initial therapy programming were standardized. Detection in the VF zone required 12 of the last 16 R-R intervals with CL < 320 ms. An FVT detection zone was defined within the VF zone (FVT via VF) for CL 240 to 320 ms. VF zone detections in which ≥1 of the previous 8 R-R intervals were < 240 ms were classified as VF and treated with immediate high-voltage shock. The first therapy in the FVT zone was 2 ATP sequences (8-pulse burst pacing train at 88% of the FVT CL). If the first ATP sequence was unsuccessful, the second sequence was delivered at 88% of the FVT CL minus 10 ms. ATP therapies were delivered at maximum voltage and pulse duration (8 V/1.6 ms). Programming of subsequent FVT therapies was left to the investigators’ discretion and usually involved shocks. All devices were programmed to store far-field electrograms before the onset of detected episodes to aid in rhythm classification. Investigators were allowed to modify FVT therapy programming after 1 recorded episode of spontaneous FVT. A slow VT zone was not requisite for study participation. If the investigator elected to program a slow VT zone, however, the first therapy was programmed identically to that of the FVT zone.

**Rhythm Classification and Definitions**

All stored far-field electrograms from spontaneous episodes were classified by predetermined criteria based on visual inspection and comparison with sinus rhythm far-field electrograms. Two additional blinded reviewers evaluated spontaneous episodes classified as supraventricular tachycardia. When the 3 reviewers did not agree, the implanting investigator was consulted for additional clinical data. The majority rule was applied to eliminate supraventricular tachycardias from further analysis. Ventricular tachyarrhythmias were then analyzed by their device classification (VF, FVT, or VT). When the number of episodes exceeded the electrogram storage capability of the device, episodes without an accompanying electrogram were analyzed on the basis of device classification without further screening.

Acceleration was defined as > 10% decrease in CL, with the device reporting CL as the mean of the last 4 intervals preceding detection. Episode duration was also defined according to the device and included time after therapy until the episode termination criterion was met. Therapy was deemed successful when the posttherapy rhythm was not a ventricular tachyarrhythmia.

**Data Analysis**

Data were analyzed on an intention-to-treat basis. ATP therapy was deemed successful if confirmed FVT was terminated by the first- or second-burst ATP sequence. CIs were calculated by use of the exact binomial distribution for percentages applied to the patients’ first episodes. To adjust for multiple episodes per patient, the generalized estimating equation was used.11,12 Mortality rate was determined by Kaplan-Meier estimation. Statistical analyses were performed by use of SAS version 6.12.

**Results**

**Patient Characteristics**

Baseline clinical and demographic characteristics of the study population are shown in Table 1.

<table>
<thead>
<tr>
<th>TABLE 1. Patient Characteristics (N=220 Patients)</th>
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<tbody>
<tr>
<td>Age, y</td>
</tr>
<tr>
<td>Male sex</td>
</tr>
<tr>
<td>LVEF</td>
</tr>
<tr>
<td>Cardiovascular medical history</td>
</tr>
<tr>
<td>CAD (required)</td>
</tr>
<tr>
<td>With MI</td>
</tr>
<tr>
<td>Without MI</td>
</tr>
<tr>
<td>Hypertension</td>
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<tr>
<td>NYHA functional class</td>
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<tr>
<td>I</td>
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<tr>
<td>II</td>
</tr>
<tr>
<td>III</td>
</tr>
<tr>
<td>IV</td>
</tr>
<tr>
<td>Unknown</td>
</tr>
<tr>
<td>Spontaneous ventricular arrhythmia history</td>
</tr>
<tr>
<td>Sustained monomorphic VT</td>
</tr>
<tr>
<td>Sustained polymorphic VT</td>
</tr>
<tr>
<td>NSVT</td>
</tr>
<tr>
<td>Ventricular flutter</td>
</tr>
<tr>
<td>Ventricular fibrillation</td>
</tr>
</tbody>
</table>

Values are n (range) or n (%).

Programming compliance was 98% for the 7 variables necessary to achieve uniform detection and initial therapy for FVT (upper and lower detection CL limits, burst therapy, number of sequences, pulses per sequence, percent FVT CL, and minimum pacing interval).

**Spontaneous Episodes Detected**

During a mean follow-up of 6.9 ± 3.6 months, 1100 episodes of ventricular tachyarrhythmia were detected in 65 patients. An additional 148 episodes of supraventricular tachyarrhythmias were detected but excluded from further analysis. Four hundred forty-six episodes (40%) were de-
detected as FVT (mean CL 301 ± 24 ms) in 52 patients (24%) (Figure 1) and were the subject of analysis. Slow VT (mean CL 374 ± 39 ms) occurred for 624 episodes (57%) in 30 patients. Only 30 episodes (3%) in 16 patients were detected in the VF zone (mean CL 236 ± 36 ms). Among the 52 patients with FVT, the median number of FVT episodes per patient was 2 (range 1 to 158). Seventeen patients (7%) had 1 FVT episode, 12 patients (5%) had 2 episodes, and 23 patients (10%) had ≥3 episodes.

