Diverse Mechanisms of Unexpected Cardiac Arrest in Advanced Heart Failure

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To define the mechanisms of unexpected cardiac arrest in advanced heart failure, we reviewed the causes of cardiac arrest as established from electrocardiographic monitoring and from clinical and autopsy data in patients hospitalized for cardiac transplantation evaluation and management of advanced heart failure (mean left ventricular ejection fraction, 0.18±0.08) who were stable while on vasodilator and diuretic therapy such that hospital discharge to home was anticipated. Twenty-one cardiac arrests occurred in 20 of 216 (9%) such patients during a 4-year period. Heart failure was due to coronary artery disease with prior myocardial infarction in 13 patients and nonischemic cardiomyopathy in seven patients. The rhythm at the time of arrest was severe bradycardia or electromechanical dissociation (BA/EMD) in 13 (62%) patients. The precipitating cause of the BA/EMD arrest was coronary artery thrombosis or embolism in two patients, pulmonary embolism in one patient, hyperkalemia in two patients, and unexplained hypoglycemia in one patient. In seven of 13 (54%) patients, a precipitating cause of the bradycardia arrest could not be established. Only eight of 21 (38%) arrests were due to ventricular tachycardia or fibrillation (VT/VF), and all occurred in patients with prior myocardial infarction (p=0.02 vs. BA/EMD arrests). Two VT/VF arrests were due to acute or recent infarction, and one patient had hyperkalemia. The patients who suffered a BA/EMD arrest were similar to those who had a VT/VF arrest in age, ventricular arrhythmia history, ventricular function, and serum potassium levels. Serum sodium levels were lower in patients with BA/EMD arrests (129±3 vs. 133±4 meq/l, p=0.025). In hospitalized patients with advanced heart failure who are considered for cardiac transplantation, unexpected cardiac arrest frequently presents with either a BA or VT/VF. The causes of cardiac arrest are multifactorial. In many patients, the precipitating factors cannot be identified, suggesting that other unidentified mechanisms play a role. (Circulation 1989;80:1675–1680)

Sudden, unexpected cardiac arrest is a major threat to the patient who has advanced heart failure and accounts for approximately half of all deaths in this population.1-2 Therapy with diuretics and vasodilators frequently produces substantial improvement in heart failure symptoms and functional status, even in patients with severely depressed ventricular function.3 However, as therapy for the congestive symptoms of heart failure has improved, prevention of sudden cardiac arrest has emerged as a major challenge in the management of the heart failure patient. Numerous studies of cardiac arrest victims and survivors of aborted cardiac arrests have identified several potential causes of cardiac arrest, the most common of which is ventricular tachycardia (VT) or fibrillation (VF) due to either acute ischemia or reentry in a healed myocardial scar.4-22 These studies have focused primarily on the patient with coronary artery disease, including patients with and without heart failure, and may not accurately indicate the frequency of various causes of death in the heart failure population. Heart failure is associated with activation of the sympathetic nervous system and electrolyte abnormalities that could affect arrhythmogenesis.1,22,24 In addition, heart failure patients are predisposed to systemic and venous thromboemboli that could precipitate cardiac arrest.25 Establishing the causes of cardiac arrest in heart failure patients is important for the development of therapeutic strategies to reduce sudden death in this population. Therefore, we reviewed clinical and autopsy data from all electrocardiographically monitored, sudden, unexpected cardiac arrests observed

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during a 4-year period in hospitalized patients with advanced but stable heart failure.

Methods

Records of all patients admitted to the UCLA Medical Center under the care of the Heart Failure Service from 1984 to 1988 were reviewed. Patients were included in this study if they suffered an unexpected cardiac arrest during telemetry electrocardiographic monitoring in-hospital and if they met the following criteria: 1) The patient had New York Heart Association class III or IV heart failure before admission. 2) The patient was referred for evaluation for cardiac transplantation or adjustment of medical therapy and improved while on medical therapy such that in the absence of intravenous inotropic medications and ventricular assist devices the patient was clinically stable during the 48 hours preceding the arrest and hospital discharge was anticipated. Thus, decompensated heart failure was absent before arrest as evident from systolic blood pressure greater than 80 mm Hg and absence of rales or dyspnea at rest. 3) Clinical evidence of uncontrolled infection was absent before the arrest and at subsequent necropsy.

