Predictors of efficacy of amiodarone and characteristics of recurrence of arrhythmia in patients with sustained ventricular tachycardia and coronary artery disease

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ABSTRACT The value of serial electropharmacologic testing during long-term oral amiodarone therapy for prediction of long-term drug efficacy as well as characteristics of arrhythmia recurrence is controversial. One-hundred four consecutive patients with coronary artery disease and sustained ventricular tachyarrhythmias (VT) underwent initial electrophysiologic (EP) evaluation in the drug-free state and again after an amiodarone loading period of 25 ± 14 days (mean ± SD). Twenty-six patients (25%) had no inducible ventricular tachyarrhythmia during therapy with amiodarone (VT control group), whereas arrhythmia inducibility persisted in the remaining 78 patients (VT noncontrol group). During 17.4 ± 13.7 months of follow-up, two patients in the VT control group either had VT recurrence or died suddenly compared with 21 VT recurrences and eight sudden cardiac deaths in the VT noncontrol group (actuarial event rates at 36 months of 0.11 and 0.56, respectively, p = .0065). The cycle lengths of recurrent VT in these 21 patients in the VT noncontrol group were compared with those observed at final EP testing. A significant linear correlation was demonstrated (r = .76, p = .0001). Subgroup analysis of patients in the VT noncontrol group showed no EP predictors of outcome, including cycle length of induced VT. However, patients dying suddenly during the follow-up period had a higher prevalence of new or worsening congestive heart failure (75%) compared with patients with VT recurrence (19%) or those with no arrhythmic event (29%) (p < .02). Patients with sudden death or VT recurrence had a less stable initial clinical course, with an increased prevalence of spontaneous VT episodes during the amiodarone loading period (50% and 43%), compared with those with no recurrent arrhythmia (20%, p < .05). These data indicate that serial EP testing during amiodarone therapy is useful for predicting arrhythmia recurrence as well as its rate in patients with persistently inducible arrhythmias in the absence of new or worsening congestive heart failure. However, EP data, other than inducibility, was not useful for predicting those patients at highest risk of sudden death.


THE ROLE of repeat electrophysiologic testing in the evaluation of amiodarone therapy in patients with sustained ventricular tachyarrhythmias (VT) remains controversial. The use of electrophysiologic testing for assessment of drug efficacy is based on the premise that suppression of the ability to induce an arrhythmia during drug administration by programmed stimulation is a predictor of clinical efficacy. Although numerous studies have supported this hypothesis, a majority of the patients included in these studies were treated with conventional antiarrhythmic drugs such as quinidine, procainamide, and disopyramide. Accurate early assessment of therapy with amiodarone has been a particular problem for several reasons: a long loading period is required to achieve steady state, plasma concentration is not a good indicator of its electrophysiologic effect, and the drug has been most commonly used only in a highly selected population of patients with one or multiple prior drug failures. Several early reports on the use of electrophysiologic testing in patients treated with amiodarone failed to demonstrate that the results of stimulation were of predictive value. However, these studies were fre-
quently limited by heterogeneous patient populations and relatively short follow-up periods. In contrast, several recent reports have suggested that the persistent ability to induce VT with stimulation may be a clinically valuable predictor of arrhythmia recurrence in patients treated with amiodarone. In these studies, however, further correlations between electrophysiologic data and follow-up observations were not detailed, characteristics of arrhythmia recurrence were not examined, and no attempts were made to predict which patients were at highest risk for dying suddenly.

To examine these issues, we evaluated 104 consecutive patients with coronary artery disease, a prior history of sustained VT or fibrillation, and reproducible induction of this arrhythmia with programmed ventricular stimulation, who were treated with amiodarone. The purposes of this study were to determine if the results of programmed ventricular stimulation were accurate predictors of arrhythmia recurrence during follow-up and to ascertain which clinical and/or electrophysiologic variables correlated with the characteristics of recurrent episodes of arrhythmia.