Figure 2 shows a CL histogram for spontaneous ventricular tachyarrhythmia episodes. Three fourths of detected FVT episodes had CL 290 to 320 ms. Only 19% had CL < 280 ms, and 6% had CL > 320 ms (possible given that CL is the mean of only the last 4 beats before detection). Seventy-four percent of VT episodes fell between 320 and 400 ms, and 26% had CL>400 ms. CL for VF episodes was evenly distributed from 170 to 310 ms.

ATP Efficacy

Of 446 FVT episodes, 378 (85%) were terminated by the first or second ATP sequence (Table 2). Ninety percent of ATP successes came after the first ATP sequence. Outside of the standard study protocol, an additional 18 episodes (4%) were terminated by a third ATP attempt, yielding a total of 89% ATP efficacy. Efficacy adjusted for the occurrence of multiple episodes per patient was 77% (95% CI 68% to 83%).

In 1 episode, the rhythm converted to a slower VT outside the FVT zone, and 1 episode terminated spontaneously before shock delivery. Forty-eight FVT episodes (11%) occurred in

Figure 3. Example of successful termination of FVT by ATP (A). Example of failed ATP accelerating FVT followed by shock termination (B).

14 patients who required a shock for episode termination, with no single episode requiring ≥3 shocks. Examples of ATP success and failure are shown in Figure 3.

Effect of CL on ATP Efficacy

Efficacy of ATP for detected CL is displayed in Figure 4. The mean FVT CL at which ATP was successful versus unsuccessful was not significantly different (301 ± 22 and 299 ± 30 ms, respectively, P = 0.72). When FVT CLs were dichotomized into two 40-ms groups, initial ATP therapy was successful in 84% of episodes with mean CL 280 to 320 ms versus 69% of episodes with mean CL 240 to 280 ms (P = 0.05).

Polymorphic VT

Among the 250 episodes with electrograms available for analysis, polymorphic VT was detected in the FVT zone in 6 (2%). ATP was delivered to all and was effective once, whereas a single shock terminated the remainder.

Nonsustained VT

Ninety-four of the 220 patients in this study had a history of nonsustained VT (NSVT). They had higher ATP efficacy than patients without a history of NSVT (90% versus 64%, respectively, P < 0.001). Patients with NSVT in their arrhythmia history had a median of 2 episodes, whereas those with a history of sustained VT or VF had a median of 1 episode.

Efficacy Within Individuals

The first ATP therapy was effective in terminating 37 of 52 patients’ first FVT episode (71%, 95% CI 53% to 83%) (Table 2). In 2 patients (4%), VT was not terminated by the first ATP sequence but ceased spontaneously before the delivery of the second sequence. Thirteen patients (25%) required a shock to terminate their first episode of FVT. Individual success rates were 0% in 6 patients, 100% in 38 patients, and 14% to 75% in 8 patients.

Shocks for FVT Episodes

Fourteen patients (6%) received shocks for FVT. Thirteen required a shock on their first episode of FVT. In patients with ATP success on their first episode, estimated probability of ATP efficacy in subsequent episodes was 99% (95% CI 96% to 100%), and the predicted efficacy after initial ATP failure was 38% (95% CI 15% to 69%, P < 0.001).

Antiarrhythmic Drugs

One hundred nineteen patients (54%) were on antiarrhythmic drug therapy at the time of ICD implantation (85 on
Discussion

Sustained monomorphic VT in CAD occurs via a macroreentrant mechanism. Pace termination success is therefore limited by ventricular refractoriness, excitable gap, conduction time to the circuit, and circuit abolition or reinitiation. Pace termination becomes more difficult as arrhythmia CL shortens. The assumption that empirical ATP therapy is ineffective for FVT has resulted in the standard practice of applying shocks as first therapy for FVT. This study demonstrated, however, that empirical ATP therapy terminated 396 of 446 episodes of FVT (89%) and did so with shorter median time to effective therapy. Syncope occurred in 2% of FVT episodes (4 patients), and acceleration occurred in only 4% of episodes. One death had the possibility of being causally related to ATP. The large reduction in number of shocks reduced morbidity caused by shock pain and increased the longevity of ICDs.

