The use of ambulatory monitoring in the prognostic evaluation of patients with sustained ventricular tachycardia treated with amiodarone

ENRICO P. VELTRI, M.D., LAWRENCE S. C. GRIFFITH, M.D., EDWARD V. PLATIA, M.D., THOMAS GUARNIERI, M.D., AND PHILIP R. REID, M.D.

ABSTRACT We recently reported a retrospective experience with serial Holter monitoring as a guide to therapy in patients with sustained ventricular tachycardia treated with amiodarone. To confirm and substantiate these findings, a prospective study was designed that included baseline 24 hr Holter monitoring and serial Holter monitoring after 1 week of therapy with amiodarone. Fifty-two patients with documented sustained ventricular tachycardia who manifest nonsustained ventricular tachycardia on baseline Holter monitoring were treated with amiodarone. Thirty-four patients (group I) had nonsustained ventricular tachycardia completely suppressed and 18 patients (group II) had continued nonsustained ventricular tachycardia on serial Holter monitoring performed on days 8, 9, and 10 of therapy. At 11.6 ± 1.0 (mean ± SE) months follow-up, three (9%) group I patients and 12 (67%) group II patients had recurrent sustained ventricular tachycardia or sudden cardiac death (p < .01). The sensitivity, specificity, positive and negative predictive value, and predictive accuracy of ventricular tachycardia on 24, 48, and 72 hr Holter monitoring over days 8, 9, and 10 for predicting recurrent sustained ventricular tachycardia or sudden cardiac death were analyzed. The positive and negative predictive values were 89% and 84%, 69% and 89%, and 67% and 91% for 24, 48, and 72 hr Holter monitoring, respectively. Overall predictive accuracy was 85%, 83%, and 83%, respectively. We conclude that early Holter monitoring is useful in assessing the clinical efficacy of amiodarone in patients with sustained ventricular tachycardia who manifest nonsustained ventricular tachycardia on baseline Holter monitoring.


AMIODARONE is a benzo-furan derivative structurally similar to thyroxine that was originally introduced in 1967 as an antianginal agent.1 It was subsequently recognized to have potent antiarrhythmic action, which appeared related to prolongation of action potential duration and refractory periods of all cardiac tissue without changing resting membrane potential.2–4

It has been used effectively in both supraventricular and ventricular tachyarrhythmias.5–16

The prediction of clinical efficacy of amiodarone in the treatment of patients with sustained ventricular tachyarrhythmias remains difficult to assess and controversial. At times therapy remains empiric.17 Although programmed electrical stimulation has been useful in guiding therapy of sustained ventricular tachycardia with several class I antiarrhythmic agents,18,19 this may not be the case with amiodarone, a class III antiarrhythmic agent. Several studies have revealed a discrepancy between the clinical and electrophysiologic efficacy of amiodarone,10–13,20–23 while others have found programmed electrical stimulation useful.24–26 Notwithstanding, electrophysiologic studies are invasive, expensive, and time-consuming; they require expertise and have attendant risks.27 Similarly, although serum amiodarone concentrations below 1.0 µg/ml may signal arrhythmia relapse, serum concentrations do not differentiate responders and nonresponders.13

In a recent retrospective study we reported that Holter monitoring appeared useful in the therapeutic management of selected patients with histories of sustained ventricular tachycardia and high-grade ventricular ectopy (nonsustained ventricular tachycardia) on baseline 24 hr Holter monitoring.28 However, because

**CIRCULATION**
of the potential impact of these preliminary findings, we felt it imperative to evaluate prospectively the clinical utility of serial Holter monitoring as a prognostic tool early in the course of amiodarone therapy.