Of 284 consecutive patients admitted to the heart failure service, 216 were stabilized on medical therapy. An unexpected sudden cardiac arrest before anticipated hospital discharge occurred in 20 (9%) of these 216 patients. The clinical characteristics of the 20 study patients are shown in Table 1. There were 16 men and four women with mean age of 49±14 years. One patient (patient 13) had two separate cardiac arrests (one from VT and the other from sinus bradycardia) that were separated by an intervening period of clinical stability. Thus, 21 cardiac arrests were evaluated.

For each patient, the etiology of heart failure was established from coronary angiography (available for 19 patients), autopsy, and history. Left ventricular ejection fractions were quantified from two-dimensional echocardiography. Three cardiologists reviewed the single-channel electrocardiographic rhythm strips recalled from telemetry monitoring (78720A SDN Arrhythmia Monitoring System, Hewlett-Packard) immediately preceding and at the time of the arrest. For the nine patients who were successfully resuscitated, the clinical course, serum electrolytes, creatine phosphokinase MB isoenzymes, and electrocardiograms were reviewed to establish the cause of the arrest. In 10 of the 12 patients who suffered a fatal cardiac arrest, necropsy data were available in addition to clinical data preceding the arrest. Death was attributed to a primary arrhythmia if subsequent clinical or necropsy evaluation failed to reveal a possible precipitating cause of the initial arrhythmia.

Definitions of the Causes of Cardiac Arrest

Cardiac arrest. Cardiac arrest required that the patient be unresponsive with no palpable pulse and no spontaneous respiration and that closed chest compression was required before any patient response.

Ventricular tachycardia. VT required a ventricular rhythm greater than 100 beats/min with discrete QRS complexes.

Ventricular fibrillation. VF required a disorganized ventricular rhythm with no discrete QRS complexes discernable.

Bradycardia. Bradycardia required any rhythm at a rate less than 55 beats/min.

Electromechanical dissociation. Electrochemical dissociation (EMD) required a cardiac rhythm at a rate of 55–100 beats/min or supraventricular tachycardia with absence of a palpable pulse.

Nonischemic dilated cardiomyopathy. Nonischemic dilated cardiomyopathy required dilated heart failure with absence of obstructive coronary artery stenoses or other structural cause of heart failure determined by either coronary angiography or necropsy.

Statistical Analysis

Continuous data are shown as mean±1 SD. Student’s t test and Fisher’s exact test were used for statistical comparisons.

Results

The clinical characteristics of the patient population are shown in Table 1. Nineteen of the 20 patients had severely depressed systolic ventricular function (mean left ventricular ejection fraction, 0.18±0.08) and by study design were receiving chronic vasodilators (captopril or hydralazine and isosorbide dinitrate) and diuretics for heart failure.

Initial Cardiac Rhythm

The initial rhythm at the time of cardiac arrest was sinus bradycardia in nine (43%) arrests, second- or third-degree atrioventricular (AV) block in two (10%) arrests, EMD in two (10%) arrests, VT degenerating to VF in seven (33%) arrests, and VF in one (5%) arrest (Figure 1). Thus, eight (38%) arrests were due to VT or VF (VT/VF group) and 13 (62%) were due to a bradycardia arrest or EMD (BA/EMD group).

Patients in the VT/VF and BA/EMD groups are compared in Table 2. All eight patients in the VT/VF group had coronary artery disease compared with only six of 13 patients in the BA/EMD group (p=0.02). No difference was found between groups in the likelihood of successful resuscitation, left ventricular ejection fraction, bundle branch block, first-degree AV block, serum potassium levels, or serum magnesium levels. Patients in the BA/EMD group had lower serum sodium concentrations than those in the VT/VF group. Four patients had a history of sustained VT, two of whom suffered BA and two of whom suffered VT/VF arrests. A history of nonsustained VT (>3 beats) during telemetry electrocardiographic moni-
Dissociation 

Etiology of

was (two group of history (six group was 

toring 

FIGURE 1. Pie chart 

resuscitated. One additional patient in each group was receiving a type I antiarrhythmic drug for atrial fibrillation prophylaxis.

