Management of Ventricular Arrhythmias

Detection, Drugs, and Devices

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Ventricular arrhythmias are ubiquitous and range from single premature ventricular complexes (PVCs) to sudden cardiac death due to ventricular tachycardia (VT) or ventricular fibrillation (VF). Data from 2 decades of clinical electrophysiological studies have allowed great progress in the evaluation and treatment of patients with sustained ventricular arrhythmias and the appropriate identification of those patients at high risk of subsequent sudden death. This review examines the history of the treatment of ventricular arrhythmias, the workup and therapies available, specific disease states, and recommended treatment strategies.

**METHODS**

A MEDLINE search of English-language publications of ventricular arrhythmias and their reference lists from 1966 through April 27, 1998, was performed. Search terms included arrhythmia, cardiac complexes premature, electrocardiography, heart failure, tachycardia, death sudden cardiac, coronary disease, defibrillators implantable, antiarrhythmic agents, ablation catheter, myocardial infarction, ventricular dysfunction, clinical protocols, and clinical trials. The search included the data source items listed of 778 potential publications to retrieve; we evaluated 310 and 73 were included as references. In addition, references in the articles were scanned. Randomized controlled trials and all large nonrandomized trials of arrhythmias and arrhythmia therapy were reviewed. In addition, studies that led to changes in approach to patients with arrhythmias were reviewed.

**Objective** To review evaluation and treatment of patients with ventricular arrhythmias, based on recent studies, with an emphasis on randomized controlled trials.

**Data Sources** MEDLINE search of English-language publications of ventricular arrhythmias and their references from 1966 through April 27, 1998. References to articles were also scanned to broaden the search.

**Study Selection** Randomized controlled trials and all large nonrandomized trials of arrhythmias and arrhythmia therapy were reviewed. In addition, studies that led to changes in approach to patients with arrhythmias were reviewed.

**Data Extraction** We reviewed articles jointly for pertinent studies and information.

**Data Synthesis** The goals of treatment of the patient with ventricular arrhythmias are to suppress symptoms and prevent a fatal event. The steps in providing such therapy include defining the cardiac anatomy, assessing arrhythmia risk through noninvasive or invasive testing, and prescribing treatment based on these results. Patients may be separated into high- and low-risk groups to help identify appropriate treatment. While low-risk groups may benefit from reassurance or medications such as β-blockers or verapamil, high-risk groups have been more difficult to treat. Recent randomized trials of implantable cardioverter defibrillators for ventricular arrhythmias suggest that they may provide better protection for high-risk patients than do antiarrhythmic medications.

**Conclusions** Treatment and understanding of risk from ventricular arrhythmias have advanced substantially in recent years. Classifying patients as being at high or low risk for fatal arrhythmias allows the physician to identify appropriate treatments for the high-risk patient without exposing the low-risk patient to unnecessary treatment-related risks.

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showed the shortcomings of warning arrhythmias. For example, 155 (59%) of 262 patients with an acute myocardial infarction (MI) had warning arrhythmias, yet only 12 (7%) had primary VF, and 8 (40%) of 20 with primary VF had no warning arrhythmias. Furthermore, most recorded episodes of VT result from midcycle rather than R-on-T PVCs, and R-on-T PVCs initiated VT in only 14 (15%) of 94 episodes in 1 study. Even in 47 patients with a history of VT, introduction of PVCs onto the T wave at electrophysiologic testing did not initiate sustained VT or VF. Recent data have shown that it is the combination of nonsustained VT or frequent PVCs in patients with substantial left ventricular dysfunction (LVEF ≤ 0.40) that identifies a high-risk group for subsequent sudden death, not the morphological aspects of the PVC itself. 

Lidocaine Prophylaxis
Primary VF (VF in the absence of other significant factors, such as heart failure) is a well-known complication of an acute MI. In a review of randomized trials, routine lidocaine use reduced the occurrence rate of primary VF by one third. However, lidocaine prophylaxis did not have any beneficial effect on early mortality and, in contrast, may even have increased mortality. In general, intravenous lidocaine prophylaxis for patients with acute MI in a coronary care unit is not warranted, but lidocaine may be useful to suppress symptomatic ventricular arrhythmias.