Methods

Study entry criteria. Fifty-two patients with refractory, recurrent ventricular tachycardia met the following entry criteria: (1) history of documented sustained ventricular tachycardia (≥30 sec) manifesting as syncope (transient loss of consciousness with spontaneous recovery), presyncope (lightheadedness accompanying the arrhythmia), or sudden cardiac death (unheralded cardiac arrest within 1 hr of symptoms requiring cardiopulmonary resuscitation and/or cardioversion from ventricular tachycardia/ventricular fibrillation) in the absence of acute myocardial infarction, acid-base or electrolyte abnormalities, or drug toxicity (digoxin, class I antiarrhythmic agents, theophylline or tricyclic antidepressants), (2) nonsustained ventricular tachycardia (≥3 beats, <30 sec duration, rate >100/min) on single baseline 24 hr Holter monitor, and (3) a minimum follow-up of 1 month on amiodarone therapy in the absence of concurrent antiarrhythmic agents (except digoxin or β-blockers) or associated surgical interventions (coronary artery bypass surgery, subendocardial resection, or aneurysmectomy).

Patient population profile. The clinical characteristics of the patient population are summarized in Table 1. All patients had at least one episode of documented sustained ventricular tachycardia within 1 yr of referral. The clinical presentations were syncope in 26 patients, presyncope in 10 patients, and sudden cardiac death in 16 patients.

Underlying cardiac disease was defined by cardiac catheterization, echocardiography, and radionuclide studies. Coronary artery disease (defined by ≥70% coronary artery narrowing) was present in 41 patients (78%), nonischemic dilated congestive cardiomyopathy (defined by diffuse hypokinesis with ejec-

tion fraction ≤40%) in five patients (10%), congenital heart disease in two patients, valvular heart disease in two patients, and no structural heart disease in two patients. The ejection fraction was 37±2% (mean±SE) (range 13% to 81%) calculated from left ventriculographic data at cardiac catheterization in all but 11 patients, who had radionuclide estimates of overall left ventricular function. Thirty-nine (95%) of 41 patients with coronary artery disease had at least one previous remote myocardial infarction and seven (17%) had left ventricular aneurysm. Thirty-three patients had undergone baseline electrophysiologic study with a programmed electrical stimulation protocol previously described. Twenty-five patients (76%) had sustained ventricular tachycardia induced, six patients (18%) had nonsustained ventricular tachycardia induced, and two patients had noninducible ventricular tachycardia.

Patients had failed 2.9±0.1 previous antiarrhythmic drugs based on (1) symptomatic arrhythmic event while on the drug with therapeutic levels, (2) continued ventricular tachycardia on subsequent serial Holter monitoring after 48 hr on drug with therapeutic levels, (3) induction of ventricular tachycardia by programmed electrical stimulation on the drug, or (4) intolerable side effects. Thirty patients had failed at least one previous investigational drug before institution of amiodarone therapy.

Baseline data. Baseline evaluation included physical examination, complete blood count, basic chemistry screen including liver and thyroid function tests, pulmonary function tests, ophthalmologic evaluation with slit-lamp examination, 12 lead electrocardiogram, and single 24 hr Holter monitoring after discontinuation of all antiarrhythmic drugs (other than digoxin and β-blockers) for at least five half lives.

Holter monitoring was performed with dual-channel recordings. The magnetic tapes were analyzed with a Trendsetter Model DCG VII Dynamic Electrocardioscanner (Del Mar Avionics, Irvine, CA). The incidence of ventricular couplets and frequency of premature ventricular contractions were quantified. All runs of ventricular tachycardia, defined by 3 or more repetitive ventricular beats at a rate of greater than 100/min, were printed out and counted, and mean and peak ventricular tachycardia rates on each Holter were determined. Random tapes analyzed independently with a Dynamic Electrocardiovalidator Model 686 (Del Mar Avionics) revealed a 95% accuracy of our technician's scan. All tapes were reviewed by at least two of the investigators.

Amiodarone administration. Each patient gave informed consent before starting amiodarone. The oral loading of amiodarone was 600 mg twice daily for 14 days and the initial maintenance dose was 400 mg/day. The maintenance dose was decreased to 200 to 300 mg/day only for symptomatic side effects. Amiodarone was the only antiarrhythmic drug used over the long term; any concomitant antiarrhythmic drugs other than digoxin or β-blockers were discontinued 2 to 5 days after starting amiodarone.

