SUMMARY Sixty-four patients with coronary artery disease (CAD) who had been resuscitated from out-of-hospital ventricular fibrillation (VF) underwent cardiac catheterization and angiography. The majority (72%) had a previous history of cardiovascular disease; in the remaining 28%, VF was the first manifestation of CAD. Advanced coronary atherosclerosis was a common finding; 94% of the patients had severe stenoses (70% or greater diameter narrowing) in one or more of the major coronary arteries, and most (70%) had ventricular wall contraction abnormalities. In over half of the patients, coronary anatomy was potentially suitable for complete revascularization.

During an average follow-up period of 20.4 months, fourteen of the 64 patients developed a second episode of VF and/or died suddenly (VF/SD). In an attempt to identify characteristics which might be of prognostic value, the clinical, hemodynamic, and angiographic characteristics of this group were compared to those patients who had a single episode of VF and survived during follow-up. Patients who developed recurrent VF/SD had more triple vessel CAD ($P < 0.01$), lower ejection fractions ($P < 0.05$), and far more severe abnormalities of left ventricular contraction ($P < 0.001$). These results indicate that angiographic findings can identify individuals at high risk for recurrent VF and also suggest that myocardial scarring may be an important factor in the initiation of ventricular fibrillation and in its recurrence.

SUDEN CARDIAC DEATH is a common manifestation of ischemic heart disease and accounts for a large proportion of deaths from coronary atherosclerosis. In recent years, recognition of this fact has stimulated the development of mobile coronary care units and rapid response emergency care systems which have demonstrated that many victims of out-of-hospital ventricular fibrillation (VF) can be resuscitated. In the first four years of operation, the Seattle emergency medical care system resuscitated 234 patients who ultimately returned home as functional individuals. In these patients, clinical evidence indicated that the majority of episodes of VF were “primary” dysrhythmic events and not secondary to acute myocardial infarction. During an average follow-up of 14 months (range 1–50 months), 26% of these 234 patients developed a second episode of VF and/or died suddenly.

Since VF might be prevented by prophylactic therapy, it is important to identify indicators predictive of this lethal dysrhythmia. Autopsy studies have demonstrated that the majority of victims of sudden cardiac death had severe coronary stenoses. Hypertension, electrocardiographic evidence of left ventricular hypertrophy, and frequent premature ventricular beats are among the clinical findings which may help identify patients with ischemic heart disease who are at greater risk to develop sudden cardiac death.

However, these factors are nonspecific in a given patient. In order to understand the underlying pathophysiologic mechanisms leading to the development of VF, we have examined the coronary anatomy and left ventricular characteristics of 64 patients successfully resuscitated from out-of-hospital VF. In addition, to identify further those angiographic and hemodynamic findings associated with VF, we have compared these observations to a subgroup of 14 patients who developed recurrent ventricular fibrillation or sudden death (VF/SD) during follow-up.

Angiographic Findings and Prognostic Indicators in Patients Resuscitated from Sudden Cardiac Death

W. DOUGLAS WEAVER, M.D., GERALD S. LORCH, M.D., HERNAN A. ALVAREZ, M.D., AND LEONARD A. COBB, M.D.
Methods

The Seattle Fire Department operates a comprehensive, rapid response emergency care system, serving a community of approximately one-half million people. Resuscitation from circulatory arrest, particularly in patients with VF, is emphasized heavily. During the four years ending in March 1974, more than 1100 patients with VF were treated outside the hospital. Forty-three percent of the patients were initially resuscitated, and two hundred thirty-four were discharged from the hospital as long-term survivors. During the follow-up period, ending April 15, 1975, the clinical status and outcome of the patients were assessed periodically.

Seventy-nine of these patients underwent cardiac catheterization and coronary angiography. Fifteen of them had valvular or presumed myocardial/metabolic disorders and were excluded from the study. This report describes the angiographic and hemodynamic findings in 64 patients with angiographically demonstrated CAD. Patients were selected for study by the physicians responsible for their care. In most cases the decision to perform arteriography was precipitated by the episode of VF. In 10 patients (16%), coronary arteriography, done for evaluation of angina pectoris, preceded the episode of VF. The patients studied were, on the average, younger than the total resuscitated group (55 vs 59 years). Although not quantifiable, individuals with overt congestive heart failure and other disabling disorders were generally not studied, whereas patients with a history of angina tended to be selected for catheterization. The time from VF to angiographic study averaged 3.8 months in fifty-four patients studied after VF. The patients have been followed for an average of 20.4 months subsequent to out-of-hospital VF.