Methods

Patient population. Patients were included in this study if they met the following four criteria: (1) a history of documented sustained VT or ventricular fibrillation not associated with acute myocardial infarction, (2) coronary artery disease diagnosed either by coronary angiography and/or by a history of an enzymatically and electrophysiologically confirmed myocardial infarction, (3) initiation of sustained VT or fibrillation by programmed ventricular stimulation at initial electrophysiologic study, and (4) repeat electrophysiologic study after oral loading with amiodarone. One hundred four consecutive patients who satisfied these criteria comprise the study group.

Electrophysiologic studies. Initial electrophysiologic studies were performed in patients in the fasting state 24 to 48 hr after discontinuation of any prior antiarrhythmic therapy. In nine patients multiple spontaneous episodes of VT complicated attempted drug withdrawal and the initial electrophysiologic study to confirm tachycardia mechanism and induction with programmed stimulation was performed in the presence of an antiarrhythmic drug. In these latter nine patients, the characteristics of the spontaneous tachycardia recorded after drug withdrawal were used for analysis. Our protocol for the electrophysiologic evaluation of patients with ventricular arrhythmias has been previously described. In brief, three or four quadripolar electrode catheters are inserted and advanced to the heart under fluoroscopic guidance. The catheters are positioned in the high right atrium, across the tricuspid valve adjacent to the bundle of His, in the right ventricular apex, and when indicated, in the coronary sinus and right ventricular outflow tract. Intracardiac signals are filtered between 30 and 500 Hz and displayed on a multichannel oscilloscope (Electronics for Medicine VR-16, Pleasantville, NY). Signals are stored on FM magnetic tape (Honeywell Model 101, Waltham, MA) and reproduced for analysis with an ink-jet recorder (Siemens Mingograf 16, Iselin, NJ). Programmed stimulation is performed with a constant-current stimulator (Bloom DTU-101, Reading, PA) that delivers rectangular 2 msec pulses at 2 mA.

Ventricular stimulation includes single, double, and triple extrastimuli during sinus rhythm and ventricular pacing at two cycle lengths (600 or 500 and 400 msec). If no sustained arrhythmia is initiated by pacing from the right ventricular apex, stimulation is repeated with a catheter positioned in the right ventricular outflow tract. The criteria used for analysis of responses to stimulation are given below.

Administration of amiodarone. All patients had failed one or more antiarrhythmic drug trials before the initiation of therapy with amiodarone. Therapy with amiodarone was begun with a loading dose of either 1200 or 1400 mg/day for 6 to 12 days and then reduced to 400 or 600 mg daily. Adjustments in amiodarone dosing were individualized on the basis of the appearance of side effects or pattern of spontaneous arrhythmia. The mean (± SD) dose during the second to fifth weeks of therapy was 466 ± 124 mg/day. Two protocols were followed for electrophysiologic testing. Sixty-two patients were studied within 20 days after initiation of amiodarone therapy. Twenty-one of 48 patients with inducible VT underwent repeat testing after an additional 3 to 5 weeks of outpatient therapy. Forty-two remaining patients who had well-tolerated arrhythmias were not hospitalized for the entire loading period and were restudied only once after 4 to 5 weeks of treatment. For the entire group, the mean duration of amiodarone therapy before their final electrophysiologic study was 25 ± 14 days. Twenty patients had rapid, poorly tolerated VT induced during amiodarone therapy that was suppressed or significantly slowed with addition of a second antiarrhythmic drug. These patients were treated over the long term with this combination. Data from the final electrophysiologic study performed during treatment with the drug regimen selected for long-term therapy were used for analysis.

Follow-up. Patients were followed at the University of Virginia by the investigators at intervals of 3 to 6 months after hospital discharge. Interval data were obtained from referring physicians and records from outside hospitals. No patient was lost to follow-up. For each patient, follow-up data were analyzed until one of the following end points was reached: electrocardiographic documentation of recurrent VT, sudden cardiac death, other cardiac or noncardiac death, alteration in the discharge drug regimen, or termination of the study. No patient underwent cardiac surgery or implantation of an automatic implantable defibrillator after initiation of amiodarone therapy but before arrhythmia recurrence. Minor dosage adjustments based on plasma level data or the appearance of side effects did not exclude continued follow-up.