PVC Suppression and CAST
The Cardiac Arrhythmia Suppression Trial (CAST) was a randomized, placebo-controlled study that tested the hypothesis that suppression of asymptomatic or minimally symptomatic PVCs after MI would reduce death due to arrhythmia. Drugs selected for study were encainide hydrochloride, flecainide acetate, and moricizine. The CAST Data Safety Monitoring Board interrupted the original study protocol prematurely and recommended that encainide and flecainide be discontinued. Even though these drugs successfully suppressed PVCs, arrhythmic death was more common in patients treated with drugs (4.5%) than placebo (1.2%), with a relative risk of 3.6. Furthermore, total mortality was also greater with encainide or flecainide (7.7%) compared with placebo (3.0%), with a relative risk of 2.5. The second Cardiac Arrhythmia Suppression Trial (CAST-II) was also prematurely discontinued due to increased mortality in patients treated with moricizine compared with placebo in the early phase, and in the long-term phase it was estimated that no survival benefit would be obtained from moricizine if the trial continued to completion.

The results from CAST and CAST-II were both surprising and discouraging to many physicians who assumed incorrectly that if PVCs were associated with an increased mortality in patients after MI, then suppression of PVCs should improve survival. However, antiarrhythmic drugs can also be proarrhythmic, which can lead to cardiac arrest. In CAST and CAST-II, proarrhythmia occurred early as well as throughout the trials. One hypothesis to explain the later, or secondary, proarrhythmic events was an interaction of the antiarrhythmic drugs and myocardial ischemia.

A negative effect of the CAST trials has been the assumption by many physicians that it is not worth pursuing risk stratification after MI to identify patients at high risk for sudden death. On the contrary, implantable cardioverter defibrillator (ICD) therapy can lead to improved survival in a subgroup of patients selected by noninvasive parameters and electrophysiologic testing.

Tests Used to Evaluate Arrhythmias
Sustained Ventricular Arrhythmias
Electrophysiologic Testing. Electrophysiologic testing involves introduction of electrode catheters for the purposes of pacing and recording electrical activity from within the heart to determine whether VT or other arrhythmias can be induced. An electrophysiologic study can provide both diagnostic and therapeutic information. For more than 2 decades, electrophysiologic testing has been used to judge drug efficacy in patients with sustained VT and survivors of cardiac arrest. The predictability of electrophysiologic study appears best for patients with a relatively stable substrate, eg, myocardial scar after infarction. Although recurrence of sustained VT in very high-risk patients can be predicted fairly accurately with electrophysiologic study, a limitation of this technique is the occurrence of false-negative results, with an inability to predict subsequent sudden death uniformly in very high-risk patients. Electrophysiologic-electropharmacologic testing has enjoyed widespread use as a method to determine adequacy of antiarrhythmic drug therapy for patients with sustained tachyarrhythmias. However, the data from the Antiarrhythmics Versus Implantable Defibrillator (AVID) Study, in which electrophysiologic testing was not done, have lessened its role in the management of many patients.

Noninvasive Tests. Use of noninvasive tests has been proposed as an alternative to serial electrophysiologic-electropharmacologic testing to guide drug therapy for patients with sustained VT or VF. Mitchell et al. in a randomized clinical trial of 57 patients with VT or VF, showed that the probabilities (mean [SD]) of remaining event-free at 1 and 2 years after the VT or VF event, respectively, were 0.76 (0.08) and 0.50 (0.10) in the noninvasively guided patients vs 0.89 (0.06) and 0.80 (0.08) for the invasively guided patients (P = .02). A second trial, the Electrophysiologic Study Versus Electrocardiographic Monitoring (ESVEM), randomized 486 (23%) of 2103 enrolled patients to either serial electrophysiologic drug testing or electrocardiographic (ECG) monitoring to guide therapy. Reasons for not enrolling patients included factors such as patient or physician refusal to participate in ESVEM and inability of patients to meet both noninvasive and invasive criteria. During follow-up, there was an inordinately high recurrence rate of ventricular tachyarrhythmias in patients predicted to have achieved drug efficacy by either technique. For ex-
example, in the electrophysiologic study group and the ECG monitoring group, the actuarial recurrence rates (mean SE) were, respectively, 32% (5%) and 41% (4%) at 1 year and 47% (5%) and 51% (4%) at 2 years.27