Coronary arteriography by either Sones or Judkins technique was done in multiple views using 35mm cineangiography and/or large cut-films. Biplane left ventricular angiograms were performed in both the anterior and lateral projections in fifteen patients, and single plane (30° right anterior oblique projection) angiograms were performed in the others. Left ventricular pressures were recorded through fluid-filled systems using pressure transducer and standard laboratory recorder.

The coronary angiograms were reviewed by at least two of the authors who evaluated the coronary anatomy, estimated the percent diameter reduction of each stenotic lesion, and judged the technical feasibility of saphenous vein bypass grafting based on the arteriographic anatomy alone, without knowledge of clinical history or ventricular function. The surgical feasibility of bypass grafting of each stenotic artery was graded as excellent, acceptable, poor, or impossible. A grade was chosen after consideration of the caliber of vessel distal to a stenosis plus the presence of distal lesions, in the same way one would select patients for surgical therapy of disabling angina pectoris. If there was disagreement in percent stenosis or surgical feasibility, a third observer entered an evaluation. The three observations were then averaged. The extent of coronary disease was determined by involvement of the left anterior descending (LAD), circumflex (CX), and right coronary (RCA) arteries. Stenosis of the LAD diagonal branches was not counted. CX system involvement was considered present if there was narrowing of either the main CX or a large obtuse marginal branch. Left main stenosis was counted as two vessel involvement. No major artery was counted more than once.

The ventriculograms were analyzed as follows: anterior, lateral, or right anterior oblique projections were each divided into four equal segments. Two or more readers determined if each segment contracted normally or demonstrated hypokinesia, akinesia, or apparent paradoxical wall motion. The extent of ventricular wall abnormality was expressed as a percentage by dividing the total number of segments in all views into the number of abnormal segments in all views. The presence of mitral regurgitation was graded qualitatively (absent, trace, moderate, or severe).

Quantitative analysis of left ventriculography was possible in 51 of 64 angiograms. Silhouettes were drawn of the left ventricular cavity when it was largest (end diastole) and when it was smallest (end systole). Volume was calculated using the area-length method and corrected for image magnification using a calibration factor derived from a grid filmed at the level of the left ventricle. If the correction factor for a patient was not known, only ejection fraction was calculated. End-diastolic volume (EDV) and end-systolic volume (ESV) were then used to compute ejection fraction: $\frac{EDV-ESV}{EDV}$. The left ventricular end-diastolic pressure was chosen as that point on the A wave preceding the rapid rise.

The 64 patients were separated into two groups. Group one contained 45 individuals who survived during the follow-up period (averaging 21 months) and who did not experience a second episode of VF. A second group consisted of 14 patients who during the follow-up period after discharge from the hospital developed another episode of VF (11 patients) and/or died suddenly (3 patients who had sustained VF but who were not immediately attended by the mobile care unit). The findings in these two groups were compared using Chi-square or Student's $t$-tests. There were five additional patients who died during follow-up but whose deaths were not due to recurrent VF/SD. Four of these deaths occurred after a prolonged period of hospitalization, and the fifth death was witnessed with the circumstances surrounding the time and mode of death unknown.

Seventy percent of the entire group of patients was on anti-dysrhythmic drug therapy at the time of their first follow-up visit, including 12 of the 14 patients who developed recurrent VF/SD. However, the drug levels and the apparent efficacy of therapy was not known in these individuals.

Results

Characteristics of the Patients

Seventy-two percent of the 64 patients with angiographically demonstrated CAD were recognized as having cardiovascular disease diagnosed prior to the first episode of VF. Twenty-nine (45%) reported a history of angina; ten (16%) had been treated for congestive heart failure; and twenty-two (34%) were known to be hypertensive (table 1). In thirty-two cases (50%), pathologic Q waves were present on the resting electrocardiogram. VF was associated with acute myocardial infarction in nineteen patients (30%); in the remainder, VF was a primary dysrhythmic event. The
The age of the patients ranged from 31 to 72 and averaged 55 years.

