Ambulatory Arrhythmias in Resuscitated Victims of Cardiac Arrest

W. Douglas Weaver, M.D., Leonard A. Cobb, M.D., and Alfred P. Hallstrom, Ph.D.

SUMMARY One hundred forty-four patients with coronary heart disease previously resuscitated from out-of-hospital ventricular fibrillation underwent 24-hour ambulatory ECG monitoring 5 months (median) after cardiac arrest. Patients were then followed for an average of 31.7 months. Fifty-one patients died, 32 from subsequent unexpected cardiac arrest.

One hundred twenty-nine patients (90%) had uniform ventricular ectopy. Two-thirds had complex ventricular ectopy (bigeminy/trigeminy, repetitive forms or frequent multiforms). Complex ectopy, present in 20% or more of the 30-minute recording intervals, occurred in 18 of the patients (56%) who developed subsequent cardiac arrest, compared with 26 of 92 (28%) who survived (p < 0.005, specificity 72%, relative risk 2.3). Other forms of ventricular ectopy, e.g., uniform, multiform and repetitive beats, were more sensitive but less specific predictors of death or recurrent ventricular fibrillation.

Complex ventricular ectopy was associated with certain clinical histories: it occurred in 95% of patients with a history of congestive heart failure and in 79% with remote myocardial infarction, compared with 59% and 56% without these histories (p < 0.001 and p < 0.01). As expected, mortality was also greater in patients who had these clinical characteristics. Complex ectopy was related to mortality regardless of the clinical history.

APPROXIMATELY ONE-THIRD of patients resuscitated from the sudden cardiac death syndrome can be expected to develop a second episode of cardiac arrest within 2 years.1 Earlier reports have shown that certain clinical histories2 and cardiac catheterization findings3 can distinguish groups of patients at relatively high risk of having a recurrent episode of ventricular fibrillation (VF). Prognosis can also be determined using noninvasive tests that detect myocardial ischemia, infarction and left ventricular dysfunction.4–6

We examined the forms and frequency of ventricular ectopy during a single ambulatory recording in previously resuscitated victims and have correlated arrhythmias with clinical histories and subsequent outcome. The purpose of this study was to determine whether particular forms of ectopy increase the risk of subsequent cardiac arrest.

Methods

One hundred forty-four patients previously resuscitated by the Seattle Fire Department’s emergency care system participated in this study. Only patients who had suspected coronary heart disease were included. This diagnosis was based on the presence of at least one of the following: history consistent with typical angina pectoris or prior myocardial infarction, Q waves on the ECG, findings from coronary arteriography, or evidence of acute myocardial necrosis associated with the episode of cardiac arrest. Patients with other cardiac diagnoses were excluded.

The episodes of VF occurred between 1972 and 1976. All patients were followed through April 1978; all had follow-up for at least 2 years.

Patients volunteered to be followed in a research clinic for VF survivors. About 70% of patients who survived out-of-hospital VF (patients discharged from any of the city’s hospitals) volunteered to be evaluated in this clinic. Clinic personnel abstracted the cardiovascular history before VF and determined the circumstances of the cardiac arrest. Physicians interviewed and examined the patients and reviewed the medical record, which included the resuscitation report. The patients had been initially managed in any of the 14 coronary care units in the city, and laboratory measurements were not uniformly available; only 110 of the 144 patients had serum lactate dehydrogenase (LDH) isoenzyme determinations during hospitalization. Coronary angiography was done for clinical indications as determined by the patient’s personal physicians. The patient’s physician gave permission for the clinic evaluation and ambulatory monitoring.

Twenty-four hours of ambulatory ECG were recorded, usually on the day after the first research clinic visit. The recordings were made using a single-channel Avionics recorder. Patients were asked to perform their usual daily activities and to keep diaries during the recording period. The average interval from the episode of VF to the ambulatory recording was 11.1 ± 12.3 months (± sd). However, most patients were monitored within the first few months of the episode; the median interval was 5 months.

The magnetic tapes were analyzed manually by a skilled technician using an Avionics Electrocardioscanner. Arrhythmias were verified by direct paper writeout and reviewed. Patients with fewer than 9 hours of technically suitable recording were excluded. Findings were validated by replicate analysis of approximately every fifteenth tape.