The poor predictability of electrophysiologic testing in ESVEM is contrary to most of the published data regarding use of this technique.21-23 For example, in a study by Haverkamp et al,23 210 patients with sustained VT or VF had sotalol hydrochloride therapy guided by electrophysiologic testing. The 1-year arrhythmia recurrence rate was 11%, which is considerably lower than the 21% 1-year recurrence rate for sotalol reported in ESVEM.28 The reason for the substantial discrepancies in the usefulness of electrophysiologic testing to guide drug therapy reported in ESVEM vs other studies21-23 is not clear and is likely related to several factors, including enrollment bias, previous drug failures, and an inadequate electrophysiologic testing protocol during drug therapy.29

**Risk Stratification for Primary Prevention**

Survival rates for out-of-hospital cardiac arrest are typically low, from 2% to 25%, in the United States.30 Thus, identification and appropriate preventive therapy for the patient at high risk for sudden cardiac death are necessary to decrease the incidence of this problem that affects nearly 300,000 individuals each year in the United States.31 In patients with coronary artery disease and documented sustained monomorphic VT, electrophysiologic testing initiates sustained VT in 90% to 95% of patients.21 The high sensitivity of electrophysiologic testing in patients with coronary artery disease has encouraged its use for risk stratification after MI.12,32-34 The theory is that induction of sustained VT at electrophysiologic study identifies a high-risk group for subsequent arrhythmic mortality, and that appropriate therapy can improve survival. Two multicenter, randomized controlled trials, the Multicenter Unsustained Tachycardia Trial (MUSTT) and the Multicenter Automatic Defibrillator Implantation Trial (MADIT), have used electrophysiologic testing for risk stratification in patients with significant left ventricular dysfunction after MI.12,32 Enrollment in MUSTT has been completed but outcome results are not yet known. The MADIT data suggest that high-risk patients can have improved survival after MI if electrophysiologic testing is used to identify those at highest risk and ICD therapy is then used.32 An important trial, the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT), has recently begun and will compare standard medical therapy with empirical amiodarone or empirical ICD implantation in individuals known to be at high risk for sudden cardiac death.33

In addition to left ventricular function, there are other noninvasive parameters that appear useful to identify patients at high risk for cardiac mortality. Signal-averaged electrocardiography is a technique that identifies ventricular late potentials, which presumably represent areas of slowed conduction in abnormal ventricular tissue that is arrhythmogenic.33 Several studies have supported the prognostic significance of SAECG for mortality after MI.36-38 Sustained VT in the first year after MI occurred in 14% to 29% of patients with an abnormal SAECG result compared with 0.8% to 4.5% with a normal SAECG result.39 Unfortunately, the relatively low positive predictive accuracy of SAECG limits its clinical applicability.

Heart rate variability is another noninvasive test used for risk stratification.30 Respiratory sinus arrhythmia can provide a noninvasive measure of parasympathetic control of the sinus node and presumably reflects parasympathetic tone on other cardiac tissue.40 Determination of heart rate variability can be as simple as a 1- to 2-minute bedside breathing test41 or more complicated by evaluation of time- or frequency-dependent values obtained during longer monitoring periods.39 Abnormal heart rate variability is an independent predictor of mortality after MI.28,42-45 The role of heart rate variability in risk stratification, as well as other noninvasive tests, such as ventricular repolarization43 and QT dispersion,44,45 remains to be determined.

**TREATING HIGH-RISK PATIENTS**

**Implantable Cardioverter Defibrillator**

The concept of the ICD (an implanted device that will recognize and quickly treat malignant arrhythmias) has not changed since its inception by Michele Mirowski, MD, but the technology has evolved quickly.46 The first ICD was implanted in 1980, and the US Food and Drug Administration approved its release in 1985.