**Coronary Angiographic Findings**

Patients who survived out-of-hospital VF usually had extensive CAD. Sixty of sixty-four patients (94%) had at least one major artery with 70% or greater reduction in diameter. Coronary angiograms in the four other patients showed only mild CAD: two showed 50% lesions and two demonstrated 20–30% stenoses. Severe stenoses involving two coronary arteries were observed in eighteen patients (28%), and twenty-one (33%) had triple vessel disease. Forty-three (67%) of the arteriograms demonstrated at least one total occlusion. Multiple occlusions were frequently apparent; nineteen patients (30%) had total occlusion of two or more of the major arteries (fig. 1).

Distribution of coronary lesions showed nearly equal numbers of stenoses in the left anterior descending (LAD), circumflex (CX), and right coronary arteries (RCA) (fig. 2). Similarly, in those twenty-one patients with severe narrowing of only a single major artery, there was no significant difference in the location of stenoses (RCA = 38%, CX = 24%; LAD = 38%). The left main artery was moderately stenosed (50–70%) in only four patients, and severely narrowed in one.

Collateral arteries were frequently observed; the selective coronaries outlined one or more collateral pathways in 49 patients (75%), and two or more collaterals in 20 patients (37%). However, considering all 165 vessels with severe stenosis, only 39% of areas distal to severe narrowings were supplied by way of an accessory circulation.

In thirty-four patients (53%), the coronary anatomy was judged potentially suitable for complete revascularization.

**Left Ventricular Function**

The end-diastolic pressure averaged 13.1 ± 0.9 (SE) mm Hg (range 2 to 33 mm Hg), and the mean ejection fraction was 0.48 ± 0.03. End-diastolic volume averaged 108 ± 8.4 ml/m² and exceeded the normal limit (100 ml/m²) in 55% of the fifty-one studies in which this measurement could be obtained (table 2).
Characteristics of Patients Developing Recurrent VF/SD

The 45 patients surviving during follow-up were compared to 14 patients who developed a recurrent episode of VF/SD. The average age of the groups was comparable, 55 years and 53.1 years, respectively. A history of congestive heart failure was significantly more common in the recurrent VF/SD group (P < 0.05); however, other manifestations of cardiovascular disease were reported in approximately equal frequency (table 1).

The angiograms of those patients who developed recurrent VF/SD during follow-up showed significantly more extensive coronary and myocardial abnormalities. Triple vessel disease (70% or greater stenosis) was seen in 64% of these patients (9 of 14), compared to 22% of the survivors (10 of 45) (P < 0.01) (fig. 3). Of the 28 patients with mild or moderate CAD (less than 70% stenosis in one or two vessels), only one developed recurrent VF/SD. Coronary collateral circulation was observed in about two-thirds of each group; however, there were fewer collaterals perfusing areas distal to severe stenoses in patients who had a recurrent episode of VF/SD (15 collaterals for 49 vessels compared to 44 collaterals for 103 vessels).

There was no appreciable difference in the average end-diastolic pressure or end-diastolic volume between the groups; however, the mean ejection fraction was significantly lower in those who developed recurrent VF/SD compared to survivors (0.39 vs 0.51, P < 0.05). The left ventricular angiogram demonstrated significant differences in contraction between the two groups (table 2). Those patients who developed recurrent VF/SD showed far greater impairment of contraction: in 10 of 14 angiograms (71%), over half of the segments contracted abnormally. Such extensive wall motion abnormality was seen in only nine of forty-five survivors (20%) (P < 0.005). In addition, paradoxical wall motion, observed in seven (50%) recurrent VF/SD patients, was seen in only four survivors (9%) (P < 0.001). Normal contraction was present in only one patient who developed recurrent VF/SD compared to 15 of 45 survivors (P < 0.06) (fig. 4).

