Predicting Sudden Death Risk for Heart Failure Patients in the Implantable Cardioverter-Defibrillator Age

William G. Stevenson, MD; Laurence M. Epstein, MD

One-third to one-half of patients with chronic, dilated heart failure will die suddenly or be resuscitated from a cardiac arrest or sustained ventricular tachycardia (VT). Implantable cardioverter-defibrillators (ICDs) offer excellent protection from sudden death by providing effective termination of the arrhythmia when it occurs, but they are not without problems. Approximately one-third of patients will experience some adverse effect, including inappropriate shocks, lead problems, and infection. The implantation and testing procedure occasionally precipitates hemodynamic deterioration. DDD or VVI pacing from the right ventricular lead of the ICD may have adverse hemodynamic effects, including increasing dys synchrony of left ventricular contraction, and may have contributed to the aggravation of heart failure observed in the Multicenter Automatic Defibrillator Implantation Trial II (MADIT II).

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As with any therapy, wider use in lower risk patients increases the number of patients who might not benefit but who still suffer adverse effects. On the other hand, many sudden deaths will be prevented, and the balance, to this point, has been positive. The substantial costs of the ICD hardware, implantation, and follow-up are also a concern. Thus, identifying those patients with depressed ventricular function who are most likely to benefit, or perhaps more importantly, those who are unlikely to benefit, is of interest.

The development of tests to identify patients at high risk for fatal arrhythmias typically follows a progression (Table). Retrospective studies determine if a positive test is more common in known high-risk groups (eg, cardiac arrest survivors) compared with lower risk groups. Second, predictive accuracy is evaluated prospectively, often as a substudy of a larger trial. Finally, the test is used to select a high-risk group for testing of a therapy. Despite the extremely high efficacy of ICDs for terminating arrhythmias, benefit cannot be automatically assumed. A new test might select patients at high risk for hemodynamic deterioration or catastrophic events with imminent death even if an arrhythmia is terminated.

With attempts to risk stratify heart failure populations, 3 general themes have emerged. First, the etiology of heart failure makes a difference. Patients with coronary artery disease and prior infarction are at risk for ventricular fibrillation during myocardial ischemia and from reentry in the old infarct causing VT. These mechanisms of arrhythmia are uncommon in “noncoronary” causes of heart failure, such as valvular heart disease, and idiopathic or familial cardiomyopathies. Secondly, the severity of electrophysiological abnormalities parallels the severity of heart failure. Thus, markers for arrhythmias are also associated with death from pump failure. Third, noninvasive tests based on the ECG recordings (T-wave alternans, signal averaged-electrocardiograms, and heart rate variability) are not interpretable in more than 20% to 30% of patients because of atrial fibrillation or limitations peculiar to the test.

The severity of left ventricular (LV) dysfunction and LV size alone is a marker of risk, but it identifies a broad segment of the heart failure population. In patients with prior infarction and LV ejection fraction ≤0.30, but without any recent New York Heart Association class IV heart failure symptoms, ICDs reduced mortality to 16% from 22% at 2 years in the MADIT II study. Nonsustained VT and frequent ventricular ectopy increase in prevalence with heart failure severity and have predicted sudden and non-sudden death. ICDs did not improve survival compared with no antiarrhythmic therapy or with amiodarone in patients with nonischemic cardiomyopathy selected for nonsustained VT (S. Adam Strickberger, MD, Washington Hospital Center, Washington, DC, oral and electronic communication, 2001) or depressed ventricular function.

Invasive electrophysiological studies detect potential reentry circuits after myocardial infarction. Approximately one-third of patients with prior infarction, LV ejection fractions ≤0.40, and spontaneous nonsustained VT have inducible sustained VT, predicting a 6% to 9% per year risk of spontaneous sustained VT or sudden death. ICDs reduce this risk to less than 3% to 5% per year. Electrophysiological study is not a useful screening tool in noncoronary causes of heart failure; fewer than 5% of patients have inducible monomorphic VT. When heart failure is advanced, the sensitivity of electrophysiological testing decreases, thereby failing to identify many high-risk patients even in the postinfarction group.

Given these limitations, other noninvasive predictors have been sought. Abnormalities of cardiac repolarization are common in heart failure. Dispersion of the QT interval in the surface ECG was initially associated with high-risk

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patients, but was of no value in a prospective study of 703 patients. Detection of small oscillations in the T-wave amplitude (T-wave alternans) during exercise is linked to susceptibility to ventricular arrhythmias. It is associated with increased mortality and, in some but not all studies, increased risk of sudden death. As long as the risks, impact on quality of life, and costs of ICDs continue to be more than minimal concerns, refining patient selection will remain of interest. However, it is a moving target. During the 10-year course of their study, La Rovere and coworkers observed a decrease in mortality and an increase in use of β-adrenergic blocker therapy. Ten years ago, ICDs required a thoracotomy for placement and were reasonable options only for patients at the highest risk who had been resuscitated from a cardiac arrest. ICDs are now warranted for many patients with depressed ventricular function who have not had a cardiac arrest. As lower risk populations are evaluated, identification of those higher risk subgroups most likely to benefit may assume more importance. At the other extreme, patients with end-stage heart failure often will have risk markers for sudden death but no benefit of an ICD when death from pump failure intervenes. New strategies for selecting patients for ICDs will continue to require evaluation in clinical trials.

### TABLE 1. Risk Factors for Sudden Death in Patients With Depressed Ventricular Function

<table>
<thead>
<tr>
<th>Abnormal in High-Risk Groups</th>
<th>Prospectively Predicts Risk</th>
<th>Useful to Select for ICD</th>
<th>Useful to Select for Amiodarone</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV size/EF C/NC</td>
<td>C</td>
<td>C</td>
<td>C? (early after MI)</td>
</tr>
<tr>
<td>BNP C/NC</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Holter ECG C/NC</td>
<td>C/NC</td>
<td>C (with EPS)</td>
<td>+/-</td>
</tr>
<tr>
<td>HRV C/NC</td>
<td>C/NC</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>TWA C/NC</td>
<td>NC</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>SAECG C/NC</td>
<td>C/NC</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>QT dispersion C/NC</td>
<td>No</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>EPS C</td>
<td>C</td>
<td>C</td>
<td>C?</td>
</tr>
</tbody>
</table>

LV indicates left ventricular; EF, ejection fraction; C, coronary artery disease patients; NC, noncoronary artery disease patients; C/NC, shown for both coronary and noncoronary artery disease patients or in studies including both groups with the finding not stated to be confined to one disease etiology; MI, myocardial infarction; BNP, brain natriuretic peptide; EPS, electrophysiologic study; HRV, heart rate variability; TWA, T-wave alternans; SAECG, signal averaged ECG; and ?, unknown.
References


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