Definitions. A ventricular arrhythmia was considered to be sustained if it lasted 30 sec or if it required earlier intervention for termination because of cardiovascular collapse. Sustained VT or ventricular fibrillation was the end point used during both initial and final electrophysiologic studies. Patients who did not manifest a sustained arrhythmia in response to stimulation at their final study on their discharge antiarrhythmic regimen were considered part of the “VT control” group. Patients with inducible sustained VT or fibrillation at their final study were considered part of the “VT noncontrol” group. Sudden cardiac death was defined as a witnessed death occurring within 1 hr of symptom onset or an unwitnessed death of a patient documented to be asymptomatic within the previous 12 hr. Documented episodes of VT and sudden cardiac death were defined as arrhythmic events during follow-up. Nonarrhythmic cardiac death was defined as death due to acute myocardial infarction or to intractable congestive heart failure. New or worsening congestive heart failure was defined as a change in the patient’s functional status due to symptoms typically associated with left ventricular failure severe enough to warrant hospitalization and/or major change in therapy.

Statistical analysis. Individual test data were compiled and
stored in a computerized data base. Continuous data are presented as the mean ± SD. For comparisons between means of independent observations, one-way analysis of variance and Duncan’s multiple-range tests were used to delineate significance of any observed differences. Discrete variables were analyzed with contingency tables with appropriate chi-square or Fisher’s exact tests. Correlations between the characteristics of VT at electrophysiologic study and during clinical follow-up were made by linear regression analysis. Follow-up event rates were calculated by Kaplan-Meier life table analysis. Significance differences between groups were tested by the product-limit method.

Results

Electrophysiologic testing. Results of the initial electrophysiologic study and pertinent clinical characteristics of the patient population are summarized in table 1. At the time of the final electrophysiologic study, sustained VT could not be initiated with programmed ventricular stimulation in 26 patients (25%, VT control group). In 21 of the 104 patients (20%), this result was achieved with amiodarone alone. In the remaining five patients, VT either occurred spontaneously or was induced during amiodarone therapy, but was suppressed at final electrophysiologic study by addition of a second antiarrhythmic drug (quinidine in two, pro-cainamide in three). Of 21 patients in whom VT was inducible at early testing and who were restudied after additional amiodarone loading, only one became noninducible. Sustained VT was persistently inducible during amiodarone therapy in 78 patients (75%, VT noncontrol group). There were no significant differences between the VT control and VT noncontrol groups with regard to pertinent clinical variables, as shown in table 1. When electrophysiologic data from the two groups were compared, no differences were seen with respect to baseline or posttreatment refractory periods, corrected QT intervals, or initial tachycardia cycle length. However, a higher proportion of patients in the VT control group required three extrastimuli for VT initiation at their baseline study.

A polymorphic VT only was initiated at baseline electrophysiologic study in 11 patients. Six of these patients had polymorphic VT or fibrillation at initial clinical presentation. Initiation of VT at baseline testing in these patients required double extrastimuli three in patients and triple extrastimuli in eight. Overall, four of 26 patients in the VT control group had polymorphic VT or ventricular fibrillation induced at baseline compared with seven of 71 of those in the VT noncontrol group (p = NS).