Each 30-minute interval of the ambulatory ECG was separately analyzed and the following findings were recorded: the forms of ventricular ectopy during the interval (i.e., uniform, multiform and repetitive) and the estimated peak rate for each form (0, 1–6, 7–30, 31 or more per half hour). Bigeminy/trigeminy, repetitive

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forms, and frequent (more than 30 per interval) multiform beats were considered to be complex ventricular ectopy. The number of 30-minute intervals that showed each form were then summed for each patient and used to calculate the proportion of intervals with arrhythmias. There was an average of 40.2 interpretable intervals (20 hours) per tape for the 144 patients studied.

The patients were followed at least 2 years (average ± SD 31.7 ± 16.2 months) after the initial recording. The clinical and ambulatory ECG characteristics of 92 patients who survived were compared to those of 32 patients who developed subsequent cardiac arrest (24 who died from unexpected cardiovascular collapse and eight who were resuscitated from a second episode of VF). Nineteen additional deaths were considered to be nonsudden (usually in-hospital events due to heart failure, myocardial infarction or shock). The status of one patient was unknown. Survival was calculated by life-table analysis.

Seventy-seven patients (53%) were taking one or more antiarrhythmic drugs during the ambulatory monitoring; subsequently, 28 were taking procainamide, 25 quinidine, 15 propranolol and nine combinations of these drugs. Therapy was prescribed by the patient’s personal physician and not controlled by the research clinic. Summaries of studies performed in the clinic were forwarded to the patent’s physician and, in turn, have influenced subsequent therapy. We compared clinical and ambulatory ECG findings in patients taking antiarrhythmic drugs with findings in patients not receiving such agents.

The significance of differences in continuous variables was determined by t test and discrete variables by chi-square analysis. A logistics model was used in a multivariate analysis of clinical history, outcome and complex ventricular ectopy. Sensitivity is the percentage of patients who died suddenly with a given abnormality. Specificity was used to indicate the ability of the test to recognize a survivor: number of true normals detected/total number of normals; i.e., number of survivors without a given abnormality/total number of survivors. Relative risk was derived as the ratio of the percentage of patients having an abnormal finding who developed subsequent cardiac arrest to the percentage of patients not having the finding who developed subsequent cardiac arrest.

**Results**

**Patients**

We studied 117 men and 27 women. Their average age at the initial resuscitation was 61.1 ± 10.3 years. One hundred nine patients (76%) had a history of cardiovascular disease before VF. Sixty-two (43%) had typical exertional chest pain; 50 (35%) had hypertension; 53 (38%) had a history consistent with remote myocardial infarction, which had occurred an average of 4.9 years (range 1 week to 20 years) before the episode of VF. Eighteen patients (12%) had VF within 1 year of the prior infarction. Twenty-six patients had congestive heart failure before the episode of cardiac arrest. These prevalences of prior cardiovascular abnormalities are similar to earlier reports in patients resuscitated from out-of-hospital VF.

Thirty-three patients (23%) had developed ECG evidence consistent with acute transmural myocardial infarction (Q waves) during hospitalization after resuscitation. Forty-four of 110 patients (40%) in whom LDH isoenzymes were measured had evidence of myocardial necrosis. The 51 subsequent fatal events included 32 episodes (63%) of unexpected cardiac arrest and 19 nonsudden deaths.

**Arrhythmias**

A normal recording was unusual in these patients. Ninety percent had one or more ventricular ectopic beats, and 62 patients (43%) showed uniform ventricular ectopy in more than half the total number of recording intervals. Other forms of ventricular ectopy were also common: 110 patients (76%) showed multiform ventricular ectopy, 70 (49%) had bigeminy or trigeminy, and 76 (53%) had couplets or triplets (two or three consecutive ectopic beats). Thirteen patients (9%) developed nonsustained ventricular tachycardia (four or more consecutive beats) (fig. 1).

**Clinical Histories, Acute Necrosis at the Time of VF, and Ambulatory Arrhythmias**

The presence of complex ventricular ectopy (i.e. high-rate multiforms, ventricular bigeminy/trigeminy or repetitive ectopy) was associated with certain clinical characteristics (table 1). Sixty-one patients (68%) who had VF without ECG evidence of acute infarction showed complex ventricular ectopy during the ambulatory recording compared to 16 of 33 patients (48%) who developed acute infarction at the time of VF (p < 0.06). Complex ectopy was more common in patients with clinical histories of heart failure, present in 25 of

![Figure 1](https://example.com/figure1.png)
26 patients (96%), or remote infarction, present in 42 of 53 patients (79%), than in patients not having these histories (in 69 of 105 patients [59%] and 49 of 87 patients [56%] respectively, $p < 0.001$ and $p < 0.01$). Neither gender nor history of angina or hypertension correlated with the occurrence of complex ectopy. Uniform ventricular ectopy was ubiquitous and not related to any particular clinical characteristic (table 1).