Serial Holter monitoring and follow-up. Serial 24 hr Holter monitoring was performed on days 8, 9, and 10 of therapy in all patients. If nonsustained ventricular tachycardia was present on any of these initial three 24 hr Holters, repeat serial 24 hr Holter monitoring was performed after the completion of amiodarone loading on days 15, 16, and 17. Patients were then entered into a long-term protocol with 24 hr Holter monitoring on days 17, 24, and 31, and at 2, 3, 4, 6, 9, 12, 18, and 24 months of therapy.

Patients were followed in the outpatient clinic of the Sudden Death Prevention Program at 1, 2, 3, 4, 6, 9 and 12 months after discharge and then every 6 months thereafter. At each visit repeat baseline variables (other than slit-lamp examination), history of interim symptomatic events (sudden cardiac death, syncope, presyncope), or any adverse side effects were recorded.

### TABLE 1

<table>
<thead>
<tr>
<th>Clinical characteristics of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patients</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Age (yr)</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
</tr>
<tr>
<td>Cardiac pathology</td>
</tr>
<tr>
<td>CAD</td>
</tr>
<tr>
<td>CAD, MI</td>
</tr>
<tr>
<td>CAD, aneurysm</td>
</tr>
<tr>
<td>CCM</td>
</tr>
<tr>
<td>VHD</td>
</tr>
<tr>
<td>CHD</td>
</tr>
<tr>
<td>NSD</td>
</tr>
<tr>
<td>Clinical presentation</td>
</tr>
<tr>
<td>Sudden cardiac death</td>
</tr>
<tr>
<td>Syncope</td>
</tr>
<tr>
<td>Presyncope</td>
</tr>
<tr>
<td>Previous drugs failed</td>
</tr>
<tr>
<td>Follow-up (mo)</td>
</tr>
</tbody>
</table>

CAD = coronary artery disease; CCM = idiopathic dilated congestive cardiomyopathy; CHD = congenital heart disease; MI = myocardial infarction; NSD = no structural heart disease; VHD = valvular heart disease.
Efficacy of amiodarone. The clinical efficacy of amiodarone was based on the absence of clinical arrhythmic events (sudden cardiac death, sustained ventricular tachycardia). Amiodarone was considered effective if the patient remained free of clinical arrhythmic events through follow-up.

Statistical analysis. The data are presented as mean ± SE. The significance of differences between two groups was determined by Student’s t test for paired and unpaired data or by the chi-square or Fisher’s exact test where appropriate; p < .05 was accepted as the limit of significance. Kaplan-Meier actuarial curves²⁹ for amiodarone efficacy were constructed and differences were assessed with the generalized Wilcoxon test.³⁰

The sensitivity, specificity, positive predictive value, negative predictive value, and predictive accuracy were defined as follows: sensitivity = TP/TP + FN, specificity = TN/TN + FP, positive predictive value = TP/TP + FP, negative predictive value = TN/TN + FN, predictive accuracy = TP + TN/total population, where TP = true positive (patients with ventricular tachycardia on Holter and subsequent clinical arrhythmic event), TN = true negative (patients without ventricular tachycardia on Holter and no clinical arrhythmic event), FP = false positive (patients with ventricular tachycardia on Holter but no clinical arrhythmic event), FN = false negative (patients without ventricular tachycardia on Holter but subsequent clinical arrhythmic event).

Results

Baseline 24 hr Holter. Baseline 24 hr Holter monitoring revealed 3047 ± 632 single premature ventricular contractions and 315 ± 105 ventricular couplets per patient. All patients had nonsustained ventricular tachycardia with 70 ± 41 episodes per patient. The longest run of ventricular tachycardia was 17 ± 4 consecutive beats (range 3 to 118). The mean and peak rates of ventricular tachycardia were 151 ± 4 and 162 ± 5 beats/min, respectively.