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Clinical and electrophysiologic characteristics of 104 patients with and without suppression of VT inducibility during amiodarone therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>VT control group (n = 26) 62 ± 10</td>
</tr>
<tr>
<td>Sex (men)</td>
<td>23 (88%)</td>
</tr>
<tr>
<td>No. of episodes VT/VF</td>
<td>4.1 ± 3.3</td>
</tr>
<tr>
<td>Clinical rhythm — VF</td>
<td>5 (14%)</td>
</tr>
<tr>
<td>No of AAD trials</td>
<td>4.2 ± 2.2</td>
</tr>
<tr>
<td>No. of coronary arteries with greater than 70% stenosis</td>
<td>2.0 ± 1.0</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>32 ± 15</td>
</tr>
<tr>
<td>LV aneurysm</td>
<td>22 (85%)</td>
</tr>
<tr>
<td>Final amio dose (mg)</td>
<td>481 ± 123</td>
</tr>
<tr>
<td>Amio+type I AAD</td>
<td>5 (19%)</td>
</tr>
<tr>
<td>Initial EPS</td>
<td></td>
</tr>
<tr>
<td>VERP (ms)</td>
<td>234 ± 18</td>
</tr>
<tr>
<td>QTc (msec)</td>
<td>435 ± 17</td>
</tr>
<tr>
<td>VT cycle length (msec)</td>
<td>267 ± 74</td>
</tr>
<tr>
<td>Initiation by triple VES</td>
<td>15 (58%)</td>
</tr>
<tr>
<td>Final EPS</td>
<td></td>
</tr>
<tr>
<td>Δ VERP (msec)</td>
<td>+47 ± 29</td>
</tr>
<tr>
<td>Δ QTc (msec)</td>
<td>+43 ± 42</td>
</tr>
<tr>
<td>Δ VT CL (msec)</td>
<td>—</td>
</tr>
</tbody>
</table>

AAD = antiarrhythmic drug; Amio = amiodarone; EF = ejection fraction; EPS = electrophysiologic study; LV = left ventricular; QTc = rate-corrected QT interval; VERP = ventricular effective refractory period; VES = ventricular extrastimuli; VF = ventricular fibrillation; Δ = change in value between initial and final EPS.

Outcome. During a median follow-up of 14.5 months (mean 17.4 ± 13.7, range 1 to 53), 31 of the 104 patients experienced an arrhythmic event. In the group of 26 patients in whom VT was controlled, only two arrhythmic events (one episode of recurrent VT and one episode of sudden death) were observed. Among the 78 patients in whom VT was not controlled, 21 patients had one or more episodes of sustained VT and eight additional patients died suddenly. As shown in figure 1, life table analysis yielded a rate for arrhythmic events at 36 months of 0.11 in the VT control group and 0.54 in the VT noncontrol group (p = .0065). The event rates of these two groups were similar if the analysis was limited to the subgroup of 93 patients in whom only monomorphic VT was induced at baseline electrophysiologic study (0.13 vs 0.52, p = .022), or to the subgroup of 84 patients who were treated with amiodarone as the sole antiarrhythmic agent (0.07 vs 0.48, p = .0098).

There was no difference between the VT control and noncontrol groups with respect to nonarrhythmic cardiac death rates during follow-up (0.09 vs 0.08). There was a trend toward a higher occurrence of death due to arrhythmia in the VT noncontrol group (0.07 vs 0.19).
However, the number of such deaths was small and statistical significance was not reached.

Characteristics of recurrent arrhythmias in the VT non-control group. Twenty-one patients had an electrocardiographically documented episode of VT not associated with sudden death during the follow-up period. Since only single-lead rhythm strips were obtained in some patients before intervention, tachycardia cycle lengths were compared with those documented at final electrophysiologic study but the QRS morphologies were not. As shown in figure 2, there was a significant and linear correlation between the cycle length of recurrent VT and that of the tachycardia observed at final electrophysiologic study.

Eight additional patients died suddenly during follow-up; the initial electrocardiogram, when obtained, showed ventricular fibrillation or asystole. Data obtained from these patients at the time of final electrophysiologic testing did not predict their poor outcome. As shown in figure 3, patients who died suddenly in follow-up had similar cycle lengths of tachycardia induced at final electrophysiologic study when compared with cycle lengths in those with recurrent VT and those who remained free of recurrent arrhythmia. Clinical observations made during tachycardia at electrophysiologic study were also not helpful in predicting outcome during follow-up. Only one of the eight patients who subsequently died suddenly had an induced VT at the time of electrophysiologic testing that caused syncope and required emergency cardioversion.