### Ambulatory Arrhythmias and Subsequent Outcome

Ninety-two patients survived the 2½-year follow-up period and 51 had a fatal event (32 cardiac arrests and 19 nonsudden deaths). Histories of congestive heart failure and remote myocardial infarction were more common in patients who died than in those who survived (table 2). Primary VF (arrest not associated with acute infarction) was a sensitive, but not a specific, predictor of outcome.

Neither presence nor absence, peak rate or number of intervals with uniform ventricular ectopy was related to survival. Other forms, however, were associated with subsequent episodes of cardiac arrest. Bigeminy/ trigeminy, multiforms and repetitive forms of ventricular ectopy during ambulatory monitoring were each associated with subsequent episodes of sudden cardiac arrest (fig. 2). Multiforms and bigeminy/trigeminy occurred at high peak rates or in more than half the total number of intervals in about a third of patients. Multiforms at rates of 30 or more per interval were a better predictor than mere presence or absence (specificity 72% vs 28% and sensitivity 62% vs 87%); however, the density of other ectopic forms did not enhance prediction. Ventricular couplets and tachycardia occurred infrequently during the 24-hour recording, usually in fewer than eight intervals.

The sensitivity of complex ventricular ectopy in predicting cardiac arrest was high (84%), but specificity was disappointing (40%) (table 2). A somewhat more useful predictor of cardiac arrest was complex ectopy, present in 20% or more of the total number of recording intervals. Patients with this amount of rhythm disorder more often died suddenly during follow-up. This was true whether we considered total outcome (table 2).

![Figure 2](http://circ.ahajournals.org/)

**Figure 2.** Subsequent cardiac arrest related to the presence (+) or absence (−) of specific forms of ventricular ectopy (VE). The rate of cardiac arrest was greatest in those patients with high-peak-rate (>30/interval) multiform ectopy and in those with complex VE present in 20% or more of the total number of recording intervals. No single ectopic form or combination of ectopic forms was of high predictive value. Patients who had subsequent nonsudden death are excluded in the comparisons.

### Table 1. Clinical Characteristics Related to Ventricular Ectopy in Patients Previously Resuscitated from Ventricular Fibrillation

<table>
<thead>
<tr>
<th>History (no. of pts in group)</th>
<th>Pts with uniform VE</th>
<th>Pts with complex VE†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>(%) of group</td>
</tr>
<tr>
<td>Angina (62)</td>
<td>53</td>
<td>85%</td>
</tr>
<tr>
<td>No angina (80)</td>
<td>76</td>
<td>95%</td>
</tr>
<tr>
<td>HT (50)</td>
<td>42</td>
<td>84%</td>
</tr>
<tr>
<td>No HT (93)</td>
<td>88</td>
<td>95%</td>
</tr>
<tr>
<td>CHF (26)</td>
<td>24</td>
<td>92%</td>
</tr>
<tr>
<td>No CHF (116)</td>
<td>105</td>
<td>91%</td>
</tr>
<tr>
<td>Remote MI (53)</td>
<td>47</td>
<td>89%</td>
</tr>
<tr>
<td>No remote MI (87)</td>
<td>78</td>
<td>90%</td>
</tr>
<tr>
<td>Acute transmural MI with VF‡(33)</td>
<td>31</td>
<td>94%</td>
</tr>
<tr>
<td>No transmural MI with VF(90)</td>
<td>86</td>
<td>96%</td>
</tr>
<tr>
<td>Men (n = 117)</td>
<td>105</td>
<td>90%</td>
</tr>
<tr>
<td>Women (n = 27)</td>
<td>24</td>
<td>89%</td>
</tr>
</tbody>
</table>

*The p values are indicated when the significance of the difference in the proportion of patients having complex VE with and without a given condition is less than 0.1.

†Complex VE is defined as bigeminy or trigeminy, repetitive VE, or highest peak rate multiform VE.

‡Twenty-one patients are not included: 14 with MI of indeterminate age, five with left bundle branch block and two for whom the initial ECGs were not available.