Suppression of nonsustained ventricular tachycardia. There were 34 patients (group I) who had complete suppression of nonsustained ventricular tachycardia on serial Holter monitoring performed on days 8, 9, and 10 of therapy. Eighteen patients (group II) continued to have spontaneous nonsustained ventricular tachycardia on Holter monitoring on days 8, 9, and 10. Of group II patients, nine had ventricular tachycardia noted on the first 24 hr monitoring, 16 had ventricular tachycardia noted on 48 hr monitoring, and two patients required 72 hr monitoring to document continued nonsustained ventricular tachycardia.

Nine (50%) of 18 group II patients had complete suppression of nonsustained ventricular tachycardia on serial Holter monitoring performed on days 15, 16, and 17. Of the remaining nine patients, one had complete suppression of nonsustained ventricular tachycardia on day 24 and two patients had complete suppression on day 31.

Clinical outcome. At 11.6 ± 1.0 months follow-up (range 1 to 24), 38 patients (73%) were alive and 14 patients (27%) were dead. There were nine cardiac deaths (seven sudden) and five noncardiac deaths (three sepsis, one cerebrovascular accident, one metastatic carcinoma). Thirty-seven patients (71%) were free of clinical arrhythmic events through follow-up. The range of follow-up was 1 to 24 months (13.3 ± 1.0) in patients free of events. Fifteen patients had clinical arrhythmic events: recurrent sustained ventricular tachycardia in eight and sudden cardiac death in seven. Figure 1 depicts the actuarial analysis of the efficacy of amiodarone therapy.

Table 2 summarizes the characteristics of patients with and without clinical arrhythmic events. There were no significant differences in age, number of previous drug failures, maintenance amiodarone dose, number of premature ventricular contractions or ventricular couplets, and characteristics of ventricular ta-

![Image](http://circ.ahajournals.org/)

**FIGURE 1.** Actuarial analysis of efficacy of amiodarone for the total study population.

**TABLE 2**

Characteristics of patients with and without clinical arrhythmic events

<table>
<thead>
<tr>
<th></th>
<th>Event</th>
<th>No event</th>
<th>p value</th>
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<tbody>
<tr>
<td>No. of patients</td>
<td>15</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>Age (yr)</td>
<td>62 ± 3</td>
<td>61 ± 2</td>
<td>NS</td>
</tr>
<tr>
<td>Previous drugs failed</td>
<td>3.0 ± 0.2</td>
<td>3.0 ± 0.3</td>
<td>NS</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>30 ± 3</td>
<td>41 ± 2</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Maintenance dose (mg/day)</td>
<td>346 ± 23</td>
<td>331 ± 16</td>
<td>NS</td>
</tr>
</tbody>
</table>

Baseline 24 hr Holter

<table>
<thead>
<tr>
<th></th>
<th>Event</th>
<th>No event</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single PVCs</td>
<td>2648 ± 921</td>
<td>3169 ± 780</td>
<td>NS</td>
</tr>
<tr>
<td>Couplets</td>
<td>309 ± 196</td>
<td>317 ± 124</td>
<td>NS</td>
</tr>
<tr>
<td>VT episodes</td>
<td>16 ± 8</td>
<td>89 ± 55</td>
<td>NS</td>
</tr>
<tr>
<td>Longest VT run (beats)</td>
<td>12 ± 8</td>
<td>19 ± 5</td>
<td>NS</td>
</tr>
<tr>
<td>Mean VT rate (beats/min)</td>
<td>153 ± 8</td>
<td>149 ± 5</td>
<td>NS</td>
</tr>
<tr>
<td>Peak VT rate (beats/min)</td>
<td>165 ± 7</td>
<td>161 ± 6</td>
<td>NS</td>
</tr>
</tbody>
</table>

PVCs = premature ventricular contractions; VT = ventricular tachycardia.
chycardia (number of episodes, longest duration, mean and peak rates) on baseline 24 hr Holter monitoring in patients with and without clinical arrhythmic events. The ejection fraction, however, was significantly lower in patients with events (30 ± 3% vs 41 ± 2%; p < .01).

