Sudden Death Prevention in Patients With Advanced Ventricular Dysfunction

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Heart failure affects 1 million to 2 million adults in the United States alone.1 In the majority of patients, an inexorable, although often slow, deterioration of ventricular function occurs, and only 60% survive 4 years.2 Although the long-term outcome is viewed with pessimism, death is classified as sudden and "unexpected" in up to 80% of patients. One may ask whether any death preceded by months or years of chronic heart failure can truly be called sudden. Sudden death is often defined as death preceded by a short duration, typically <1 hour, of acute symptoms.3,4 In the adult United States population, ventricular fibrillation in the setting of coronary artery disease is the most common scenario identified by this definition. Many heart failure patients periodically suffer mild exacerbations of heart failure that require adjustment of their medical regimen but have good functional status between exacerbations. In such circumstances, out-of-hospital ventricular fibrillation during a mild heart failure exacerbation may not meet everyone's definition of sudden death. Even if one focuses on "arrhythmic death," the clinical implications are not always straightforward. Preventing ventricular fibrillation in a patient with mild dyspnea on climbing hills is clearly desirable. Preventing ventricular fibrillation in a patient with no option for cardiac transplantation who is bedridden with resting dyspnea despite maximal medical therapy may not be an appropriate therapeutic goal. From a clinically practical standpoint, sudden death could be considered an unexpected death that occurs without sufficient warning to allow an ambulatory patient to seek medical assistance before the fatal collapse.

Is Sudden Death Prevention Desirable When Ventricular Dysfunction Is Advanced?

The risk of sudden death increases with the severity of heart failure.5-9 In patients who are referred for possible cardiac transplantation, an increased risk of sudden death has been associated with lower left ventricular ejection fraction, elevated pulmonary capillary wedge or pulmonary artery pressures, and hypotension. When sudden death is produced by a reversible arrhythmia that is not the last gasp of an end-stage ventricle, then prevention of sudden death may prolong survival in heart failure patients. With recent advances in heart failure management, symptoms of dyspnea can now be relieved with vasodilators and diuretics in the majority of patients with depressed ventricular function.10 The functional capacity and quality of life of these patients, once stabilized on medical therapy, are frequently comparable to that of patients after cardiac transplantation.10 Angiotensin-converting enzyme inhibitors reduce total mortality in heart failure.11 Their effect specifically to reduce sudden death was most apparent when compared with a hydralazine/isosorbide dinitrate combination tailored to similar hemodynamic goals.12 However, mortality remains high. The population of heart failure patients who have an acceptable quality of life but significant mortality is growing. The major risk without cardiac transplantation is not hemodynamic decompensation, which generally occurs slowly in adult patients under careful supervision, but instead sudden death. Sudden death accounts for 28% to 68% of all deaths in heart failure patients treated with converting enzyme inhibitors.11-16 Thus, even for patients with advanced ventricular dysfunction, prevention of sudden death could allow more patients to defer or avoid transplantation until hemodynamic symptoms made daily life intolerable.

When heart failure symptoms are severe despite medical therapy, the prevention of sudden death remains important when transplant is planned. The number of available donor hearts is limited, however. Almost twice as many patients are accepted onto transplantation waiting lists each month than actually undergo transplantation.17 Sudden death may occur before a suitable donor can be found for a patient who would otherwise enjoy prolonged survival and improved quality of life after transplantation. Thus, even for patients with advanced ventricular dysfunction, medical therapy could allow transplantation to be reserved for those patients who require in-hospital monitoring and hemodynamic support, while transplantation is deferred for the majority until necessitated by functional deterioration.