Subsequent studies confirmed the efficacy of the ICD to prevent recurrent sudden death.47-49 Winkle et al47 reported a sudden death survival of 90% at 1 year and 96% at 5 years and an overall survival of 92% at 1 year and 74% at 5 years in 270 patients. Retrospective reports compared the ICD with amiodarone therapy and found improved survival in the ICD group.50 However, there were clinical problems noted by all centers that used these early devices, which required a thoracotomy for implantation. Complications included a small but important operative mortality of 2% to 7%, a small risk of device infection, and postoperative atrial and ventricular arrhythmias.

In the largest retrospective series of cardiac arrest survivors, Powell et al51 compared survival in 331 patients receiving either electrophysiologically guided antiarrhythmic drugs (and appropriate therapy for coronary artery disease) or an ICD. In the 150 patients receiving an ICD, the total mortality was 29% vs 62% in the 181 patients without an ICD. The effect was most striking in patients with an LVEF of 0.40 or less. This study also showed that left ventricular function was more important in predicting long-term survival than the presence of an ICD because patients with high LVEF (>0.40) without a device had better survival than patients with low LVEF (≤0.40) with an ICD.

Implantable cardioverter defibrillator technology has become increasingly sophisticated during the last decade and has made the device easier to use for both the patient and the physician. The lead system can now be implanted transve-
nously, which obviates the need for a thoracotomy. The generators have become smaller and are now 40 cm³ in size and positioned in the pectoral position, as is a pacemaker generator. Generator function has also become very complex in what are known as third-generation devices. Extensive programmability of arrhythmia detection features and delivered therapies to convert either VT or VF is standard. Programmable antitachycardia pacing can be used as first-line therapy to convert pace-terminable VT. Stored electrograms give accurate diagnostic information about the cause of device activation (FIGURE 1). The newest ICDs feature single- or dual-chamber pacing capability with rate response, and more than half of the devices being implanted are now dual-chamber. The device complication profile has improved significantly. An occasional lead fracture is encountered and ICD infection is a problem on rare occasion.

**Direct VT Surgery**

Prior to the widespread use of the ICD, a direct surgical approach to VT was used in many centers. Cox² examined 5 large published series, including 483 patients who underwent map-directed surgical ablation of the VT focus. The majority of these patients also had coronary artery bypass surgery. The major clinical drawback of the procedure was the high operative mortality, which averaged 13.4% (range, 6%-21%), even in these high-volume centers. Therapy with ICDs has largely supplanted direct ablative surgery for the treatment of patients with sustained VT because of the low operative risk of ICD implantation (<1%), as well as the excellent long-term patient survival with the ICD, which was 75% at 36 months in the AVID trial.

**Catheter Ablation**

The early 1990s were an era of explosive growth in the successful application of radio frequency (RF) catheter ablation to cure supraventricular rhythms. This procedure is performed in a cardiac catheterization laboratory and uses a form of electricity generated from low-power, high-frequency alternating current that delivers high temperature to the targeted tissue. Patients with VT who are younger and have healthy hearts are routinely treated with RF ablation. The origin of their VT is either in the right ventricular outflow tract or in the left ventricle near the septum. Before ablation, these cases present with a characteristic ECG pattern (left bundle-branch block–inferior or right axis from right ventricular outflow tract, right bundle-branch block–left axis deviation from the left ventricle); RF therapy results in a success rate of more than 90%.

The application of RF ablation techniques in patients with VT due to coronary artery disease and a prior MI is much more problematic, although this area is changing rapidly. The indications to ablate VT in this population are not agreed on and generally include either incessant VT that cannot be controlled with drugs or episodes of VT (in a patient with an ICD) that cause frequent device discharges. Most experienced centers can successfully ablate the target VT in such patients 60% to 70% of the time. New technology using special catheters that will deliver a larger lesion likely will improve rates of success.