Abbreviations: CHF = congestive heart failure; HT = hypertension; MI = myocardial infarction; VE = ventricular ectopy; VF = ventricular fibrillation.
TABLE 2. Clinical and Ambulatory Electrocardiographic Findings in 143 Patients with Out-of-Hospital Ventricular Fibrillation: Comparison of Those Who Developed Subsequent Sudden Death and Those Who Survived

<table>
<thead>
<tr>
<th>Clinical characteristics*</th>
<th>Ambulatory arrhythmias</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Uniform VE</td>
</tr>
<tr>
<td>Angina</td>
<td></td>
</tr>
<tr>
<td>Remote MI</td>
<td></td>
</tr>
<tr>
<td>CHF</td>
<td>83 (90%)</td>
</tr>
<tr>
<td>No ATMI with VF</td>
<td>13 (42%)</td>
</tr>
</tbody>
</table>

92 survivors (n = 92 group) 

32 sudden cardiac arrest (n = 32 group) 

19 nonsudden deaths (n = 19 group) 

$p^\dagger$ The $p$ values are indicated when $p < 0.01$ for survivors vs sudden cardiac arrest victims. 

Abbreviations: ATMI = acute transmural infarction (new Q waves); CHF = congestive heart failure; MI = myocardial infarction; VE = ventricular ectopy; VF = ventricular fibrillation.

| Relative risk$^\ddagger$ | 0.9 | 2.4 | 1.8 | 2.5 | 0.7 | 2.2 | 2.0 | 3.0 | 2.8 | 2.3 |

*Clinical history unknown in up to four cases; percentages adjusted for known cases. 

†Complex VE is expressed as occurring in one or more of the 30-minute recording intervals (VE) and in 20% or more of the intervals (VE_{20}). 

‡Includes 24 patients who died from unexpected cardiac collapse and eight others resuscitated from a second episode of VF. The percentage figure also denotes sensitivity of an observation related to the prediction of recurrent cardiac arrest.

Drug Therapy and Arrhythmias

Probably as a result of nonrandom assignment, different clinical history profiles were present in the treatment groups. Patients who were taking procainamide, quinidine or combinations of antiarrhythmic drugs more often had clinical histories that would place them at risk for subsequent cardiac arrest than did patients who were taking propranolol or no antiarrhythmic treatment. The incidence of complex ventricular ectopy was similar in all five treatment groups. There were significantly more fatal events in the procainamide and combination drug groups than in those receiving no antiarrhythmic drug. This difference in mortality probably reflects the greater prevalence of clinical risk factors for recurrent VF in the drug groups. Mortality was lowest in the group that received propranolol (table 3).

Discussion

Mortality in the months after acute myocardial infarction has been shown to be associated with ventricular ectopy during ambulatory monitoring. This relationship appears to pertain to both sudden and
nonsudden deaths. Recent infarction may enhance ventricular ectopy, and, accordingly, the predictive value of arrhythmias in that setting may not be representative of the majority of patients who develop cardiac arrest outside the hospital. We found that uniform ventricular ectopy was ubiquitous in patients previously resuscitated from VF. Quantitation of both peak rates and number of half-hour intervals with uniform ectopy was not helpful. Uniform ectopy is thus a poor predictor of subsequent cardiac arrest.

More than half of our patients had complex ectopy. In this prospective evaluation, both repetitive beats and frequent multiform ectopy were more prevalent in those who died suddenly compared with survivors. However, no single ectopic form was both a sensitive and specific predictor. The best means of predicting sudden death was quantitating the rate of occurrence of multiforms and the number of intervals of complex ectopy. Over half the patients who died suddenly demonstrated these findings. Although a strong statistical association exists between complex ectopy during ambulatory monitoring and subsequent cardiac arrest, ambulatory arrhythmias are of limited value in predicting outcome because they are neither highly sensitive nor specific. In addition, complex ventricular ectopy was only associated with subsequent cardiac arrest when recorded within a year of the prior episode of VT. Nonetheless, dynamic monitoring can be used to stratify risk in these patients. Histories of heart failure and remote infarction are associated with both outcome and the occurrence of complex ectopy. However, the risk of sudden death increased as the number of intervals with complex ectopy increased, in patients with and without these risk histories.

We have not systematically examined the reproducibility of 24-hour studies in all patients, although many have had multiple recordings, with few differences displayed from tape to tape. Others have reported that patients with coronary heart disease who have both complex and high-peak-rate ectopy on one tape show similar arrhythmias on subsequent recordings. Therefore, we believe that the findings in 24-hour tapes in our groups of patients are likely to be reproducible. We do not suspect that the forms and frequency of ectopy change dramatically on the day of cardiac arrest; instead, conditions that allow VF to be manifest may change. Ectopy that was benign on one day may initiate cardiac arrest on another.