Clinical predictors of arrhythmia recurrence in the VT noncontrol group. Clinical markers that might predict recurrent arrhythmic events in the group of VT non-control patients were examined. Comparisons between the patients suffering sudden death, the patients with VT recurrence, and those with no arrhythmia recurrence during follow-up are shown in figure 4 and table 2. The most striking finding was that patients who died suddenly during follow-up were more likely to have had new or worsening congestive heart failure at an earlier point in the follow-up period (p < .02). There were trends toward lower ejection fractions and an increased number of diseased coronary arteries in these patients compared with the other groups, but these differences did not reach statistical significance. In addition, patients who subsequently died suddenly were discharged on a higher mean dose of amiodarone. Both patients suffering sudden death and patients with recurrent VT had a greater prevalence of spontaneous episodes of sustained VT during the period of amio-
Amiodarone loading and had a tendency for more frequent treatment with a second antiarrhythmic agent than those patients with no recurrence. There were no significant differences between the groups with regard to any other clinical or electrophysiologic variables.

**Discussion**

The data in this report demonstrate that the use of electrophysiologic testing to evaluate amiodarone therapy in patients with sustained ventricular arrhythmias and coronary artery disease identifies patients at risk for arrhythmia recurrence, and in these patients characterizes the rate of arrhythmia recurrence provided that their functional class has not deteriorated. In contrast, electrophysiologic variables other than the persistent ability to induce VT during amiodarone therapy did not identify patients at risk for sudden death since other clinical factors, especially progressive congestive heart failure, seem to play a significant role.

**Previous studies.** Early reports on the use of oral amiodarone therapy in the treatment of recurrent life-threatening VT stressed its efficacy, even in patients resistant to multiple-drug regimens. An additional observation was that many patients had a favorable long-term clinical outcome despite a continued ability to induce ventricular arrhythmias at electrophysiologic testing during long-term drug therapy. 10-14 This led some authors to conclude that there was little benefit...
TABLE 2
Clinical and electrophysiologic characteristics of 78 patients in the VT noncontrol classified group by arrhythmic events in follow-up

<table>
<thead>
<tr>
<th></th>
<th>SCD (n = 8)</th>
<th>VT (n = 21)</th>
<th>No arrhythmia (n = 49)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>66 ± 7</td>
<td>65 ± 9</td>
<td>64 ± 8</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (men)</td>
<td>6 (75%)</td>
<td>13 (62%)</td>
<td>41 (84%)</td>
<td>NS</td>
</tr>
<tr>
<td>No. of episodes VT/VF</td>
<td>5.1 ± 3.9</td>
<td>4.6 ± 3.1</td>
<td>3.9 ± 3.3</td>
<td>NS</td>
</tr>
<tr>
<td>Clinical rhythm — VF</td>
<td>1 (12%)</td>
<td>2 (10%)</td>
<td>10 (20%)</td>
<td>NS</td>
</tr>
<tr>
<td>No of AAD trials</td>
<td>4.3 ± 2.1</td>
<td>4.5 ± 2.8</td>
<td>3.8 ± 2.3</td>
<td>NS</td>
</tr>
<tr>
<td>No. of coronary arteries with greater than 70% stenosis</td>
<td>2.8 ± 0.4</td>
<td>1.9 ± 0.9</td>
<td>2.1 ± 0.9</td>
<td>0.048*</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>25 ± 10</td>
<td>33 ± 10</td>
<td>34 ± 13</td>
<td>0.059*</td>
</tr>
<tr>
<td>Final amio dose (mg)</td>
<td>575 ± 198</td>
<td>471 ± 151</td>
<td>440 ± 123</td>
<td>0.013*</td>
</tr>
<tr>
<td>Amio + type I AAD</td>
<td>2 (25%)</td>
<td>7 (33%)</td>
<td>6 (12%)</td>
<td>NS</td>
</tr>
<tr>
<td>Initial EPS VT CL (msec)</td>
<td>298 ± 96</td>
<td>306 ± 95</td>
<td>293 ± 78</td>
<td>NS</td>
</tr>
<tr>
<td>Final EPS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Δ VERP (ms)</td>
<td>+27 ± 22</td>
<td>+41 ± 30</td>
<td>+36 ± 35</td>
<td>NS</td>
</tr>
<tr>
<td>Δ QTc (msec)</td>
<td>+66 ± 39</td>
<td>+54 ± 77</td>
<td>+46 ± 45</td>
<td>NS</td>
</tr>
<tr>
<td>Δ VT CL (msec)</td>
<td>+80 ± 129</td>
<td>+85 ± 94</td>
<td>+59 ± 112</td>
<td>NS</td>
</tr>
</tbody>
</table>