Discussion

Rapid response emergency care systems can be effective in resuscitating victims of out-of-hospital VF. In Seattle, over a fourth of persons found in VF will ultimately return home as functional individuals. While pre-hospital emergency care can substantially reduce the number of out-of-hospital sudden cardiac deaths, prevention of this syndrome would be a preferable approach; however, this cannot be realized until individuals at high risk can be recognized. Although it is not possible to identify the immediate physiologic events that result in VF, it is important to define the pathologic conditions present in the sudden cardiac death syndrome in order to understand the mechanisms leading to this dysrhythmia. While studies have been done in autopsied

**Table 2. Angiographic and Hemodynamic Observations**

<table>
<thead>
<tr>
<th>Coronary anatomy</th>
<th>All patients</th>
<th>VF X 1</th>
<th>RVF/SD</th>
<th>RVF/SD</th>
</tr>
</thead>
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<tr>
<td></td>
<td>No. (percent)</td>
<td>No. (percent)</td>
<td>No. (percent)</td>
<td>No. (percent)</td>
</tr>
<tr>
<td>≥70% stenosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 vessel</td>
<td>21 (33)</td>
<td>18 (40)</td>
<td>2 (14)</td>
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<tr>
<td>2 vessel</td>
<td>18 (28)</td>
<td>13 (29)</td>
<td>3 (21)</td>
<td></td>
</tr>
<tr>
<td>3 vessel</td>
<td>21 (33)</td>
<td>10 (22)</td>
<td>9 (64)</td>
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</tr>
<tr>
<td>100% stenosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 vessel</td>
<td>24 (38)</td>
<td>18 (40)</td>
<td>4 (29)</td>
<td></td>
</tr>
<tr>
<td>2 vessel</td>
<td>11 (17)</td>
<td>7 (16)</td>
<td>4 (29)</td>
<td></td>
</tr>
<tr>
<td>3 vessel</td>
<td>8 (12)</td>
<td>4 (9)</td>
<td>3 (21)</td>
<td></td>
</tr>
<tr>
<td>No. of collaterals</td>
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<td>32 (71)</td>
<td>9 (64)</td>
<td></td>
</tr>
<tr>
<td>No. with anatomy suitable for total revascularization</td>
<td>34 (53)</td>
<td>25 (56)</td>
<td>3 (21)</td>
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<td>Left ventricular function</td>
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<tr>
<td>EDP &gt;15 mmHg</td>
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<tr>
<td>EDV &gt;100 mL/m²†</td>
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<td>6 (67)</td>
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<tr>
<td>Ejection fraction</td>
<td>&lt;0.50‡</td>
<td>30 (50)</td>
<td>20 (47)</td>
<td>9 (64)</td>
</tr>
<tr>
<td>Moderate mitral regurgitation</td>
<td>4 (6)</td>
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<tr>
<td>Extent of left ventricular contraction abnormality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None (normal)</td>
<td>19 (30)</td>
<td>15 (33)</td>
<td>1 (7)</td>
<td></td>
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<td>&lt;25% abnormal</td>
<td>10 (16)</td>
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<tr>
<td>Types of contraction abnormalities</td>
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<tr>
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<td>15 (33)</td>
<td>1 (7)</td>
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<td>12 (27)</td>
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<td>14 (31)</td>
<td>3 (21)</td>
<td></td>
</tr>
<tr>
<td>Paradoxical wall motion</td>
<td>11 (17)</td>
<td>4 (9)</td>
<td>7 (50)</td>
<td></td>
</tr>
</tbody>
</table>

*VF X 1 = Patients who survived during follow-up after VF.*
†RVF/SD = Patients who developed recurrent VF or died suddenly after discharge from the hospital during the follow-up period ending April 1975.
‡Ejection fraction determined in 60 patients.
§Ejection fraction determined in 51 patients.
††End-diastolic volume measurements possible in 51 patients.
‡‡Abbreviations: EDP = end-diastolic pressure; EDV = end-diastolic volume.

**Figure 3. Extent of coronary stenosis in patients surviving during follow-up (VF X 1) and in patients who developed recurrent ventricular fibrillation and/or sudden death (RVF/SD). The latter group showed significantly more extensive coronary artery disease.**
populations there are no previous reports on the angiographic characteristics of survivors of VF. Autopsy provides some information of the coronary anatomy and myocardial scarring. However, to be of clinical prognostic value, assessment of ventricular function, coronary arteries, coronary collateral circulation, and mitral valve apparatus must be obtained by cardiac catheterization in a group of survivors of VF/SD.