The magnitude of the problem is illustrated by our experience at the University of California at Los Angeles (UCLA) Medical Center. From 1984 to 1992, we evaluated 615 patients with advanced dilated heart failure sufficiently severe to warrant hospitalization for adjustment of medical therapy and evaluation for possible cardiac transplantation (Table 1). These patients underwent placement of a pulmonary artery flotation catheter and adjustment of vasodilator and diuretic
therapy to achieve hemodynamic goals and had sufficient improvement in symptoms to allow hospital discharge.\textsuperscript{6-10} Cardiac transplantation was deemed an appropriate option for 53\% of patients. The average time from hospital discharge to transplantation was 152±133 days. While on the cardiac transplant waiting list, 15\% of patients died suddenly. Sudden death accounted for 75\% of all mortality for candidates initially listed as outpatients. The mean time to sudden death was 202±306 days. The actuarial risk of sudden death for patients waiting 1 year was 21±3\% (±SEM) (Fig 1). Of the 288 patients who were not cardiac transplantation candidates, 15\% died suddenly during a mean follow-up of 430±477 days. Sudden death accounted for 19\% of the total mortality, and the 3-year actuarial risk of sudden death was 29±4\% (Fig 2).

| Table 1. Patients Hospitalized for Heart Failure and Transplantation Evaluation Who Survived to Hospital Discharge |
| N | 615 |
| Age, y | 51±31 |
| Male, % | 79 |
| Pathogenesis, % | 
| Ischemic CAD | 48 |
| Nonischemic CM | 45 |
| Valvular | 5 |
| Other | 1 |
| CAD not excluded | 0.5 |
| LV ejection fraction, % | 0.20±0.07 |
| NYHA class | 3.4±0.7 |
| Na <135 mEq/L, % | 41 |
| PCWp Initial, mm Hg | 25±10 |
| PCWp final, mm Hg | 16±6 |

CAD indicates coronary artery disease; CM, cardiomyopathy; LV, left ventricular; NYHA, New York Heart Association; and PCWp, pulmonary capillary wedge pressure.

Fig 1. Graph showing actuarial probability of sudden death for 327 patients with advanced heart failure who were accepted for cardiac transplantation at UCLA Medical Center between 1984 and 1992. All patients were stabilized on medical therapy and discharged from hospital to wait for a donor heart to become available. One standard error is represented by the vertical bars. See text for discussion.

Fig 2. Graph showing actuarial risk for all causes of mortality (dotted line) and sudden death (solid line) in 288 patients with advanced heart failure who were not candidates for cardiac transplantation. All patients were stabilized on medical therapy and discharged to their homes. One standard error is indicated by the vertical bars. See text for discussion.

Causes of Sudden Death: Should Arrhythmias Be the Primary Target for Prevention?

There are a variety of potential causes of sudden death.\textsuperscript{18,19} If initial attempts at cardiac resuscitation are prompt and successful, the underlying cause of the arrest and neurological recovery largely determine prognosis. When ventricular fibrillation occurs as a primary electrical event, such as reentry in a chronic infarct scar, prompt conversion to normal rhythm usually restores the heart to the functional and physiological state that existed before the arrest. This is illustrated by the success of implantable cardioverter-defibrillators in terminating ventricular tachycardia or ventricular fibrillation, providing dramatic evidence that many “fatal” arrhythmias are unfortunate electrical accidents in predisposed hearts. In contrast, when ventricular fibrillation is the manifestation of massive myocardial infarction, preventing or promptly terminating the arrhythmia is unlikely to alter the eventual outcome.

How frequently does a primary arrhythmia cause sudden death? Patients who suffer out-of-hospital cardiac arrest have been most extensively studied but are a somewhat heterogeneous group.\textsuperscript{19-22} The majority have coronary artery disease, some have prior myocardial infarction, ventricular function before the event ranges from normal to depressed, and in many patients sudden death is the initial presentation of coronary artery disease. Ventricular fibrillation is found in two thirds of cases and is most commonly caused by acute myocardial ischemia, often in the early phase of myocardial infarction. In patients with prior myocardial infarction, ventricular fibrillation is often caused by reentry in the infarct scar, producing ventricular tachycardia, which degenerates to ventricular fibrillation. Other causes of sudden death are distinctly less common.\textsuperscript{18}