Etiology of Bradycardia and Electromechanical Dissociation

Four of the patients with sinus bradycardia were resuscitated. One patient had a serum potassium level greater than 6.0 meq/l at the time of arrest. After the arrest, she developed pneumonia and died in severe heart failure 8 weeks later. Of the remaining three resuscitated patients, no clear cause of the arrest could be established. One patient remained in hospital and received a cardiac transplant 10 days later without recurrent arrest. In the remaining two patients, electrocardiographic monitoring revealed no evidence of sinus or AV node dysfunction, and the attending physicians attributed the arrests to severe vasovagal reactions, which once hypotension was present required prolonged resuscitation. Neither patient received a permanent pacemaker. One is alive and well 14 months after the arrest, and the other was lost to follow-up. An autopsy was performed in three of the four patients who suffered fatal sinus bradycardic cardiac arrests. Pulmonary emboli and a small acute myocardial infarction were identified in one patient. The second patient had a permanent pacemaker that had been functioning normally before the arrest but failed to capture as sinus bradycardia developed, and the serum potassium level was 6.2 meq/l. No precipitating cause of the arrest was identified in the third patient.

One of the patients with AV block was found to be hypoglycemic (serum glucose level, <20 mg/dl) without apparent cause (no diabetes mellitus or hypoglycemic agents) and was resuscitated. Her electrocardiogram showed a normal PR interval and left axis deviation before and after resuscitation.

**Table 1. Patient Characteristics**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Etiology</th>
<th>Na (meq/l)</th>
<th>LVEF (%)</th>
<th>Initial rhythm</th>
<th>Survived arrest</th>
<th>Autopsy</th>
<th>Cause of arrest</th>
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<td>1</td>
<td>M</td>
<td>36</td>
<td>IDCm</td>
<td>131</td>
<td>12</td>
<td>SB</td>
<td>+</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>55</td>
<td>CAD</td>
<td>133</td>
<td>22</td>
<td>SB</td>
<td>+</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>50</td>
<td>IDCm</td>
<td>129</td>
<td>22</td>
<td>SB</td>
<td>+</td>
<td>-</td>
<td>K 6.4 meq/l</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>31</td>
<td>IDCm</td>
<td>126</td>
<td>12</td>
<td>SB</td>
<td>+</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>78</td>
<td>Amyloid</td>
<td>132</td>
<td>47</td>
<td>SB</td>
<td>-</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>55</td>
<td>CAD</td>
<td>131</td>
<td>20</td>
<td>SB</td>
<td>-</td>
<td>+</td>
<td>PE,AMI</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>57</td>
<td>CAD</td>
<td>134</td>
<td>20</td>
<td>SB</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>40</td>
<td>IDCm</td>
<td>126</td>
<td>12</td>
<td>SB</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>52</td>
<td>CAD</td>
<td>127</td>
<td>25</td>
<td>AVB</td>
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<td>-</td>
<td></td>
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<tr>
<td>10</td>
<td>F</td>
<td>18</td>
<td>IDCm</td>
<td>122</td>
<td>12</td>
<td>AVB</td>
<td>+</td>
<td>-</td>
<td>Hypoglycemia</td>
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<td>11</td>
<td>M</td>
<td>54</td>
<td>CAD</td>
<td>128</td>
<td>14</td>
<td>EMD</td>
<td>-</td>
<td>+</td>
<td>AMI</td>
</tr>
<tr>
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<td>F</td>
<td>22</td>
<td>IDCm</td>
<td>131</td>
<td>15</td>
<td>EMD</td>
<td>-</td>
<td>+</td>
<td>AMI,PE</td>
</tr>
<tr>
<td>13*</td>
<td>M</td>
<td>54</td>
<td>CAD</td>
<td>131</td>
<td>15</td>
<td>SB</td>
<td>-</td>
<td>+</td>
<td>K 6.2 meq/l</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>56</td>
<td>CAD</td>
<td>136</td>
<td>12</td>
<td>VT</td>
<td>-</td>
<td>+</td>
<td>AMI</td>
</tr>
<tr>
<td>15</td>
<td>M</td>
<td>59</td>
<td>CAD</td>
<td>135</td>
<td>9</td>
<td>VT</td>
<td>-</td>
<td>+</td>
<td>Recent MI</td>
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<tr>
<td>16</td>
<td>M</td>
<td>52</td>
<td>CAD</td>
<td>135</td>
<td>17</td>
<td>VT</td>
<td>-</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>M</td>
<td>61</td>
<td>CAD</td>
<td>128</td>
<td>15</td>
<td>VT</td>
<td>-</td>
<td>+</td>
<td>K 6.3 meq/l</td>
</tr>
<tr>
<td>18</td>
<td>F</td>
<td>52</td>
<td>CAD</td>
<td>130</td>
<td>22</td>
<td>VT</td>
<td>+</td>
<td>-</td>
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<tr>
<td>19</td>
<td>M</td>
<td>55</td>
<td>CAD</td>
<td>130</td>
<td>13</td>
<td>VT</td>
<td>+</td>
<td>-</td>
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<tr>
<td>20</td>
<td>M</td>
<td>45</td>
<td>CAD</td>
<td>137</td>
<td>23</td>
<td>VF</td>
<td>+</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1. Pie chart of initial rhythm at 21 cardiac arrests (see text for discussion).**
She died suddenly at home 2 weeks later. An autopsy on the patient who died of AV block failed to reveal a precipitating cause for the arrest.

