

# Survivors of sudden cardiac death: a rational approach to evaluation and therapy of patients surviving ventricular fibrillation

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■ Survivors of out-of-hospital cardiac arrest that is not associated with acute myocardial infarction are at high risk for subsequent life-threatening ventricular tachyarrhythmias. A rational approach to evaluating the underlying disease processes and to formulating a specific treatment plan for these patients is presented. A protocol is suggested whereby existing cardiac conditions are appropriately treated and hemodynamic parameters are optimized. Myocardial ischemia is minimized with drugs or revascularization; this may suffice to prevent recurrence of sudden cardiac death in a small group of patients. For remaining patients at high risk of recurrence, the implantable cardioverter-defibrillator is the therapy associated with the lowest rate of mortality.

□ INDEX TERMS: DEATH, SUDDEN; HEART ARREST; ARRHYTHMIA; CORONARY DISEASE □ CLEVE CLIN J MED 1992; 59:166-172

**O**F THE 700,000 DEATHS each year in the United States from heart disease, approximately 450,000 (60% to 65%) are sudden. With the advent of community education programs in cardiopulmonary resuscitation, the potential for rapid arrival of ambulance-based advanced cardiac life support, and improvements in in-hospital coronary care units, increasing numbers of patients are being resuscitated successfully and discharged alive. In urban areas with well-trained paramedic units, as many as 25% to 30% of patients

sustaining out-of-hospital cardiac arrest may survive to leave the hospital.<sup>1-6</sup> Potentially, therefore, clinicians may be faced with 135,000 new patients each year who have survived sudden cardiac death.

The prognosis for these patients has traditionally been quite grim. Up to one third die within 1 year of the initial episode, and up to one half are dead within 2 years, with three fourths of the deaths being sudden.<sup>7-11</sup> The outlook is more favorable if the initial arrest occurred in the setting of an acute myocardial infarction (MI). In this case, the prognosis is the same as would be expected in a patient with a comparable infarction without cardiac arrest; that is, the presence of ventricular fibrillation or ventricular tachycardia in the acute stage of MI appears to have no prognostic significance.<sup>7</sup> Contrary to popular belief, however, MI is not the most common cause of sudden cardiac death.

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Even though coronary artery disease is found in the majority of sudden cardiac death patients, most of these (whether successfully resuscitated or not) do not have clinical or pathological evidence of acute infarction.<sup>7,8,12</sup>

What is needed, then, is a rational approach to identify underlying disease processes, stratify risk of recurrence, and formulate a specific treatment plan for patients who survive nonacute-MI sudden cardiac death, in order to reduce the risk of future sudden death.

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## EVALUATION

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### Identify the arrhythmia

Tachyarrhythmias (ventricular tachycardia, ventricular fibrillation) are the most common causes of sudden cardiac death. Ventricular fibrillation is the most common rhythm to be identified initially, but most episodes probably begin with ventricular tachycardia, which then degenerates into ventricular fibrillation.<sup>13-15</sup> Bradyarrhythmias (including asystole due to atrioventricular block or sinus arrest), with or without electromechanical dissociation, account for fewer than 20% of episodes.<sup>14,15</sup> Primary bradycardia, asystole, and electromechanical dissociation may result from overwhelming mechanical insult such as pulmonary embolism, massive MI, or cardiac rupture; successful resuscitation from these rhythms is extremely rare.<sup>16</sup> Therefore, most patients who are resuscitated from cardiac arrest are presumed to have experienced a ventricular tachyarrhythmia.

### Identify underlying disease

Coronary artery disease is present in over 80% of patients who die suddenly,<sup>11</sup> and cardiac catheterization is almost always warranted soon after resuscitation from sudden death to assess the presence and severity of atherosclerotic lesions. A subgroup of survivors of sudden cardiac death are those in whom myocardial ischemia alone is thought to have precipitated the arrest. These patients tend to have normal or near-normal left ventricular function and do not have inducible arrhythmias during electrophysiological testing. Their prognosis is quite favorable when therapy is directed at preventing further ischemia.<sup>17-20</sup> The remaining majority of survivors is likely to have significant LV dysfunction secondary to previous MI, have inducible arrhythmias, and receive less benefit, if any, from anti-ischemic measures alone.<sup>20</sup>

In patients without coronary disease, underlying conditions span the range of cardiac diseases: dilated

and hypertrophic cardiomyopathies, valvular heart disease, congenital heart disease, and disease of the electrical system (long QT syndromes and Wolff-Parkinson-White syndrome are seen). Routine evaluation, along with cardiac catheterization and echocardiography, will satisfactorily identify most of these. A small percentage will be found to have no underlying structural heart disease.