There is comparatively little information, however, on the frequency of various causes of sudden death in patients with heart failure.\textsuperscript{23} We have observed 29 sudden unexpected cardiac arrests during electrocardiographic telemetry monitoring in patients with advanced heart failure who were hospitalized for adjustment of medical therapy and evaluation for cardiac transplantation between 1984 and 1991. Although the patients were hospitalized, none were in pulmonary edema or cardiogenic
TABLE 2. Unexpected Cardiac Arrests in Hospitalized Heart Failure Patients

<table>
<thead>
<tr>
<th>Heart Failure State</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>29</td>
</tr>
<tr>
<td>Ventricular tachycardia/ventricular fibrillation</td>
<td>15</td>
</tr>
<tr>
<td>Primary</td>
<td>7</td>
</tr>
<tr>
<td>Ischemia/infarction</td>
<td>3</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>1</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>1</td>
</tr>
<tr>
<td>Torsade de pointes</td>
<td>3</td>
</tr>
<tr>
<td>Bradyarrhythm</td>
<td>12</td>
</tr>
<tr>
<td>Primary</td>
<td>8</td>
</tr>
<tr>
<td>Ischemia/infarction</td>
<td>1</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>2</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>1</td>
</tr>
<tr>
<td>Electromechanical dissociation</td>
<td>2</td>
</tr>
<tr>
<td>Pulmonary and coronary emboli</td>
<td>1</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1</td>
</tr>
</tbody>
</table>

Shock at the time of arrest. The initial rhythm at arrest was ventricular tachycardia or ventricular fibrillation in 52% and bradyarrhythmias or electromechanical dissociation in the remainder. Causes of cardiac arrest were established from clinical evaluation in the event of successful resuscitation and from necropsy in several cases of unsuccessful resuscitations (Table 2). In 7 (47%) of the 15 arrests presenting with a ventricular tachyarrhythmia and 8 (67%) of 12 arrests presenting with a bradyarrhythmia, no clear precipitating factor could be identified, suggesting that these were primary arrhythmias. In 14 arrests (48%), a variety of potential causes were identified, including coronary thrombosis or embolism producing acute myocardial infarction, pulmonary embolism, torsade de pointes caused by hypokalemia or drugs that prolong the QT interval, and hyperkalemia. This is, however, a small series of hospitalized patients. The relative frequency of different mechanisms of sudden death in outpatients with heart failure is unknown.

The potential for causes of sudden death other than tachyarrhythmias has important implications. Sudden death does not always reflect failure of therapy directed at prevention or termination of an arrhythmia. Deaths caused by pulmonary embolism and bradyarrhythmias will not be reduced by amiodarone or implantable cardioverter-defibrillators. By diluting the number of arrhythmic sudden deaths, trials of antiarrhythmic therapies may require larger numbers of patients than expected to detect improvements in survival. Some therapies that do not impact specifically on arrhythmias could be beneficial. Anticoagulation, coronary revascularization, and antianginal drugs may prevent some sudden deaths. Careful attention to potassium balance, especially in the face of changing renal perfusion and angiotensin-converting enzyme inhibitors is also clearly important.

**Is Heart Failure Cause an Important Consideration When Ventricular Dysfunction Is Advanced?**

Of patients with advanced, dilated heart failure referred to our institution, 48% have coronary artery disease with prior myocardial infarction and the remainder have nonischemic causes, predominantly idiopathic cardiomyopathy (Table 1). Patients with dilated cardiomyopathy have had a lower mortality than patients with a similar degree of ventricular dysfunction caused by coronary artery disease in some but not all studies. Although risk of sudden death was slightly higher in the coronary artery disease patients, this did not reach statistical significance in this population (P = .22 by the Mantel-Cox test). One standard error is indicated by the vertical bars. See text for discussion.