**Adjunctive Therapy**

β-Adrenergic blockers have been demonstrated for decades to reduce total mortality and sudden death mortality after MI. More recently, Packer et al² demonstrated in patients with heart failure that carvedilol reduced the risk of death from 7.8% in controls to 3.2% in the carvedilol group. Angiotensin-converting enzyme inhibitors have been shown to decrease total mortality by 18% to 27% in patients with diminished LVEF and heart failure. Trandolapril also reduced sudden death, with a relative risk of 0.76 compared with placebo. Finally, lipid lowering with simvastatin in patients with coronary artery disease decreased total mortality, with a relative risk of 0.70 vs placebo.

**CURRENT APPROACHES**

**General Evaluation**

The patient with a suspected arrhythmia poses a special challenge for the clinician at many levels. There are no published practice guidelines on this subject, and our approach is summarized herein. Where suggestions are based on specific studies, the study is cited.

The physician needs to carefully evaluate prior clinical episodes that may suggest the occurrence of a tachyarrhythmia. Taking a careful family history is also critical to identify family members who may have died suddenly. Establishing the presence of a cardiac arrhythmia may carry considerable survival risk for a patient, and special attention needs to be given to the fears of the patient and family.

The medical evaluation of a patient with an arrhythmia typically involves a standard set of tests to evaluate cardiac structure and arrhythmia prevalence. Causes are listed in TABLE 1. The cardiac anatomy is defined, usually through an echocardiogram (or a stress echocardiogram or nuclear study if ischemia is suspected). An ECG may reveal caus-
tation (eg, long QT syndrome or right bundle-branch block with ST-segment elevation). If the patient’s cardiac symptoms are present on a frequent basis, a Holter monitor result is obtained, but if the symptoms are infrequent and paroxysmal, an event recorder is useful. Such monitoring can be used for weeks, and there are now subcutaneous monitors that can be used for months at a time. It is important to assess serum potassium and magnesium levels. The need for electrophysiological testing or cardiac catheterization is determined through this evaluation.

**Treatment by Patient Type**

The proposed treatment algorithm incorporates data from randomized clinical trials whenever they are available (Figure 2). In the absence of such data, the approach is that of the authors, based on published data and our own experience in treating such patients for a combined 50 years.

**Minimally Symptomatic or Asymptomatic With Low Mortality Risk.** The patient with PVCs or nonsustained ventricular arrhythmias and few or no symptoms who has normal cardiac function can be reassured of an excellent long-term prognosis. Patients with palpitations secondary to PVCs and normal cardiac function (a common clinical situation) also have an excellent prognosis. Kennedy et al followed up a cohort of 65 patients with palpitations for a mean of 7.5 years, with only 1 death. The preferred treatment in such patients is reassurance alone or the use of a β-blocker for symptomatic control of ventricular premature beats. It is important to normalize magnesium or potassium levels. Some patients with very marked symptoms may require more aggressive therapy with drugs such as moricizine or sotalol for symptomatic relief alone. This group of patients is often the most difficult to reassure.

**High Mortality Risk.** Patients who have had an MI need careful evaluation in the weeks after the MI to determine future arrhythmic risk. The most important risk factor is left ventricular function, and those with impairment of LVEF (eg, ≤0.40) are excellent candidates for risk stratification. The workup should include a measurement of ambient ventricular ectopy and/or VT. The risk of a future serious event is low if the LVEF is more than 0.40 and there is no VT. Such patients can be treated with reassurance and appropriate post-MI therapy, including aspirin and a β-blocker.

During the past decade, several small studies have suggested that the prophylactic use of amiodarone in high-risk patients who have had an MI would be beneficial in terms of arrhythmia prophylaxis and improved survival. The European Myocardial Infarction Amiodarone Trial