### Ambulatory monitoring

Attempts to use Holter monitoring to stratify the risk of recurrent sudden cardiac death have been disappointing. Most investigators using the Holter monitor have found no significant difference in frequency or severity of ventricular arrhythmias between survivors of nonacute-MI sudden cardiac death who sustain recurrent arrest and those who do not.<sup>21-23</sup> More elaborate methods of analysis have been used, such as dividing the monitoring period into smaller recording intervals and examining the cumulative number of these intervals in which complex ectopy is present. This technique has identified differences between patients with recurrence and those without, but with a sensitivity of only 56%; thus, almost half of those at risk of recurrent arrest are not identified.<sup>24</sup>

Perhaps a more important role for ambulatory monitoring is found in the follow-up of antiarrhythmic drug therapy. The persistence of nonsustained ventricular tachycardia in a patient on therapy is usually a poor prognostic sign, since it is associated with an annual rate of recurrence up to 20 times higher than in those in whom it is absent.<sup>25</sup> However, Holter monitoring, while safe and well tolerated, is less effective in predicting drug efficacy than is electrophysiological testing. Using the presence or absence of nonsustained VT on Holter monitoring vs presence or absence of inducible arrhythmias at electrophysiological study (EPS), the positive predictive value of recurrence for Holter monitoring is only 70%, compared to 88% for EPS, and the negative predictive value is 50%, compared to 94% for EPS.<sup>26</sup>

### Electrophysiologic study

Programmed electrical stimulation (PES), performed as part of an invasive EPS, involves inducing ventricular arrhythmias by inserting one or more premature extrasystoles via a pacing electrode in the right (or left) ventricle. If ventricular arrhythmias are induced, serial drug testing may be performed, directed at finding an antiarrhythmic agent that renders the patient noninducible.

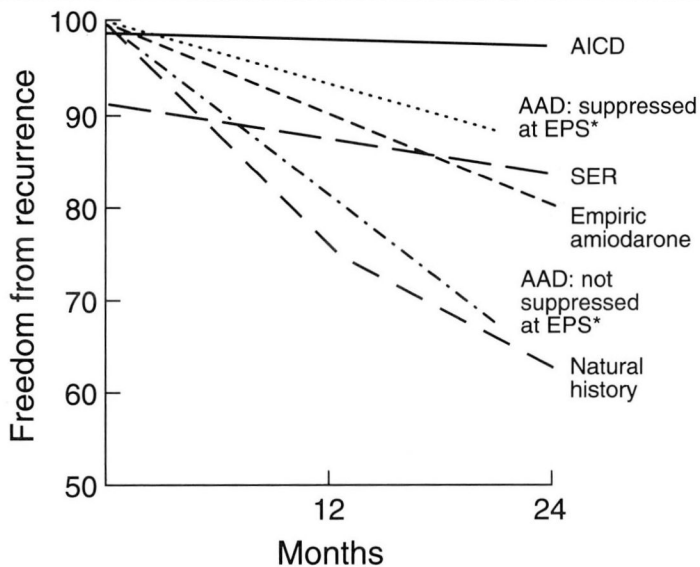


FIGURE 1. Freedom from recurrent cardiac arrest or sustained ventricular tachycardia. Starting points include operative mortality, if applicable. (AICD, automatic implantable cardioverter-defibrillator; AAD, antiarrhythmic drugs; EPS, electrophysiological study; SER, subendocardial resection.)

Two thirds to three fourths of patients with previous sudden cardiac death have inducible arrhythmias that are believed to be of clinical significance.<sup>27-38</sup> Patients are more likely to have inducible arrhythmias if the earliest identified arrhythmia at the time of arrest was sustained ventricular tachycardia rather than ventricular fibrillation.<sup>28,37</sup> In addition, patients with inducible arrhythmias are more likely to be male, have coronary artery disease with previous MI, as well as lower ejection fractions and a higher incidence of ventricular aneurysms than their noninducible counterparts.<sup>28,32,34,37,39</sup> Patients with inducible arrhythmias have high rates of arrhythmia recurrence, but these can be reduced if an antiarrhythmic agent is found which renders the arrhythmia noninducible.