**Fig 3.** Graph showing actuarial risk of sudden death (ordinate) for patients with advanced heart failure resulting from coronary artery disease (CAD) (dashed line) or idiopathic dilated cardiomyopathy (IDCM) (solid line). Although risk of sudden death was slightly higher in the coronary artery disease patients, this did not reach statistical significance in this population (P = .22 by the Mantel-Cox test). One standard error is indicated by the vertical bars. See text for discussion.
is relatively infrequent. Subendocardial ischemia could also result from inadequate capillary proliferation, abnormal microvascular regulation, or small-vessel disease accompanying hypertension.32-34

Several factors that promote arrhythmias are common to both ischemic and nonischemic heart failure. Ventricular hypertrophy is present in the noninfarct regions of ischemic heart disease patients and is present throughout the ventricles of nonischemic heart failure patients. Ventricular hypertrophy has been associated with an increased risk of sudden death in patients with hypertension.35 A number of abnormalities have been identified in hypertrophied myocardium that could slow conduction and alter refractoriness to promote reentrant arrhythmias.32,36-39 Depressed resting membrane potential, increased excitability threshold, and interstitial fibrosis may slow conduction. Action potential duration is prolonged, and there is increased temporal dispersion of refractoriness. Hypertrophy is accompanied by abnormal intracellular calcium handling and an increased susceptibility to afterdepolarizations and triggered activity in some animal models.40-43 Stretching of myocytes, as could occur because of increased wall tension accompanying ventricular dilation and high filling pressures, opens membrane channels that are nonselective for sodium and potassium ions.44 This may partially depolarize the membrane, altering conduction and refractoriness, and could theoretically also contribute to afterdepolarizations.45-48

Regardless of pathogenesis, advanced heart failure is accompanied by high sympathetic tone and abnormalities of baroreceptor responsiveness, which could influence arrhythmogenesis.49-51 Sympathetic stimulation increases susceptibility to ventricular fibrillation during ischemia, promotes afterdepolarizations and triggered activity, and alters ventricular conduction and refractoriness.50,52

Patients with heart failure are subject to fluctuations in potassium and magnesium balance, influenced by administration of diuretic drugs, potassium supplements, and drugs that inhibit angiotensin-converting enzyme.28 Hypokalemia and hyperkalemia have important electrophysiological effects.53 Hypokalemia may increase the risk of ventricular fibrillation during ischemia.54

Considering the variety of potential arrhythmia mechanisms, it is of interest to explore differences between patients with ischemic and nonischemic causes of heart failure. In our patients who suffered in-hospital, monitored cardiac arrest, the initial rhythm was ventricular tachycardia or fibrillation in 10 of 16 patients (63%) who had prior myocardial infarction, compared with 4 of the 12 patients (33%) with nonischemic cardiomyopathy. In 3 of the 4 nonischemic cardiomyopathy patients who suffered a ventricular tachycardia, the initial rhythm was torsade de pointes caused by drug-induced QT interval prolongation. This polymorphic ventricular tachycardia is not inducible by programmed electrical stimulation and may be a result of triggered automaticity arising from early afterdepolarizations.40,42 Of 458 consecutive patients evaluated for cardiac transplantsations, a documented episode of hemodynamically tolerated sustained monomorphic ventricular tachycardia had occurred in 7% of patients with prior myocardial infarction, compared with 0.5% of patients with nonischemic cardiomyopathy (P < .01).55 In a consecutive series of 72 advanced heart failure patients who had no history of cardiac arrest or sustained ventricular tachycardia, programmed ventricular stimulation induced sustained monomorphic ventricular tachycardia in 5 of 20 patients (20%) who had prior myocardial infarction but in only 1 of 45 (2%) with nonischemic cardiomyopathy (P = .057).56 In a similar group of heart failure patients, signal-averaged ECG detected late potentials in 16 (40%) of 40 patients with prior infarction but in only 3 (14%) of 22 patients with nonischemic cardiomyopathy.57