This study also demonstrates that rapid monomorphic VT is common, representing 40% of all ventricular tachyarrhythmia episodes. Because previous studies have shown 90% to 96% ATP success rates for VT with CL > 320 ms, and these data demonstrated an ATP success rate of

Table 2. Outcome of ATP Therapy for FVT (n = 446 Episodes)

<table>
<thead>
<tr>
<th>Terminating Therapy</th>
<th>Efficacy</th>
<th>Acceleration*</th>
<th>Syncope</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATP therapy (1st or 2nd sequence)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raw, n (%)</td>
<td>378 (85)</td>
<td>10 (4)</td>
<td>3 (0.6)</td>
</tr>
<tr>
<td>Adjusted† % (95% CI)</td>
<td>77 (68–83)</td>
<td>7 (3–14)</td>
<td>...</td>
</tr>
<tr>
<td>Shock, n (%)</td>
<td>48 (11)</td>
<td>...</td>
<td>6 (1.3)</td>
</tr>
</tbody>
</table>

*Acceleration evaluated in 244 episodes of monomorphic FVT with electrogram stored by the ICD.
†Results adjusted for the occurrence of multiple episodes in the same patient.

β-blockers, 34 on amiodarone, 10 on sotalol, 6 other). In 3 of the 14 patients who received shocks after failed ATP for FVT, the antiarrhythmic drugs were changed after a shock. Limited duration of follow-up prevents us from drawing conclusions as to the effect of the change in drug regimen.

Acceleration

Acceleration was defined as >10% decrease in CL of monomorphic FVT after delivery of therapy. In 244 episodes of monomorphic FVT treated by ATP for which stored electrograms were available for analysis, acceleration occurred in 10 cases (4%, generalized estimating equation adjusted 7%) in 7 patients. All accelerated episodes were re-detected in the VF zone (CL < 240 ms); 1 self-terminated during capacitor charging, 8 were successfully terminated by a single shock, and 1 required 3 shocks to terminate. Acceleration was associated with syncope in 1 episode terminated by a single shock after 22 seconds.

Episode Duration

The durations of VF and FVT episodes are shown in Figure 5. Episodes initially detected in the VF zone and immediately shocked had a median duration of 10 seconds (range 5 to 16 seconds). Episodes of successful ATP had a median duration of 6 seconds (range 3 to 282 seconds). Episodes in which ATP was unsuccessful and high-voltage shocks were necessary had a median duration of 21 seconds (range 18 to 24 seconds). Each of these durations is statistically different from the others (P < 0.001). The median duration of all FVT episodes (ATP successful or failed) was 6 seconds (range 3 to 282 seconds).

Syncope

Remarkably, most FVT episodes were found incidentally on device interrogation at follow-up because they were asymptomatic. Lightheadedness or dizziness was experienced during 29 of 446 FVT episodes (7%) in 9 patients. The median duration of these episodes was 6 seconds (range 5 to 32 seconds). Syncope occurred in 4 patients during 9 FVT episodes (9 of 446, 2%) (Table 2). In 2 patients with a single syncopal episode and in 1 patient with 2 syncopal episodes, syncope occurred after ATP failure resulted in shock. Each of these patients also had additional episodes of FVT that were successfully pace-terminated without syncope. One patient experienced syncope with each of 5 FVT episodes independently of ATP success or failure. The median duration of syncopal FVT episodes was 17 seconds (range 5 to 33 seconds).

Syncope occurred twice in 1 patient during slow VT and once in each of 2 patients during VF. In addition to the 13 syncopal episodes associated with tachyarrhythmia, there were 6 episodes of syncope not associated with tachycardia.

Death

Thirteen patients died during the study. The cumulative 6-month survival probability for all-cause mortality was 95% (95% CI 90% to 97%). The cause of death was classified by an independent committee as sudden cardiac in 2 patients, non-sudden cardiac in 8 patients, non-cardiac in 2 patients, and unknown in 1 patient for whom adequate documentation could not be obtained. One sudden cardiac death occurred in a hospitalized patient whose ICD had been intentionally deactivated. A second patient was unexpectedly found dead at home and classified as sudden cardiac; no postmortem, ICD interrogation, or autopsy data were available.
89% for VT<320 ms, the combined outcome suggests an opportunity to markedly reduce shocks in ICD patients by optimizing ATP therapy. Furthermore, only 30 episodes (3%) were diagnosed as VF with CL<240 ms. These were the only episodes in this trial that used shock as initial therapy. Given that 13 VF episodes terminated spontaneously, only 17 of 1100 episodes (1.5%) received shock as initial therapy. The ICDs in this trial were used principally as ATP devices with occasional, yet critical defibrillation capabilities.