CL = cycle length; SCD = sudden cardiac death; other abbreviations are as in table 1.
*ASignificant statistical difference between “SCD” and “VT” patients.
*Significant statistical difference between “SCD” and “no arrhythmia” patients only.

from electrophysiologic testing in patients treated with amiodarone and that therapy based on other criteria might be indicated in these patients.11, 13, 18–20

More recently, McGovern et al.14 observed that the response to programmed ventricular stimulation during amiodarone therapy was predictive of VT recurrence in follow-up in a group of 42 patients with a variety of types of structural heart disease. Borggreffe and Breithardt15 reported similar data in a group of 36 patients. Horowitz et al.16 described their results in a larger series of 100 consecutive patients with coronary artery disease. Of 80 patients with inducible VT during amiodarone therapy, there were 26 patients with recurrence of VT and 12 additional patients who died suddenly during follow-up. There were no arrhythmia recurrences during follow-up in the remaining 20 patients whose tachycardias were controlled by amiodarone according to electrophysiologic criteria. In a review by Fisher et al.,21 data on 390 patients in 14 studies were pooled. In this group, VT was found to be inducible by programmed ventricular stimulation during amiodarone therapy in 75% of patients, with arrhythmia recurrence in approximately 40% of these patients. This compared with a 10% arrhythmia recurrence rate in the 25% of patients without inducible arrhythmias. Differences in electrophysiologic study methods and definitions in these reports, however, make the value of such pooled data questionable.

The data in the present study, in which patients with a single cardiac diagnosis and studied with a uniform electrophysiologic protocol were enrolled, are consistent with these previous studies in that 78 of 104 patients (75%) continued to have inducible tachycardias during amiodarone therapy. Arrhythmia recurrence rates in this series were concordant with the pooled data compiled by Fisher et al: two of 26 patients in the VT control group (8%) vs 29 of 78 of those in the noncontrol group (37%) (actuarial rates at 36 months of 0.11 and 0.56, respectively).

Value and limitations of serial electrophysiologic testing during amiodarone therapy. The data from this consecutive series of 104 patients treated with amiodarone, either alone or in combination, who were evaluated with serial electrophysiologic testing show an overall rate of response by electrophysiologic criteria of 25%. These patients in whom VT was controlled have a prognosis that is highly favorable and similar to the prognosis for patients who have had successful suppression of their arrhythmias during electrophysiologic testing using other antiarrhythmic agents.1–3 In contrast, patients in whom arrhythmias are induced with programmed stimulation after an appropriate oral loading regimen with amiodarone have a significantly higher rate of VT recurrence and sudden cardiac death.

It should be noted that 49 of the 78 patients in the noncontrol group in the present study had no arrhythmias.
nia recurrence during the 17.4 ± 13.7 month follow-up period, despite continued inducibility by programmed stimulation. This recurrence rate is lower than that reported in some early studies that followed patients treated with agents such as quinidine, procainamide, and disopyramide. However, since no randomized trial has been reported comparing outcomes of patients receiving amiodarone and those receiving alternative antiarrhythmic agents, no greater efficacy rate can necessarily be claimed for amiodarone compared with these other agents for long-term arrhythmia suppression in patients in whom VT is not controlled by electrophysiologic criteria.

Patients with clinical sustained tachyarrhythmias and inducible polymorphic VT or ventricular fibrillation at baseline electrophysiologic evaluation were included in the present analysis. Despite the possible lack of specificity of this finding and potential for treatment of “nonclinical” arrhythmias, this reproduced the patient’s clinical rhythm in a majority of cases. Also, the prevalence of inducible polymorphic VT or ventricular fibrillation was comparable between groups.