Ventricular tachycardia is, however, a potentially important cause of sudden death in patients with nonischemic cardiomyopathy, as illustrated by three studies including 67 patients with idiopathic dilated cardiomyopathy who were resuscitated from sustained ventricular tachycardia or ventricular fibrillation and were referred for electrophysiological testing.58-60 Of 35 patients presenting with ventricular fibrillation, sustained monomorphic ventricular tachycardia was initiated in 20%. Of the 37 patients presenting with sustained ventricular tachycardia, this arrhythmia was initiated by programmed stimulation in 89%. The signal-averaged ECG often reveals late potentials in patients with nonischemic cardiomyopathy who have suffered sustained ventricular tachycardia.61,62 Cancers et al.63 reviewed 285 patients with inducible sustained ventricular tachycardia referred for electrophysiological investigation. Only 22 patients (8%) had nonischemic dilated cardiomyopathy. Interestingly, macroreentry within the bundle branches, a relatively uncommon mechanism of ventricular tachycardia in coronary artery disease, accounted for 36% of the ventricular tachycardias in nonischemic cardiomyopathy. The mechanisms of ventricular tachycardia not caused by bundle branch reentry in nonischemic cardiomyopathy patients are unknown.

Sustained monomorphic ventricular tachycardia inducible by programmed electrical stimulation is thus more common in post–myocardial infarction patients than in patients with nonischemic dilated cardiomyopathy. Monomorphic ventricular tachycardia suggests repetitive activation of the ventricles from a stable arrhythmia focus or reentry circuit. This is consistent with reentry arising from a relatively fixed anatomic substrate, such as slow conduction through a large infarct scar. In both post–myocardial infarction patients and patients with nonischemic dilated cardiomyopathy, ventricular hypertrophy may set the stage for arrhythmias caused by triggered automaticity or random reentry, which is more likely to present as ventricular fibrillation or polymorphic ventricular tachycardia.64 These arrhythmias may be more susceptible to modulation by fluctuating sympathetic tone, electrolyte abnormalities, and wall tension. Because the proper combination of factors is required for arrhythmia initiation, susceptibility may not be detected by programmed electrical stimulation.

The relative incidence of arrhythmogenic and nonarrhythmogenic mechanisms of sudden death in heart failure patients is undefined. A classification relating the presenting arrhythmia to associated factors, heart disease, and predictive tests is shown in Table 3.
**Do All Causes of Sudden Death Increase as Heart Failure Severity Progresses?**

In patients with prior myocardial infarction without advanced heart failure, ventricular tachycardia inducible by programmed electrical stimulation and abnormal signal-averaged ECGs indicate an increased risk of sudden death. Convervally, absence of these risk factors is associated with a low risk of sudden death. This has been clearly shown for patients studied early after myocardial infarction. In patients with nonsustained ventricular tachycardia and variably depressed ventricular function late after infarction, absence of inducible sustained ventricular tachycardia has often been associated with a low incidence of sudden death, typically <6% over a period of 2 years. Patients with inducible tachycardia were generally treated with antiarrhythmic drugs and experienced a higher incidence of sudden death during follow-up. In patients with advanced ventricular dysfunction, however, programmed electrical stimulation is less useful. We performed programmed ventricular stimulation in 24 patients who had advanced heart failure and prior myocardial infarction. Of 19 patients who did not have inducible sustained ventricular tachycardia, 5 died suddenly over a mean follow-up of only 6 months.

Patients resuscitated from ventricular fibrillation or ventricular tachycardia who have markedly depressed ventricular function have a markedly increased risk of sudden death compared with cardiac arrest survivors with better ventricular function. Wilber and coworkers found a 3-year risk of recurrent cardiac arrest of 22% in patients with left ventricular ejection fraction <0.3 despite suppression of inducible ventricular tachycardia at electrophysiological testing. Similarly, the risk of sudden death during therapy with amiodarone or implantable cardioverter-defibrillators is higher in patients with markedly depressed ventricular function than in patients with left ventricular ejection fraction >0.3. This may not indicate that such therapy is without benefit, however. We recently analyzed survival of heart failure patients resuscitated from ventricular tachycardia/ventricular fibrillation some time before cardiac transplantation evaluation who were treated with implantable defibrillators or selected antiarrhythmic drugs (commonly amiodarone). Although the risk of sudden death was substantial, 17% at 1 year, it was identical to that of patients who had comparably severe heart failure who had not previously suffered a cardiac arrest. It is possible that mechanisms other than those that produced the initial cardiac arrest contribute to the high mortality in patients with depressed ventricular function after resuscitation from cardiac arrest.