Prediction of clinical arrhythmic events by serial Holter monitoring. Three (9%) of 34 group I patients compared with 12 (67%) of 18 group II patients had clinical arrhythmic events (p < .01). There were two recurrent sustained ventricular tachycardia episodes and one sudden cardiac death in group I; six recurrent sustained ventricular tachycardia episodes and six sudden cardiac deaths occurred in group II. Six (67%) of nine group II patients with complete suppression of nonsustained ventricular tachycardia on days 15, 16, and 17 had clinical arrhythmic events; similarly, six (67%) of nine group II patients with continued nonsustained ventricular tachycardia on days 15, 16, or 17 had events.

Of the 15 patients with clinical arrhythmic events during follow-up, eight (53%) had ventricular tachycardia on 24 hr Holter monitoring (day 8) compared with one (3%) of the 37 patients without events, (p < .04). Eleven (73%) of 15 patients with clinical arrhythmic events compared with five (14%) of the 37 patients without arrhythmic events had ventricular tachycardia on 48 hr Holter monitoring (days 8 and 9) (p < .001). Twelve (80%) of 15 patients with clinical arrhythmic events compared with six (16%) of 37 patients without arrhythmic events had ventricular tachycardia on 72 hr Holter monitoring (days 8, 9, and 10) (p < .001). Figure 2 depicts the actuarial analysis of amiodarone efficacy in patients with and without ventricular tachycardia on 72 hr (days 8, 9, and 10) Holter monitoring.

Table 3 summarizes the sensitivity, specificity, positive and negative predictive value, and overall predictive accuracy of nonsustained ventricular tachycardia on 24, 48, and 72 hr Holter monitoring performed after 1 week of amiodarone therapy for determining long-term clinical efficacy.

Seventy-two hour Holter monitoring after 1 week of amiodarone revealed an 82 ± 3% decrease in single premature ventricular contractions and a 90 ± 3% decrease in ventricular couplets per patient from baseline 24 hr monitoring in the study population. Patients without clinical arrhythmic events had significantly greater suppression of single premature ventricular contractions and ventricular couplets than patients with arrhythmic events. Of patients with continued nonsustained ventricular tachycardia on days 8, 9, or 10, the peak ventricular tachycardia rate was significantly slower from baseline (160 ± 6 vs 144 ± 5 beats/min; p < .025); however, the mean ventricular tachycardia rate was not significantly slower (146 ± 6 vs 139 ± 5). The mean and peak ventricular tachycardia rates on Holter monitoring performed on days 8, 9, or 10 in patients with and without clinical arrhythmic events were not significantly different. Table 4 summarizes the results of 72 hr Holter monitoring after 1 week of amiodarone therapy.

**TABLE 3**
Determination of long-term clinical efficacy based on nonsustained ventricular tachycardia on serial Holter monitoring after 1 week of therapy

<table>
<thead>
<tr>
<th></th>
<th>24 hr</th>
<th>48 hr</th>
<th>72 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>53</td>
<td>73</td>
<td>80</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>97</td>
<td>86</td>
<td>84</td>
</tr>
<tr>
<td>Positive predictive value (%)</td>
<td>89</td>
<td>69</td>
<td>67</td>
</tr>
<tr>
<td>Negative predictive value (%)</td>
<td>84</td>
<td>89</td>
<td>91</td>
</tr>
<tr>
<td>Predictive accuracy (%)</td>
<td>85</td>
<td>83</td>
<td>83</td>
</tr>
</tbody>
</table>

**TABLE 4**
Results of 72 hr Holter monitoring on amiodarone therapy (days 8, 9, and 10)

<table>
<thead>
<tr>
<th>Event</th>
<th>No. of patients</th>
<th>No event</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>% PVCs suppression</td>
<td>68 ± 3</td>
<td>87 ± 4</td>
<td>&lt;.02</td>
</tr>
<tr>
<td>% Couplet suppression</td>
<td>80 ± 7</td>
<td>94 ± 3</td>
<td>&lt;.03</td>
</tr>
<tr>
<td>Mean VT rate (beats/min)(^a)</td>
<td>139 ± 6</td>
<td>137 ± 12</td>
<td>NS</td>
</tr>
<tr>
<td>Peak VT rate (beats/min)(^a)</td>
<td>144 ± 6</td>
<td>143 ± 14</td>
<td>NS</td>
</tr>
</tbody>
</table>

Abbreviations as in table 2.