Both EMD arrests were fatal. One patient (patient 1) had a normally functioning permanent pacemaker. Autopsies revealed both pulmonary and coronary emboli in one patient and a fresh right coronary artery thrombosis overlying atherosclerotic plaque in the second patient.

Thus, after BA/EMD arrest, five patients were resuscitated, and an autopsy was performed in six of the eight patients who had a fatal arrest. Of these 11 patients, cardiac arrest was attributed to an acute structural cause (coronary artery thromboemboli or pulmonary emboli) in three patients. Two patients had hyperkalemia, and one had hypoglycemia potentially contributing to the arrest. But in five of these 11 patients and in two others who had arrests in which an autopsy was not performed, no precipitating factor for BA could be established.

Etiology of Ventricular Tachycardia and Ventricular Fibrillation

Four of the 8 patients with VT/VF arrests were resuscitated. One (patient 13) had serum enzyme evidence of acute myocardial infarction. He suffered a fatal BA 3 weeks after the VT arrest. The remaining three survivors received antiarrhythmic medications. One received a cardiac transplant (patient 20), and one died suddenly at home (patient 18) within 2 weeks of initial arrest. The third patient is alive 3 years later without recurrent cardiac arrest (patient 19). Autopsies were performed in all four of the patients with fatal arrest. All had areas of old infarction, and one had evidence of a recent infarction (a few days old) that had not been suspected before death. One patient had hyperkalemia (6.3

TABLE 2. Comparison of Bradycardia and Electrochemical Dissociation Groups With Ventricular Tachycardia and Fibrillation Groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>BA/EMD</th>
<th>VT/VF</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>13</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Age (yr)</td>
<td>46±16</td>
<td>54±5</td>
<td>0.02</td>
</tr>
<tr>
<td>Old MI</td>
<td>6</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>History of sustained VT</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>History of nonsustained VT</td>
<td>6</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Antiarrhythmic treatment</td>
<td>9</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Bundle branch block</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>PR&gt;0.2 sec</td>
<td>3</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>0.19±0.09</td>
<td>0.15±0.13</td>
<td>0.02</td>
</tr>
<tr>
<td>Na (meq/l)</td>
<td>129±3</td>
<td>133±4</td>
<td></td>
</tr>
<tr>
<td>K (meq/l)</td>
<td>4.6±1.2</td>
<td>4.4±1.1</td>
<td>0.02</td>
</tr>
<tr>
<td>Mg (meq/l)</td>
<td>2.1±0.7</td>
<td>1.8±0.1</td>
<td></td>
</tr>
<tr>
<td>Resuscitated</td>
<td>5</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

BA/EMD, initial rhythm at arrest was bradycardia or electromechanical dissociation; LV, left ventricular; MI, myocardial infarction; VF, ventricular fibrillation; VT, ventricular tachycardia.

Patient number 13, who survived a VT/VF arrest and later suffered a bradycardiac arrest, is included in both columns.
meq/l) at the time of arrest. Thus, five arrests were attributed to a primary arrhythmia.

Discussion

Sudden, unexpected cardiac arrest is a major risk confronting the patient with advanced heart failure. Several studies have examined precipitating causes of cardiac arrest. These studies focused primarily on patients with coronary artery disease and included patients with and without heart failure. In out-of-hospital cardiac arrests, the initial cardiac rhythm was VF in approximately 60% of victims, VT in less than 10%, and bradycardia or asystole in the remaining 30%. However, fortuitously obtained ambulatory electrocardiographic recordings immediately preceding and during sudden cardiac arrests have shown VT degenerating to VF in more than 80% of arrests. Thus, VT degenerating to VF appears to be the mechanism of the arrest in the large majority of out-of-hospital sudden cardiac arrests. Studies of patients resuscitated from cardiac arrest and necropsy studies have suggested that the VT episode was due to either acute ischemia or reentry arising in an area of healed infarction.