**Figure 2. Treatment Algorithm for Patients With Ventricular Arrhythmias**

Table 1. Causes of Sustained Ventricular Tachycardias

<table>
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<th>Cause</th>
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<tr>
<td>Coronary artery disease</td>
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<tr>
<td>Idiopathic dilated cardiomyopathy</td>
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<tr>
<td>Hypertrophic cardiomyopathy</td>
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<tr>
<td>Right ventricular dysplasia</td>
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<tr>
<td>Long QT syndrome</td>
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<tr>
<td>Electrolyte abnormalities and proarhythmia from antiarrhythmic drugs</td>
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<tr>
<td>Infiltrative heart disease (amyloid, sarcoid)</td>
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<tr>
<td>Valvular heart disease</td>
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VT indicates ventricular tachycardia; VF, ventricular fibrillation; AA, antiarrhythmic; CAD, coronary artery disease; CM, cardiomyopathy; EPS, electrophysiologic study; LVEF, left ventricular ejection fraction; PVC, premature ventricular complex; VT-NS, nonsustained ventricular tachycardia; VT-S, sustained ventricular tachycardia; RFCA, radio frequency catheter ablation; and ICD, implantable cardioverter defibrillator. Asymptomatic patients with PVCs require no therapy. If palpitations are present, we prefer reassurance and β-blockers as a first-line approach. If the patient still has symptomatic PVCs, other AA agents can be used and the choice of drug depends on physician preference and patient characteristics. Patients at low risk (eg, LVEF >0.40) need only reassurance or β-blockers with symptoms and no therapy without symptoms. Patients with symptoms in whom this approach does not work may be treated with AA drugs or RFCA, especially if the site is in the right ventricular outflow tract. In higher-risk patients with lower ejection fractions and CAD, EPS is used. If VT-S is initiated, an ICD is recommended. In patients without VT-S, in the absence of symptoms we prefer reassurance or without β-blockers. In symptomatic patients, β-blockers or AA drugs may be used. Patients with VT-S and healthy hearts have primarily right ventricular outflow tract sites or idiopathic left ventricular focus. Sotalol is an excellent agent for patients with idiopathic left VT, and either β-blockers or verapamil may be used for a patient who has right ventricular outflow tract VT. Alternatively, RFCA can cure these individuals. If neither approach is effective, other AA drugs may be tried. In patients with cardiomyopathy, we do not have confidence in serial electrophysiologic-electropharmacological testing and recommend an ICD as initial therapy. For patients with CAD, we stratify based on the LVEF if >0.35 and the patient has neither presyncope or syncope, EPS is performed. If VT-S is reproducibly initiated, guided therapy by EPS with either sotalol or amiodarone may be used. If the arrhythmia becomes noninducible or markedly slowed with stability identified at EPS, the patient may be discharged receiving this drug. If neither result occurs, an ICD is recommended. In patients in whom VT-S cannot be initiated, an ICD is used. For patients in whom the LVEF is less than 0.35, especially with syncope or presyncope, an ICD is recommended as initial therapy. For patients who have had cardiac arrest, rule out a reversible cause such as an acute myocardial infarction. If a clear-cut reversible cause is identified, correction of the underlying problem may be all that is necessary. In most cases, no obvious reversible cause is present and an ICD is recommended.

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(EMIAT) enrolled 1482 patients with an LVEF of less than 0.40 within 5 to 21 days of their MI. The Canadian Myocardial Infarction Amiodarone Trial (CAMIAT) enrolled 1202 patients and was similar, except that patients had no LVEF cutoff but did have a criterion of more than 10 PVCs per hour. Analyzed on an intention-to-treat basis, EMIAT data showed no effect on all-cause mortality while CAMIAT data showed a reduction of 18% and did not reach statistical significance. However, both of these studies showed reductions in sudden death: 35% for EMIAT (P = .05) and 48.5% for CAMIAT (P = .02). Also, in both trials, 43% of the patients discontinued amiodarone by 2 years because of adverse effects or intolerance. Sotalol is a class 3 antiarrhythmic agent that has nonsselective β-blocker activity and also blocks the rapid component of the delayed rectifier potassium current. In an early post-MI trial, Julian et al randomized 1456 patients to either placebo or sotalol hydrochloride, 320 mg/d. After 12 months, the mortality rate was 18% lower in the sotalol group than the placebo group, although this difference did not reach statistical significance. Thus, sotalol, like amiodarone, appears safe to use in the early post-MI period if needed, but neither should be routinely given as prophylaxis to prevent mortality.