Our study was not designed to test the efficacy of conventional antiarrhythmic therapy. However, in ex-
amining for its effect, we found no differences in the frequency of complex ectopy occurring in each treatment group. This may not be surprising, as there is little convincing evidence that routine chronic administration of widely available membrane-active drugs either eliminates complex ectopy in previously resuscitated patients or enhances survival. Some have reported that antiarrhythmic drugs may prevent the recurrence of cardiac arrest in these victims, with \(^22\) and without \(^22,23\) altering the occurrence of complex ectopy during ambulatory monitoring. The value of reports such as these and ours however, is limited because in the former, patient entry was selective, and in all, drug therapy was not randomized. \(^24\) The procainamide-treated patients in this report actually fared worse than those who received no drugs, but this may be due to the greater prevalence of clinical risk histories in the procainamide treatment group.

Complex ectopy in resuscitated patients is frequent compared to the incidence of recurrent VF. Our findings suggest that further characterization of ambulatory arrhythmias is unlikely to enhance the ability to predict the sudden death syndrome. Efforts should be aimed at clarification of the electrophysiologic environment in which complex forms and VF are generated. \(^25-29\)

**References**

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Sudden Death Recorded During Holter Monitoring

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SUMMARY Six instances of sudden death were recorded by Holter monitoring, which showed ventricular fibrillation in five and a bradyarrhythmia in one. Complex ventricular ectopic activity preceded cardiac arrest in five patients, including the one with the bradyarrhythmic arrest. Two patients with chronic bifascicular block arrested as a result of ventricular fibrillation. Fifteen case reports from the literature are reviewed. The composite profile includes advanced myocardial disease (present in all cases), complex ventricular ectopic activity, R-on-T initiation of the terminal rhythm except in patients with prolonged QT interval, and variations in cycle length preceding the onset of ventricular tachycardia or fibrillation. The role of supraventricular mechanisms in sudden death is uncertain.

A few reported cases of sudden death outside of intensive care units have been documented. In this report, we describe the clinical and electrocardiographic features of six additional patients.

Materials and Methods

Sudden death is defined as unexpected death within 60 minutes of the onset of symptoms. Six patients whose Holter monitors showed arrhythmias incompatible with life and who died or required advanced life support for resuscitation between January 1, 1977, and December 31, 1980, were identified. All the patients were ambulatory. Three episodes occurred at St. Vincent Hospital, Worcester, with one survival; the other three occurred at the patient's home, again with one survival. The clinical information was obtained from the hospital records.

The Holter monitoring was performed by Del Mar Avionics Model 445 recorders. The tapes were analyzed using an Advance Med Model Techniscan 7000 scanner.

Case Reports

Case 1

The patient was a 57-year-old white man with a 4-week history of angina pectoris who was admitted with acute anterior myocardial infarction complicated by runs of ventricular tachycardia and transient heart failure. During an uneventful recovery, medications were reduced to digoxin, 0.25 mg/day, and quinidine sulphate, 300 mg four times daily. A modified stress test 24 days after admission elicited frequent multiform and repetitive ventricular ectopic complexes (VECs) associated with further ST-segment elevation. A Holter monitor study on the same day showed infrequent unifocal VECs and episodes of atrial fibrillation. Two days later a repeat study was in progress when palpitations signaled the onset of ventricular tachycardia (fig. 1). He had no other symptoms until carotid sinus massage was applied, when he suddenly collapsed, pulseless; the tachycardia continued at a faster rate, resisted cardioversion and degenerated into frank fibrillation 40 minutes after its onset. Asystole occurred 3 minutes later. The recording made before cardiac arrest showed frequent multiform VECs, some in dimorphic couplets (fig. 1). The T-wave inversion became pronounced before ventricular tachycardia initiated by an R-on-T VEC in the wake of a postextrasystolic pause. The autopsy showed left ventricular hypertrophy and extensive recent anterior infarction.

Case 2

This 83-year-old white man was admitted for recurrent colonic bleeding. The physical examination showed mild left-sided weakness, a grade 3/6 aortic systolic murmur and a blood pressure of 150/100 mm Hg. He subsequently had episodes of cyanosis, unresponsiveness and restlessness. During one of them, he was apneic in his chair, apparently pulseless; immediately afterwards he became alert, with a heart rate of 100 beats/min and a blood pressure of 190/100 mm Hg. The ECGs, unchanged from the previous year, showed left ventricular hypertrophy and ST-T-wave...
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