Ninety-four percent of our patients had severe (70% or greater stenosis) coronary artery atherosclerosis involving one or more vessels — a finding in agreement with previous autopsy series. Stenoses in multiple vessels were frequently noted; 61% had two or more major vessels with severe stenosis; a third had triple vessel disease. Total occlusion of one or more of the major coronary vessels was found in 67% of patients. It is difficult to interpret the extent of coronary disease in this group of patients as compared to published reports of CAD in patients undergoing angiography for the evaluation of angina pectoris. Selection of patients for catheterization and utilization of techniques to determine the severity of coronary stenosis vary among institutions. However, three prior reports showed that about 25% of patients had three vessel disease with greater than 30% stenosis. Over half of our patients who survived out-of-hospital VF had comparable three vessel CAD, suggesting more extensive disease than that observed in patients studied for the evaluation of angina.

Previous reports of nonresuscitated patients have been in disagreement over the distribution of coronary stenoses. One report has suggested an association of stenosis in the LAD with sudden cardiac death; however, this was not observed in another similar series, but differences in the clinical criteria of sudden death make comparisons difficult to interpret. In our series of resuscitated patients, the distribution of stenoses was nearly equal in the three coronary arteries. We found only one patient with severe stenosis of the left main coronary artery (1.6%), a figure lower than in autopsy series of sudden death. This difference may be due to the probability that patients with significant stenoses of the left main coronary artery frequently cannot be resuscitated; in addition, coronary angiography may underestimate the presence of left main disease.

Patterns of regional left ventricular contraction were of prognostic value in this series of patients with VF. In one-third of the angiograms, extensive contraction abnormalities were present. Over one-fourth demonstrated akinesia, and an additional 17% showed apparent paradoxical wall motion. These severe disturbances of left ventricular wall motion are more numerous than in patients evaluated for angina. This suggests that extensive scarring of the ventricular wall may lead to intramyocardial conduction asynchrony, a condition that is important experimentally in initiating and sustaining VF.

Compared to the patients who survived during follow-up, those who experienced recurrent VF/SD had a similar incidence of angina, hypertension, and electrocardiographic evidence of prior myocardial infarction. However, congestive heart failure was significantly more common in the latter group. This is similar to the mortality characteristics of our total population of individuals resuscitated from VF. The coronary angiograms of the patients who developed recurrent VF/SD showed significantly more extensive disease; nine had severe stenoses in three major vessels, and seven had two or more total occlusions. Equally striking was the high frequency of extensive and severe wall motion abnormalities in those persons who developed recurrent VF/SD. Seven of fourteen (50%) showed apparent paradoxical wall motion, and diffuse contraction abnormalities were detected in ten patients (71%). Such advanced and extensive degrees of myocardial fibrosis may well be important in establishing the milieu that leads to fibrillation or other lethal ventricular dysrythmias. Ejection fraction was significantly reduced in those patients who developed recurrent VF/SD. This association of higher mortality and decreased ejection fraction is similar to other groups of patients with ischemic heart disease.

It has been proposed that VF may originate in ischemic, nonnecrotic areas of myocardium which are distal to critical arterial narrowing and perfused by a collateral circulation. If this were the case, one might expect to find a relatively greater number of collaterals in patients who have experienced VF. Our patients, however, showed a similar incidence of collaterals compared to patients with severe CAD undergoing angiography for the evaluation of angina; in addition, patients who developed recurrent VF/SD had slightly fewer collaterals than those who survived. Thus, our observations on collateral circulation are not supportive of the above hypothesis.
The present study shows a strong association of certain angiographic and functional abnormalities with the development of VF and recurrent VF. In view of the incidence of sudden cardiac death in patients with CAD, effective therapeutic interventions would be highly desirable in those who demonstrate high risk findings. In addition, patients who have been resuscitated from one episode of VF and who have high risk coronary and left ventricular characteristics for developing a recurrent episode, need to be placed on prophylactic, rigorously-controlled medical therapy. Also, many of these patients have significant coronary stenoses that would be technically feasible for bypass grafting (fig. 5). Those individuals who have suitable anatomy may benefit from prophylactic bypass surgery or excision of akinetic or dyskinetic areas. However, the efficacy of any of these therapies in preventing VF is not predictable from our own experience.

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