The MADIT studied a group of 196 patients from 1989 to 1996. The hypothesis was that patients with prior MI with both an LVEF of no more than 0.35 and nonsustained VT on Holter monitoring had a high risk of sudden death. To further define high risk, all patients were studied in the electrophysiology laboratory. Patients who could be induced into sustained VT and not suppressed with intravenous procainamide hydrochloride were considered to be at the highest risk. Per protocol, these patients were randomized either to empirical (usually amiodarone) or ICD therapy. After an average patient follow-up of 27 months, the study was prematurely terminated because the ICD group had 15 deaths vs 39 deaths in the conventional group, a 54% reduction (P = .009; Figure 3).

There is little doubt that the MADIT population was at high risk. The mean LVEF of the conventional group was only 25% and that of the ICD group was 27%. The survival of the patients in the conventional group (all-cause mortality) was only 51% at 4 years. In contrast, the survival in the defibrillator group was 86%. This is because the number of deaths due to primary arrhythmia was reduced by the ICD from 13 in the conventional group to 3 in the defibrillator group. The trial has been criticized because many of the control patients stopped taking amiodarone and there was a higher incidence of β-blocker use in the ICD group.

There are many clinical situations in which antiarrhythmic drugs are needed, especially when caring for patients with supraventricular arrhythmias (eg, atrial fibrillation). There is ample evidence in the literature that both sotalol and amiodarone are safe, with a very low incidence of proarrhythmia. Ethmozine may be used safely if at least 2 weeks has elapsed since a patient had an MI. The class 3 agent dofetilide may be clinically useful for such patients in the future. Data from CAST-I prohibit the use of type-IC drugs if myocardial ischemia is a clinical consideration. Opinion varies about whether such drugs must be started under direct hospital monitoring or whether outpatient drug initiation with careful attention to ECG changes in the QT interval is sufficient. As a general rule, the greater the left ventricular dysfunction, the greater the need to initiate drugs in the hospital.

Sustained VT. Patients with sustained VT have been studied by clinical electrophysiologists for the past 20 years. The subsequent arrhythmic mortality rate is generally estimated to be 20% at 2 years.

The AVID Trial studied cardiac arrest survivors, patients with sustained VT and syncope, and patients with sustained VT and an LVEF of less than 0.40 who had hypertension, chest pain, or pre-syncope during VT. The trial screened 6035 patients and eventually enrolled a total of 455 patients with VF and 561 with VT. The mean LVEF of the entire population was 0.31; more than half had congestive heart failure, and the majority were taking an angiotensin-converting enzyme inhibitor.

Patients were randomized to receive either amiodarone or sotalol (based on LVEF >0.40 or ≤0.40) or an ICD. Amiodarone was given empirically and only 74 patients received sotalol; thus, the results of the trial actually reflect the benefits of amiodarone vs ICD. Total mortality was the measured end point. The
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Table 2. Indications for Implantable Cardioverter Defibrillator Therapy, 1998: After the ACC/AHA Guidelines

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<th>Condition</th>
<th>Indication for ICD Therapy</th>
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<tr>
<td>Cardiac arrest due to VF or VT and not due to a transient or reversible cause</td>
<td>ICD if VF or VT is hemodynamically significant sustained VT. The syncopal episode is not suppressible by a class-1 antiarrhythmic drug (confirmed by electrophysiologic testing).</td>
</tr>
<tr>
<td>Spontaneous sustained VT (confirmed by AVID)</td>
<td>ICD if the syncope of undetermined origin is hemodynamically significant sustained VT or VT induced at electrophysiologic testing when low dose is ineffective.</td>
</tr>
<tr>
<td>Nonsustained VT with coronary artery disease, prior left ventricular dysfunction, inducible VF, or sustained VT at electrophysiologic testing that is not suppressible by a class-1 antiarrhythmic drug (confirmed by the Multicenter Automatic Defibrillator Implantation Trial)</td>
<td>ICD if VF or sustained VT is the cause of the cardiac arrest, myocardial revascularization alone may be the treatment of choice.</td>
</tr>
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</table>

*Data are from Gregoratos et al.* ACC indicates American College of Cardiologists; AHA, American Heart Association; VF, ventricular fibrillation; and VT, ventricular tachycardia. Class 1 indicates general agreement that an implantable cardioverter defibrillator is warranted.