Quality-of-life scores in the ICD population are poor and are significantly affected by the occurrence of shocks. Shock pain, anticipation of the next shock, antiarrhythmic drugs, and hospitalizations due to shocks are all contributors. A recent trial demonstrated that the principle cause (26%) of all hospitalizations for ICD patients in a 12-month span was due to appropriately detected VT/VF and consequent shocks from their ICD. The results of this trial indicate the possibility of significant hospitalization reduction by empirical ATP for FVT.

The incidence of acceleration of monomorphic VT increases with decreasing VT CL. To successfully reset VT within the limit of ventricular refractory period, the pacing algorithm in this trial was set at a relatively nonaggressive 8 pulses at 88% VT CL, which yielded an acceleration rate of 4%. Although not desirable, this rate of acceleration compares favorably to previous studies that have shown acceleration rates between 7% and 18% for treatment of spontaneous rapid VT. Given the greater success for FVT between 280 and 320 ms, it is possible that both success and acceleration could be improved by different CL cutoffs. The greatest danger may be that acceleration will lead to a rhythm refractory even to shocks. It is possible that 1 patient who died suddenly did so by this mechanism, because no data exist regarding the circumstances of that patient’s death. Defibrillation thresholds have been shown to increase with episode duration. In this trial, however, every episode reviewed was terminated successfully by shock when ATP failed, although 4 episodes required 2 shocks and 1 required 3 shocks. Given the probabilistic nature of defibrillation, this is not a disproportionate number of episodes requiring >1 shock to terminate.

Another risk associated with ATP therapy for FVT is the potential for syncope due to delay of shock therapy. In the 6.9 months of follow-up, syncope occurred in 4 patients and 9 episodes. This 2% incidence of syncope is not significantly different from that reported in other ICD patient groups. Bansch et al reported 4% syncopal rate at 6 months and 10% at 12 months. Although failed ATP causes delay, every shock delivered for a rhythm that could have been pace-terminated also represents delay because it required charging a capacitor, whereas ATP is delivered immediately on detection. It has been assumed that on a population scale, effective therapy could be delivered more quickly as shock rather than ATP because of the higher failure rate of the latter. In this trial, the median duration of VF episode was 10 seconds, compared with an FVT episode duration of 6 seconds. Thus, the strategy of using ATP as first therapy and shock as backup did not lead to longer episodes. An empirical ATP approach seems to present less shock risk without increased syncope or acceleration (although in this study, all devices were in their first year of use and thus had minimal charge times). Despite these efforts, tachycardic syncope is not likely to be eradicated in these patients, as exemplified by 1 patient who experienced syncpe with episodes lasting 5 and 6 seconds. Delivery of ATP therapy during capacitor charging may be 1 method to prevent episode duration from increasing. Shocks can be aborted when ATP is successful, or a shock can be delivered without delay when ATP fails.

Study Limitations
The trial was not randomized. Even assuming 100% success rate of shock therapy, however, ATP compares favorably, because efficacy was high and risks of syncope, acceleration, and sudden death were low. One possible confounding factor in estimating ATP success is the possibility for nonsustained FVT rhythms to appear as ATP success. It was recognized that older ICDs with committed therapies were shocking after NSVT had terminated. Although shocks require time for capacitor charge before delivery, ATP is delivered immediately on detection. Therefore, ATP may appear to successfully treat VT that would have otherwise self-terminated. It is interesting that the subgroup of patients with a history of NSVT had a higher ATP efficacy than the patients with no history of NSVT (90% versus 64%, P<0.001). This result may suggest that some of the successfully treated FVT rhythms were actually episodes of NSVT. If true, then one would expect an unusually high occurrence of FVT episodes. Patients in this study, however, exhibited 0.7 episodes of VT/FVT/VF per patient per month, similar to the 0.5 episodes per patient per month reported by Schaumann et al for patients with empirical ATP programming. Regardless, even if NSVT was in fact detected as FVT and treated by ATP, the value of programming ATP for FVT remains, because the energy cost is trivial, there was minimal acceleration and syncope, and there is significant benefit in terminating the sustained rhythms.

The ATP parameters were specifically designed for rapid reentrant arrhythmias. Thus, only patients with CAD were enrolled. The application of ATP for FVT in the non-CAD patient population needs to be tested.

Clinical and ICD Design Implications
ICD patients may be spared the majority of painful shocks if ATP is programmed as the first therapy for FVT. The longevity of ICDs may be improved by fewer capacitor charges. Future development of ICDs may benefit from algorithms that distinguish polymorphic from monomorphic FVT, more sophisticated ATP with closed loop capability to evaluate the effect of each ATP pacing pulse, and by ATP during capacitor charging. Further trials are needed for VT with even shorter CL. Reduced incidence of shock may improve acceptance of ICDs, currently a major barrier to application of ICD therapy to those at risk for sudden death.

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