Recurrence rates among those with no inducible arrhythmias at baseline PES vary considerably and are currently the source of disagreement. Some investigators have found very favorable long-term outcomes with or without antiarrhythmic therapy,<sup>27,29,31,34,36</sup> while others have found poor outlooks with recurrence rates as high as 32%.<sup>32,33,35</sup> Patients with noninducible arrhythmias represent a very heterogeneous group, with relatively few having coronary disease and most having no identifiable structural heart disease.<sup>32,36,37,40</sup> Within this group are most patients with idiopathic dilated

cardiomyopathy, who, for reasons not well understood, are much less likely to have inducible arrhythmias than their counterparts with coronary artery disease; they remain at high risk for recurrence whether the arrhythmias are inducible or not.<sup>41</sup> Also within this group are patients with transient, reversible causes of sudden cardiac death, including ischemia,<sup>17-20,31</sup> drug-induced arrhythmias,<sup>27,31,34</sup> and surgically correctable valvular disease.<sup>31</sup> As would be expected, these patients fare well with treatment or removal of the precipitating cause. Noninducibility, therefore, is not automatically a favorable prognostic sign, but within this group

of patients are subgroups at low risk for arrhythmic recurrence when they are properly characterized and treated.

#### THERAPY

##### Antiarrhythmic drugs

Empiric therapy with antiarrhythmic drugs is to be avoided, as it is generally ineffective<sup>24,32</sup> or dangerous. The proarrhythmic effects of most antiarrhythmic drugs are well illustrated in reports of patients undergoing drug therapy for nonlethal arrhythmias who then experience aborted sudden death: the patient is later found to be "inducible" on the therapeutic agent, and when the drug is discontinued the patient is rendered free of recurrence.<sup>27,34</sup> When possible, drug therapy should be guided by the results of EPS. In patients with inducible arrhythmias, identification of an antiarrhythmic drug that suppresses inducibility confers a recurrence rate of 0% to 33%, compared to recurrence rates of 20% to 80% in those whose inducibility cannot be suppressed.<sup>27,29-33,35</sup>

Empiric therapy with amiodarone may be efficacious, for it results in annual recurrence rates around 10%,<sup>42</sup> somewhat better than might be expected from natural history studies. Use of amiodarone is limited by

its toxicity: adverse effects occur in over 80% of patients, and discontinuation of the drug is necessary in up to 37%.<sup>43</sup> It is commonly used as a last-line agent, given "empirically" after standard antiarrhythmic agents have failed or proved ineffective by EPS. With amiodarone, recurrence rates in this extremely high-risk group range from 8% to 24%.<sup>32,44,45</sup> The degree of benefit conferred by amiodarone in this group is controversial; it may be no better than that which would be achieved with a standard antiarrhythmic drug shown to be "ineffective" at EPS.<sup>46</sup> However, for those whose arrhythmias are rendered noninducible by amiodarone where other drugs have failed, the recurrence rate appears low.<sup>45</sup>

### Surgery

Map-assisted subendocardial resection (SER) is currently used in some centers in the treatment of patients with recurrent, usually drug-refractory, malignant ventricular arrhythmias. Aneurysmectomy alone is seldom effective in preventing recurrence of arrhythmia. This may be because the focus of the arrhythmia generally lies in the endocardium bordering the aneurysm rather than in the aneurysm itself. In selected patients, this focus can be mapped by electrophysiologic study. The focus can then be surgically obliterated by resection, cryoablation, or a combination of the two, with or without aneurysmectomy. Operative mortality rates are approximately 10%. In one series of 100 patients undergoing SER, 70 became non-inducible at EPS, while the remainder were generally more easily suppressed with drug therapy than they were preoperatively. After surgery, 90 of the patients were arrhythmia-free, although many continued to require antiarrhythmic therapy.<sup>47</sup> However, among these patients, only one fourth had sustained prior cardiac arrest, the remainder having presented with recurrent ventricular tachycardia. This restricts the interpretation of these data in regards to sudden cardiac death survivors.