The AVID trial was terminated prematurely in April 1997, when it was apparent to the data safety and monitoring board that survival in the ICD group overall was better than in the drug group. At a mean (SD) follow-up of 18.2 (12.2) months, the crude death rates were 15.8% (3.2%) in the ICD group and 24.0% (3.7%) in the drug group. Patients treated with ICD had better survival throughout the course of the study (P = .01; Figure 4). This effect was noted in each of the various subsets as well (VT with syncope and VT with symptoms). These survival figures represent a decrease in death rates (93% confidence limit) of 39% (±20%), 27% (±21%), and 31% (±21%) at 1, 2, and 3 years, respectively. The effect was most prominent in patients with an LVEF of 0.35 or less. There was no survival benefit in patients with an LVEF of more than 0.35. Thus, the AVID trial finally established the superiority of the ICD to amiodarone in the survival of patients with VT.

Cardiac Arrest Survivor. The treatment for patients resuscitated from out-of-hospital cardiac arrest is very similar to the treatment for patients with hemodynamically significant sustained VT. The etiologies of the 2 events are similar, although there is a greater incidence of ischemic events causing VF in patients with coronary artery disease. Patients with resuscitated VF have a recurrence rate approaching 30% at 2 years, which mandates an aggressive clinical approach. However, in this patient group, it is very important to rule out reversible causes, such as acute MI or ischemia, that may not require specific long-term therapy.

The AVID trial defines the preferred therapy for VF patients. Among the 1016 randomized patients, 454 were enrolled with VF as the index arrhythmia. As in the VT patients, the ICD conferred a survival advantage for the VF population.

In patients with coronary artery disease and documented ischemia as the cause of the cardiac arrest, myocardial revascularization alone may be the treatment of choice. A postrevascularization electrophysiologic test is recommended only in patients with low LVEF.

Although the ICD is first-line therapy for patients with cardiac arrest and most patients with sustained VT, approximately one third of these patients will receive antiarrhythmic drugs as well. Antiarrhythmic drugs such as amiodarone and sotalol are needed because of repetitive episodes of VT causing frequent ICD discharges or the appearance of other arrhythmias, especially atrial fibrillation. Indications for ICD therapy are provided in Table 2.

UNRESOLVED ISSUES

The approach to patients with ventricular arrhythmias has changed dramatically in the last 10 years because of both new therapies and the studies cited herein that demonstrate their utility. However, many challenges remain. Patients with a dilated cardiomyopathy and reduced LVEF, especially with heart failure, have a risk of arrhythmia approaching 20% at 2 years, yet we are unsure which, if any, prophylactic therapy is of benefit. The SCD-HeFT trial will help answer that therapeutic question. There are also important issues of cost and quality of life that need to be interpreted by both physicians and insurers. Both the MADIT and AVID trials have strong cost and quality-of-life components. They demonstrated that although device therapy is effective, it is also costly. How we integrate this cost into the health care system and, in turn, how it affects the actual cost of the ICD itself are important issues that have not been fully resolved.

Other scientific issues were not addressed in the trials. The AVID trial did not have any provision for testing electrophysiologically guided therapy. There is uncertainty as to whether electrophysiologically guided amiodarone or sotalol therapy is as legitimate an approach to the high-risk patient with ventricular arrhythmia as empirical ICD therapy. This clinical trial has not been performed and, because of cost issues, probably never will be.

Despite these uncertainties, we now can approach the most commonly seen patients with arrhythmia, from those with simple PVCs to those who have survived sustained VT or VF, and have a deliberate strategy for caring for them based on evidence-based scientific study. The clinical electrophysiology trials completed in the 1990s have resulted in a much more clinically streamlined approach to the high-risk patient.

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