The causes of sudden cardiac arrest in patients with advanced heart failure have not been specifically studied previously. The present study shows that the causes of cardiac arrest in heart failure are multifactorial. A primary ventricular arrhythmia accounted for only 38% of arrests. All VT arrests occurred in patients with prior myocardial infarction. In a prior study of patients with advanced heart failure, we found that programmed electric stimulation initiated sustained VT in 20% of patients who had a previous infarction but only in 6% of patients with heart failure in the absence of prior myocardial infarction. Although patients with heart failure in the absence of prior infarction do occasionally develop sustained VT, this is relatively uncommon compared with the coronary artery disease population. Thus, infarction may produce the appropriate substrate for reentrant arrhythmias more frequently than does nonischemic cardiomyopathy. Of the 15 patients with heart failure due to prior myocardial infarction, VT/VF was the mechanism of cardiac arrest in only eight (53%), fewer than might have been expected based on studies of the overall cardiac arrest population. BA/EMD accounted for most cardiac arrests in our heart failure patients. Bradycardic arrests in heart failure patients have been anecdotally reported, but our study is the first series of monitored cardiac arrests in advanced heart failure that provides some perspective on the frequency of the various mechanisms of sudden death in this population. A coronary artery thrombus or pulmonary embolism accounted for approximately a quarter of these arrests. Iseri et al. identified acute infarction as the cause of bradycardic out-of-hospital arrests in 65% of 20 autopsied patients. Heart failure patients are predisposed to systemic embolization of mural thrombi from the dilated left ventricle and atrium and to venous thrombosis. Hence, the frequency of emboli in our patients is not unexpected.

In 54% of BA/EMD arrests, a clear cause for the arrest was absent. This is in striking contrast to the findings of Iseri et al. in victims of out-of-hospital BA, nearly all of whom had an acute structural lesion that was believed to be the cause of the arrest. This suggests that as yet unknown factors, which may include vagally mediated reflexes, are important precipitating causes of BA in the heart failure population.

Serum electrolyte fluctuations are common in advanced heart failure probably because of large doses of diuretic drugs, fluctuating renal perfusion, and neurohumoral factors. Hyperkalemia may have contributed to 14% of arrests in this series, two due to sinus bradycardia, and one due to VT. This emphasizes the importance of careful attention to serum K+ levels in these patients and avoidance of excessive potassium supplementation. Patients receiving angiotensin converting enzyme inhibitors may be especially susceptible to hyperkalemia with excessive potassium administration. By diminishing angiotensin II stimulation of aldosterone secretion, these drugs can reduce urinary potassium excretion.

Limitations

Our patients are a selected group of hospitalized patients with severe ventricular dysfunction, most of whom were referred for possible cardiac transplantation. All required vasodilators and large doses of diuretics to control symptomatic heart failure. We attempted to exclude patients who were clinically unstable. However, most referrals are precipitated by some deterioration in outpatient status. Although we included only those patients who showed stability such that hospital discharge was anticipated, it is possible that BAs are less common in stable outpatients and in patients with less severe ventricular dysfunction. Our findings should not be extrapolated to the larger population of outpatients and patients with less severe heart failure.

Clinical Implications

This study is especially relevant to the population of patients with severe ventricular dysfunction who are considered for cardiac transplantation. Because the number of donor hearts is limited, only the minority of eligible patients can receive a cardiac transplant. For transplant candidates, as well as those who are denied transplantation, medical therapy often improves functional status and allows hospital discharge. We have previously shown that 24% of these patients will die suddenly within 6 months without transplantation. This study shows the diversity of causes of unexpected cardiac arrest in these patients, which has important implications for risk stratification and patient management.
Unfortunately, the type of arrest may be difficult to predict from the patient’s prior arrhythmia history. Two of our patients with a prior history of sustained VT suffered BA. There was no correlation between nonsustained VT during electrocardiographic monitoring in-hospital and the type of arrest. Thromboembolic events were an important cause of cardiac arrest, reemphasizing the potential role for anticoagulants in advanced heart failure.

References

15. Wannas CA, Roberts WC: Sudden coronary death: Relation of amount and distribution of coronary narrowing at necropsy to previous symptoms of myocardial ischemia, left ventricular scarring and heart weight. Am J Cardiol 1984;54:65–73

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