As cardiac function deteriorates, the risk of sudden death increases, but the relative contributions of different causes of sudden death may vary. The impact on the incidence of sudden death of therapies targeting ventricular arrhythmias will depend not only on antiarrhythmic efficacy but also on the frequency of other causes of sudden death in the heart failure population and the incidence of adverse effects. In a recent randomized trial, low-dose amiodarone (200 mg/d) failed to reduce sudden death in patients with advanced heart failure. Two patients died suddenly during ECG monitoring, and the terminal event was a bradyarrhythmia in both. It is conceivable that amiodarone reduced the incidence of ventricular fibrillation but increased deaths from bradyarrhythmias.

**Predicting Arrhythmia Risk**

**Cardiac Arrest Survivors**

Patients with depressed ventricular function who have been resuscitated from a cardiac arrest are at high risk for recurrent cardiac arrest. In general, this excludes patients whose arrest is caused by acute myocardial infarction, in whom the risk of recurrent arrest does not appear to be increased if they survive to hospital discharge, although this has not been specifically investigated in heart failure patients. Resuscitated patients...
who have depressed ventricular function but do not have inducible ventricular tachycardia and in whom the cause of the arrest is obscure have a risk of recurrent cardiac arrest > 30% over a period of 1 to 3 years.20,76 Those in whom inducible ventricular tachycardia is implicated as the cause of the arrest have a 15% to 50% risk of recurrent arrest during the next 2 to 3 years despite therapy with drugs that suppress inducible arrhythmias or with amiodarone.20,70,71 Patients with advanced heart failure who are resuscitated from a "secondary" cardiac arrest attributable to a remediable factor, such as hypoxia during pulmonary edema or torsade de pointes during antiarrhythmic drug therapy, also have a high risk of sudden death, 39%, over the next year despite attempts to prevent precipitating factors.55

Syncope

Syncope in a patient with structural heart disease is a serious symptom and is of particular concern in patients with heart failure.77 Of 491 consecutive patients with advanced heart failure referred for cardiac transplantation evaluation, 12% had a history of syncope. In 35% of cases, syncope was attributable to ventricular tachycardia. The actuarial risk of sudden death at 1 year for patients with a history of syncope was 45%. The risk of sudden death was comparable in patients with syncope from an identified cardiac cause and in those with syncope attributed to noncardiac causes or unidentified mechanisms. Syncope may identify a patient who is at high risk for arrhythmias or who has impaired ability to maintain adequate cerebral perfusion in response to physiologic stresses.51,78

Patients With No History of Cardiac Arrest or Syncope

A variety of tests have been applied to predict arrhythmia risk in heart failure patients. In patients with prior myocardial infarction, frequent ventricular ectopy on ambulatory ECG monitoring, late potentials on signal-averaged ECG, ventricular tachycardia inducible by programmed electrical stimulation, and depressed heart rate variability all are associated with an increased risk of sudden death.30,65,79 As discussed above, a negative test does not confer a low risk of sudden death when heart failure is advanced. Furthermore, the value of prophylactic arrhythmic therapy is unknown. The Cardiac Arrhythmia Suppression Trial (CAST) and post hoc analysis of the Stroke Prevention in Atrial Fibrillation (SPAF) trial have emphasized the potential for antiarrhythmic drugs to increase mortality.80,81 Initial trials of amiodarone in postinfarct survivors are encouraging, but further information is needed for patients with markedly depressed ventricular function.82,83

In patients with nonischemic causes of heart failure who have not suffered a spontaneous sustained ventricular arrhythmia, ventricular ectopy on ambulatory ECG monitoring has been related to sudden death in some but not all studies.8,9,84 Screening for ventricular arrhythmias with programmed electrical stimulation is not useful because of the low incidence of inducible ventricular tachycardia.56,58 Yet the risk of sudden death is high, especially when heart failure is advanced. The prognostic use of signal-averaged ECG requires further evaluation.