\(^a\)Mean and peak ventricular tachycardia rate in patients with continued nonsustained ventricular tachycardia.
sion of ventricular tachycardia. Twenty-one patients from group I were maintained on 400 mg/day amiodarone. Three (14%) of these patients compared with eight (62%) of the remaining 13 group I patients receiving a maintenance dose of less than 400 mg/day had recurrence of nonsustained ventricular tachycardia on follow-up Holter monitoring (eight patients) or clinical sustained ventricular tachycardia (three patients; p < .02). Recurrence of nonsustained ventricular tachycardia was noted within 1 month of decreasing the dose in two patients, within 2 months in five patients, within 3 months in seven patients, and within 6 months in all. Recurrent sustained ventricular tachycardia developed in only one patient receiving 400 mg/day maintenance and in two patients receiving less than 400 mg/day maintenance.

Side effects. Adverse side effects (excluding corneal microdeposits) were noted in 33 patients (63%). These included elevated liver enzymes in 16 patients (31%), abnormal thyroid function tests in 12 patients (23%) (with associated clinical hypothyroidism in five patients), central or peripheral nervous system side effects in six patients (12%), visual disturbances in five patients (10%), symptomatic bradycardia necessitating temporary or permanent pacemaker insertion in four patients (8%), skin discoloration in two patients (4%), and pulmonary toxicity in one patient (2%). Side effects required discontinuation of amiodarone in three patients (6%).

Discussion

This prospective study confirms and substantiates the results of an earlier retrospective study that found early Holter monitoring useful in the long term prognostic assessment of patients with life-threatening ventricular tachycardia treated with amiodarone. The findings indicate that in patients with histories of documented sustained ventricular tachycardia who manifest nonsustained ventricular tachycardia on baseline 24 hr Holter monitoring, complete suppression of this high-grade ectopy on serial Holter monitoring after 1 week of high-dose amiodarone therapy predicts long-term clinical efficacy. Continued spontaneous nonsustained ventricular tachycardia portends a high risk for recurrent sustained ventricular tachycardia or sudden cardiac death and could therefore dictate a change in management strategy early in the course of therapy.

Heterofore, few studies have assessed the value of Holter monitoring in predicting the clinical outcome of a therapeutic intervention in patients with malignant ventricular arrhythmias. Platia and Reid reported the predictive accuracy of suppression of ventricular tachycardia on Holter monitoring by antiarrhythmic agents to be only 55% compared with 91% as assessed by programmed stimulation. However, only two of 44 patients studied were treated with amiodarone. Similarly, Chua et al. reported a predictive accuracy of 41% in suppression of ectopy of Lown grade III severity or greater on Holter monitoring compared with 82% as assessed by programmed stimulation in 89 patients. These authors did not state how many patients, if any, were treated with amiodarone. For a group of patients not on amiodarone, Herling et al. reported that the response of ventricular ectopic activity on 24 hr Holter monitoring to antiarrhythmic drug or surgical therapy did not predict therapeutic success.

In contrast to these above-mentioned studies, other investigators have reported reliability of Holter monitoring in predicting clinical outcome. In a series of 123 patients treated with agents other than amiodarone, Grabois et al. concluded that suppression of advanced grades of ventricular ectopy (Lown grade IVB and V) provided an effective discriminant of clinical outcome. More recently, Vlay et al. reported that early abolition of asymptomatic ventricular tachycardia on 24 hr Holter monitoring can be used to predict a good long-term clinical response. These investigators reported a 73% predictive accuracy of 24 hr Holter monitoring at 1 month of therapy in 44 survivors of ventricular tachycardia and ventricular fibrillation treated with selected antiarrhythmic agents other than amiodarone.