Careful patient selection for this procedure is essential. To be mapped in the EP lab, the patient must display inducible, sustained, monomorphic, hemodynamically stable ventricular tachycardia. These criteria are met in only a small percentage of survivors of sudden cardiac death. Ventricular fibrillation and polymorphic ventricular tachycardia cannot be mapped. If the patient's ventricular tachycardia is hemodynamically unstable, it can be mapped in the operating room after the patient is placed on cardiopulmonary bypass. However, 25% of patients who

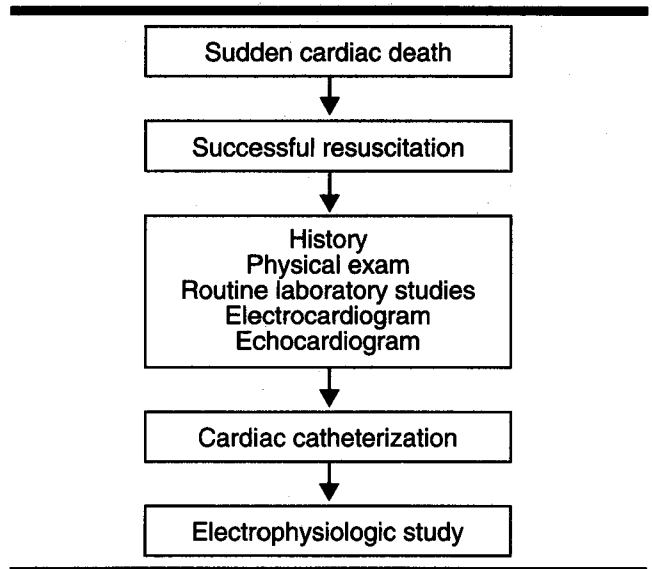


FIGURE 2. Suggested sequence of evaluation for survivors of ventricular fibrillation without acute myocardial infarction or other reversible cause.

are inducible in the EP lab can no longer be induced under these circumstances. Thus, although this procedure is effective in appropriate patients, it has limited applicability to survivors of sudden cardiac death.

### The implantable defibrillator

Introduced in 1980, the automatic implantable cardioverter-defibrillator (ICD) has been implanted in over 10,000 patients worldwide. It is clearly the most effective means available for preventing recurrent sudden cardiac death (Figure 1). Earlier devices were associated with an annual arrhythmic death rate of around 2%.<sup>48</sup> The current generation of devices seem to reduce this rate to less than 1%.<sup>49</sup> This reduction is probably attributable both to improvements in the technology and to a broadening of patient selection criteria. As previously stated, most survivors of sudden cardiac death have left ventricular dysfunction; the degree of left ventricular dysfunction is a powerful independent predictor of both subsequent arrhythmic and non-arrhythmic death.<sup>35,38</sup> The ICD is effective in reducing the rate of arrhythmic death, thereby improving overall survival regardless of the degree of left ventricular dysfunction.<sup>50</sup>

The device is currently implanted via an open-chest procedure, either through a lateral thoracotomy or a median sternotomy. Operative mortality is around 1% when implantation is performed as an isolated proce-