Prior authors have speculated that characteristics of arrhythmias induced at electrophysiologic testing might predict characteristics of arrhythmia recurrence. The present study confirms this hypothesis in the patients whose recurrence was documented to be sustained monomorphic VT. The cycle length of the tachycardia induced at electrophysiologic study during amiodarone therapy was found to correlate well with the VT cycle length in patients in whom this arrhythmia recurred during follow-up. This observation supports the presumption that electrophysiologic testing reproduces arrhythmias that are likely to occur clinically. Our analyses of other clinical variables associated with arrhythmic recurrence indicate that, in the absence of significant intervening changes in functional status, tachycardia cycle length is relatively constant over time. Similar data in another population have recently been reported by Miles et al. However, when the anatomic substrate for VT is not stable, such as during exacerbation of congestive heart failure, this relationship may not hold true.

Electrophysiologic testing alone was not useful in predicting which patients with arrhythmic recurrence would die suddenly as opposed to manifesting a well-tolerated VT. Patients who died suddenly during follow-up in the current report were similar to those with or without arrhythmia recurrence with regard to electrophysiologic characteristics, including the cycle length of VT induced at final electrophysiologic testing during antiarrhythmic drug therapy. Although this observation is contrary to an earlier report, a recent prospective study of the use of amiodarone alone vs amiodarone in combination with a type I drug in the treatment of sustained VT demonstrated that the risk of dying suddenly was similar in both groups, despite a longer cycle length of induced VT in the latter group. From the present data and those previously reported, it would appear that factors other than the rate of the inducible VT must determine of the likelihood of survival in the event of an arrhythmic recurrence. To further investigate this observation, clinical variables of patients in the present study were examined. A history of new or worsening congestive heart failure during follow-up was found to be strongly associated with subsequent sudden death. Trends toward worse resting global left ventricular function and more extensive coronary artery disease were also observed in this group. Although these findings might be associated with a higher risk of sudden death in the VT control group also, the event rate was too low in this group to allow for statistical analysis. The possibility that amiodarone therapy contributed to these patients’ hemodynamic decompensation cannot be excluded.

However, long-term amiodarone is generally associated with minimal net adverse hemodynamic effects. Thus, patients who had evidence of an unstable hemodynamic substrate appeared to be at highest risk for dying suddenly, independent of the cycle length of their tachycardia observed during electrophysiologic testing.

Patients who manifest evidence of continued electrical instability, as defined by the recurrence of one or more episodes of spontaneous VT after initiation of amiodarone therapy but before final electrophysiologic evaluation, had a higher incidence of sudden cardiac death or VT recurrence in follow-up as compared with those without this finding. These observations in part explain the higher mean discharge of sudden death subgroup, and the higher prevalence of combination therapy in the sudden death and VT recurrence subgroups.

Clinical implications. The results of the present study support previous observations that the response to serial electrophysiologic testing during amiodarone therapy in patients with coronary artery disease is a strong predictor for future arrhythmic events, and therefore is a valuable tool in the risk stratification of these patients. Cycle lengths of VT induced during amiodarone therapy strongly correlate with cycle lengths of recurrent arrhythmias in patients with a stable hemodynamic/anatomic substrate and may be useful in the assessment.
of the utility of adding of a second antiarrhythmic agent to slow a rapid tachycardia.

It must be emphasized, however, that the goal of slowing the tachycardia with the addition of a second antiarrhythmic agent may not be fully protective against sudden death, since patients with slow VT do not necessarily appear to have a lower risk, particularly if they experience exacerbation of congestive heart failure.

Among patients with coronary artery disease and sustained VT treated with long-term amiodarone therapy, a subgroup of patients at high risk for sudden death can be identified. These individuals are characterized by persistently inducible VT and unstable ventricular hemodynamics. In these patients, a careful reevaluation of therapy with aggressive management of symptoms of heart failure is indicated. Additionally, other therapeutic options for arrhythmia management, including more aggressive pharmacologic therapy, surgical or catheter ablation of the tachycardia focus, or implantation of the automatic implantable defibrillator may be warranted.

References


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