Several recent reports have attempted to correlate the effects of amiodarone on spontaneous ventricular ectopy in predicting clinical efficacy in patients with malignant ventricular arrhythmias. DiCarlo et al., in a large series of 104 patients, reported the presence of ventricular tachycardia on predischarge Holter monitoring in conjunction with an ejection fraction under 40% and previous history of syncope or cardiac arrest as significant predictors of subsequent sudden death or cardiac arrest. Marchinski et al. reported that the predictive value of a good Holter response at a mean of 11 days of amiodarone therapy was 82% in 55 patients with histories of sustained ventricular tachyarrhythmias. In both of these studies, however, the investigators did not report the incidence of nonsustained ventricular tachycardia on baseline Holter monitoring, and the range for repeat Holter monitoring after therapy in the latter study was wide (5 to 60 days). Thus the lack of baseline Holter monitoring does not permit one to conclude whether the absence of ventricular tachycardia was or was not a drug effect. In contrast, we pre-
presented a preliminary report from a group of patients with documented ventricular tachycardia on baseline Holter monitoring, correlated clinical outcome based on the results of serial Holter monitoring performed at a relatively early period after amiodarone therapy (days 8 to 13), and found an overall predictive accuracy of 76% to 79% for 24 to 72 hr Holter monitoring. The present results substantiate these earlier findings.

The early period of Holter monitoring (days 8 to 10) in the present study coincides with the mean time (9.5 days) required to achieve complete suppression of spontaneous ventricular tachycardia on continuous electrocardiographic monitoring reported by others using comparable initial amiodarone doses. Suppression of nonsustained ventricular tachycardia on these Holters was noted in approximately two-thirds of patients and correlated with good clinical outcome as evidenced by a negative predictive value of 84% to 91%. Continued nonsustained ventricular tachycardia on these Holters identified a high-risk group for subsequent clinical arrhythmic events; the positive predictive value on 24 to 72 hr Holter monitoring was 67% to 89%. Of note, group II patients with complete suppression of nonsustained ventricular tachycardia after the full loading period continued to be at high risk for clinical arrhythmic events. The overall predictive accuracy of 24 to 72 hr Holter monitoring after 1 week of amiodarone therapy was 83% to 85%, similar to that previously reported.

Sensitivity increased and specificity decreased progressively from 24 to 72 hr Holter monitoring, as one would expect. Use of 72 hr Holter monitoring would markedly increase sensitivity to 80% and mildly decrease specificity to 84% compared with the sensitivity and specificity of 53% and 97%, respectively, for 24 hr Holter monitoring. Thus, in light of the serious and potentially devastating consequences of missing true positives on 24 hr Holter monitoring, we would favor identifying more false positives with 72 hr Holter in clinical practice.

Overall left ventricular function is clearly an important determinant of clinical outcome in patients with ventricular tachyarrhythmias. Emphasizing the importance of this in prognosis is the fact that patients with clinical arrhythmic events in our population had significantly lower ejection fractions. However, further analysis has revealed Holter results to be a significant independent discriminator of outcome.

In summary, it appears that in select patients with a history of sustained ventricular tachycardia who manifest nonsustained ventricular tachycardia on baseline Holter monitoring, the ability to predict the clinical efficacy of amiodarone by early serial Holter monitoring is reliable and provides a noninvasive, practical, cost-effective method that would be accessible to most medical communities. Despite the long half-life of amiodarone, early suppression of nonsustained ventricular tachycardia would identify low-risk patients for recurrent events and thus promote hospital discharge within 2 weeks of institution of therapy. Patients considered at continued high risk, based on persistent ventricular tachycardia on Holter, could be considered for alternative therapy (other antiarrhythmic drugs, surgery, or implantable cardioverter-defibrillator) early in the course of treatment, thereby obviating amiodarone side effects frequently seen with long-term therapy.

The extension of the use of Holter monitoring in evaluating efficacy in patients with a history of sustained tachyarrhythmias but who do not manifest spontaneous nonsustained ventricular tachycardia on baseline Holter monitoring must be viewed with caution. Such patients may represent approximately 12% to 45% of the sustained ventricular tachyarhythmia populations previously reported. In these patients serial Holter monitoring during amiodarone therapy may be of limited value and the optimal means of assessing clinical efficacy is not known.

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