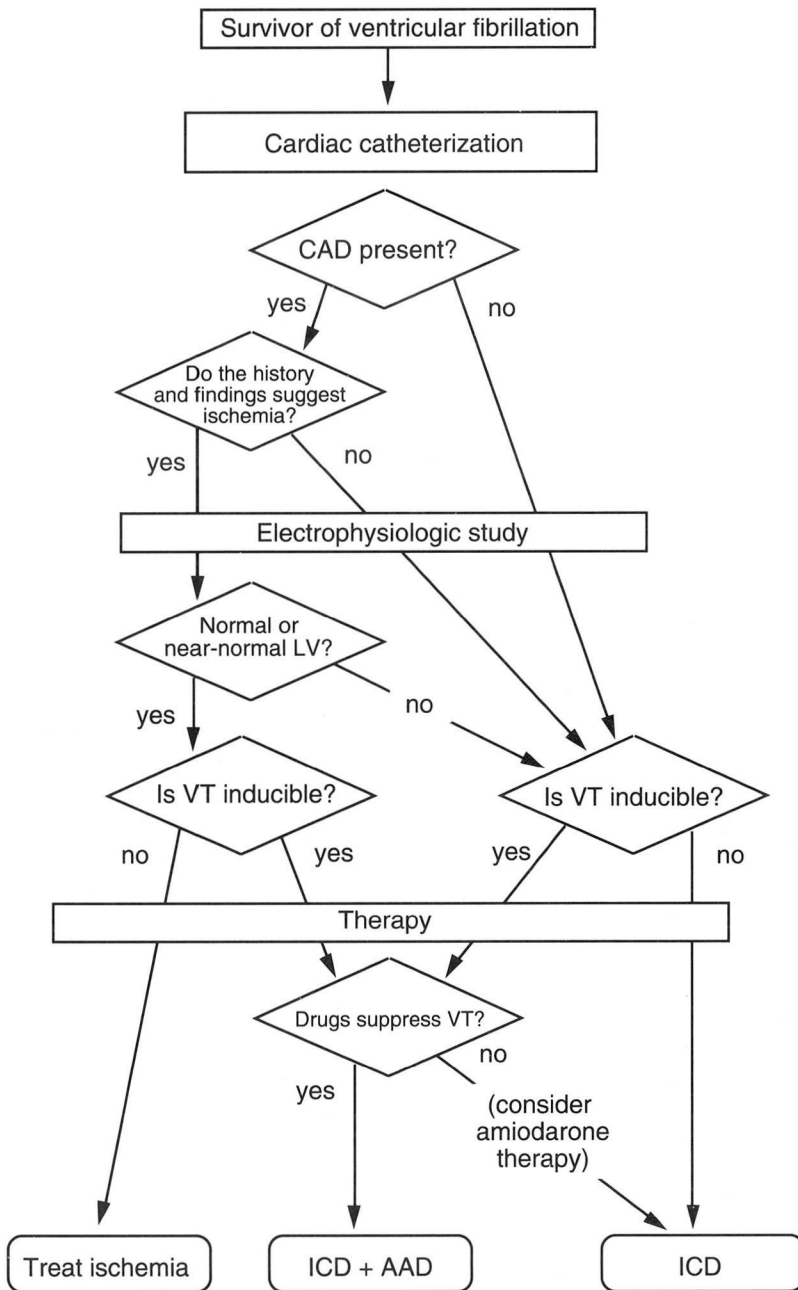


FIGURE 3. Suggested evaluation and treatment protocol. (CAD, coronary artery disease; AICD, automatic implantable cardioverter defibrillator; AAD, antiarrhythmic drugs.)

procedure; mortality rates are higher when implantation is combined with other open-heart operations. A transvenous system currently in clinical investigation employs subcutaneous rather than epicardial charge-delivering patches, thus obviating the need for major

physiological profile, and therapy should be individualized based on these findings (Figure 3). On following this protocol, existing cardiac conditions are appropriately treated, and hemodynamics are optimized. Myocardial ischemia is minimized with drugs

surgery. Further improvements are expected, such as increased programmability, better arrhythmia-sensing capabilities, and anti-tachycardia and -bradycardia pacing.

Most patients with the ICD require concomitant antiarrhythmic drug therapy. The discharge is painful in an awake individual, and frequent or inappropriate shocks can have a negative psychological impact<sup>48</sup> and lead to premature battery depletion. Current devices rely primarily on heart rate for arrhythmia detection, and care must be taken to avoid discharges for inappropriate rhythms (eg, supraventricular tachycardia, nonsustained ventricular tachycardia).

#### SUMMARY

The need for prompt evaluation and therapy of survivors of nonacute-MI sudden cardiac death is underscored by data that suggest that the highest risk of recurrence is in the first 6 months following the initial episode.<sup>38</sup> This evaluation should begin in the hospital as soon as it appears certain that resuscitation has been successful (Figure 2). The patient should be characterized with regard to underlying cardiac status and electro-

or revascularization; in a small group of patients with well-preserved left ventricular function and negative EP studies, this may suffice to prevent recurrence.

For the remaining patients, who remain at high risk of recurrence, the ICD is the therapy associated with the greatest reduction in mortality, and its use has been advocated as the treatment of choice in survivors of cardiac arrest.<sup>51</sup> EP studies and Holter monitoring

should be used (both prior to implantation and in follow-up) to optimize patient-device interaction and to assess concomitant antiarrhythmic drug therapy, when necessary. The goal of ICD therapy is to minimize the risk of arrhythmia recurrence, and to maximize the chance of survival on recurrence. Thus, the ICD may be thought of as a "first line of therapy but a last line of defense."

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