Amiodarone

Of currently available antiarrhythmic agents, amiodarone appears to have the greatest potential for reducing sudden death and possibly the lowest risk in heart failure patients. It is well tolerated hemodynamically even if heart failure is advanced.85 In contrast to class I antiarrhythmic drugs, it has not been found to increase mortality and may decrease mortality in post–myocardial infarction patients, suggesting that the incidence of proarrhythmia is low.82,83 Its well-known side effects, which increase progressively over time, are more easily justified in a patient population with a 5-year survival of <50% and a high risk of sudden death. Although there is concern that amiodarone has the potential for increasing perioperative pulmonary complications, it does not appear to increase the perioperative morbidity and mortality of cardiac transplantation.86,87 Although initial studies in post–myocardial infarction patients have shown benefit, a randomized trial of advanced heart failure patients found similar survival with placebo and amiodarone.74 At present, routine treatment of asymptomatic arrhythmias in advanced heart failure cannot be recommended, and trials addressing this issue are in progress.

In advanced heart failure patients, atrial fibrillation has been associated with increased mortality in some but not all studies.7 The low proarrhythmia risk and high efficacy make amiodarone an attractive option for treating atrial fibrillation in advanced heart failure patients, but the effect on survival is unknown.88

Implantable Cardioverter Defibrillators in Heart Failure Patients

Implantable devices hold great promise for preventing sudden death in heart failure patients. These devices are likely to terminate ventricular tachycardia or ventricular fibrillation regardless of the precipitating cause. Backup bradycardia pacing can be incorporated to deal with bradyarrhythmias, a potentially important cause of sudden death in this population. Cautious optimism, however, is warranted. In initial studies with devices that used one or more epicardial patch electrodes and therefore required thoracic surgery, the perioperative mortality was up to 11%,72,73,89 At 3 to 4 years, the actuarial mortality attributed to arrhythmias was 2% to 30%. The total mortality was 24% to 43% even though the majority of patients had New York Heart Association functional class I or II symptoms, reflecting appropriate reluctance to subject sicker patients to surgery. It is possible that prevention of an arrhythmic death may simply alter the mode of death without substantially reducing mortality, such that patients are resuscitated from ventricular fibrillation only to die of refractory pump failure in hospital a short time later.72

Implantable device technology is rapidly advancing. Nonthoracotomy lead systems and improvements in arrhythmia detection and termination methods will probably further improve their efficacy. Careful patient selection will be crucial. Considering the high risk of sudden death in advanced heart failure patients, an interesting approach may be to focus on identifying the patients who will suffer progressive hemodynamic deterioration, who would be better served with cardiac
transplantation rather than an implantable cardioverter-defibrillator.°

Conclusions
Sudden death in heart failure patients can result from any of a variety of potential mechanisms. It is possible that the relative importance of these mechanisms differs in various patient groups according to the cause of heart failure and that the relative incidence of individual causes changes over time with the progression of severity of heart failure. Preventing deaths from primary arrhythmias will meaningfully extend survival of some patients, but the overall benefit will be limited to an as yet unknown degree by "nonarrhythmic" sudden deaths. Trials evaluating amiodarone and implantable devices will provide valuable insights and much-needed guidance and are in progress. As clinicians attempt to decide whether cardiac transplantation, an implantable cardioverter-defibrillator, or amiodarone is the best option for an individual patient, it will be important to consider both the cause and the severity of heart failure.

References

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43. Lubbe W, Porterait T, Towle LH. Potential arrhythmogenic role of cyclic adenosine monophosphate (AMP) and systolic calcium overload: implications for prophylactic effects of beta-blockers in myocardial infarction and prorarrhythmic effects of phosphodies-}

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