The “modern” era of the treatment of ventricular tachyarrhythmias with device-based therapy may have begun in 1899, when Prevost and Battelli noted, almost as an afterthought, that direct current shock could terminate ventricular fibrillation (VF) in dogs. Three decades later, pioneering work in the field of defibrillation concluded that the passage of electrical current across the heart can both initiate and terminate VF. Still, little attention was paid to this phenomenon, as evidenced by Paul Dudley White’s Heart Disease, which devoted less than half a page to VF and characterized the arrhythmia as “a condition of little importance so far as we know now.” In 1947, the thoracic surgeon Claude Beck saved the first human life by the successful use of cardiac defibrillation in a 14-year-old boy who developed VF during a thoracic surgical procedure and went on to achieve a full recovery. These early accomplishments provided the foundation for the landmark work of Mirowski and Mower that ultimately led to the development of the implantable cardioverter-defibrillator (ICD) and its introduction in humans in 1980.

Permanent Pacing for Sudden Cardiac Death Prevention

Pacing may prevent sudden cardiac death due to bradyarrhythmias and in certain circumstances such as torsade de points associated with congenital long-QT syndrome (LQTS) and pause-dependent ventricular tachycardia (VT). Although no controlled studies exist, retrospective analyses suggest that recurrent torsade de points in patients with LQTS may be prevented by continuous pacing. Early clinical data on small numbers of patients suggested that the combination of beta-adrenergic blockade plus continuous pacing reduced the number of syncopal events and the anticipated rate of sudden death in high-risk LQTS patients. The beneficial effects of pacing may be limited to patients with LQT2 and LQT3, in which the transmural dispersion of repolarization worsens steeply during bradycardia. Genotype-phenotype correlation confirms that pause-dependent torsade de points is rare or absent in LQT1 and predominant in LQT2. Recent work has called into question the long-term benefits of pacing in this population, with the largest series to date demonstrating an overall 24% incidence (17% in compliant patients) of sudden death and aborted sudden death despite continuous pacing and maximally tolerated doses of beta-blockers in a nonrandomized cohort of patients with LQTS, the majority of whom failed beta-blockers alone and nearly all of whom were symptomatic before therapy. These results suggest that although the combination of beta-blockers and pacing may reduce the incidence of recurrent arrhythmic episodes, the failure rate appears to be high enough to warrant backup ICD therapy for high-risk individuals with LQTS. Current guidelines recommend the use of permanent pacing for the treatment of high-risk patients with congenital LQTS and pause-dependent VT with or without prolonged QT intervals.

Implantable Defibrillators for Sudden Cardiac Death Prevention

In contrast to the limited indications for the use of permanent pacemakers in the prevention of sudden cardiac death, expanding use of ICDs has been observed after the publication of a series of landmark studies. These studies have targeted either patients who have already survived a potentially life-threatening arrhythmic event or are considered to be at high risk owing to significant underlying structural heart disease. However, it is a well-recognized paradox that the majority of sudden cardiac deaths occur in those individuals with intermediate risk factors and those without known risk factors. Conversely, the highest-risk subgroups, on which much attention is focused because of the magnitude of the risk of death, actually constitute only a small proportion of the total number of deaths annually.

Patients in whom ICD implantation may be considered can generally be categorized into 1 of several broad groups: (1) patients who have been resuscitated from sudden cardiac arrest or have previously manifested potentially life-threatening ventricular arrhythmias not related to a transient or correctable cause; (2) patients with moderate to severe structural heart disease, including ischemic, nonischemic, and hypertrophic cardiomyopathy; and (3) those with miscellaneous cardiac disorders, genetic and otherwise, for which the risk of arrhythmic death is considered high. We will briefly describe the data supporting the use of ICDs in each of these groups, but caution must be exercised in extrapolating these results to individual patients, because these studies enrolled highly selected individuals who may not be entirely representative of the population at large. Furthermore, underrepresentation of certain cohorts, such as women, minorities, and patients with chronic kidney disease, underscores the challenges in generalizing these findings.

Secondary Prevention

Survivors of sudden cardiac death due to arrhythmia carry a high risk of recurrence. Attempts to significantly reduce this risk with antiarrhythmic drugs yielded disappointing results,
except perhaps in the case of amiodarone. The recognition of the limitations of antiarrhythmic drugs for secondary prevention was paralleled by the development of smaller, transvenous ICDs with tiered therapies, bradycardia pacing, and success rates of >95% in terminating VT and VF. Thus, the stage was set for randomized trials comparing the 2 treatments. The Antiarrhythmics Versus Implantable Defibrillators (AVID) study provided the first controlled evidence of the superiority of ICDs compared with antiarrhythmic drug therapy. The study randomized patients with resuscitated VF, sustained VT with syncope, or sustained VT with ejection fraction ≤40% and evidence of hemodynamic compromise to receive either an ICD or antiarrhythmic therapy, predominantly amiodarone. Overall mortality in the ICD arm was decreased by 39% and 31% at 1 and 3 years, respectively. Subgroup analyses of the AVID data demonstrated that the survival benefit of ICDs was confined to the group with ejection fractions between 20% and 34%. Two additional trials, the Canadian Implantable Defibrillator Study (CIDS) and The Cardiac Arrest Study Hamburg (CASH), both had similar study designs as AVID but showed only nonsignificant trends toward reduced mortality in the ICD arms. A meta-analysis of all 3 trials showed a significant risk reduction of 28% in total mortality and a 51% reduction in the risk of arrhythmic death. Interestingly, whereas the AVID study excluded patients with a transient or correctable cause for their VT or VF from randomization, a registry of all screened patients was maintained that yielded important results. Adjustment for multiple variables revealed that patients with transient or correctable causes, such as new ischemia or infarction, proarrhythmic drug reaction, electrolyte imbalance, or other causes, actually had worse survival than those considered to have primary VT or VF, thus highlighting the inherent challenges in identifying patients at low risk of recurrent arrhythmias and the limited long-term success in treating presumed transient causes.23

Primary Prevention

Primary Prevention in Ischemic Cardiomyopathy

Although survivors of sudden death represent a high-risk group for recurrent events, at-risk patients who have not yet suffered an event are in far greater abundance. Furthermore, given the low survival rate of out-of-hospital cardiac arrest, the potential for impact in terms of absolute number of lives saved is greater overall for primary prevention. Perhaps the only challenge that has rivaled that of the development of the ICD has been in determining who benefits most from its use. Although it now seems obvious that patients with significant underlying structural heart disease stand to gain the most from prophylactic ICD implantation, the medical community was divided over the potential impact of ICDs in the early years after its inception. In light of the fact that pump failure deaths increase and the proportion of deaths attributable to arrhythmias decreases as heart failure worsens, some argued that the impact of ICDs on mortality would be limited in a heart failure population. However, the rationale for using post–myocardial infarction (MI) patients with low ejection fraction as the first group to study is supported by the pathophysiological and observational data. Prior MI may result in both reduced ejection fraction and abnormalities of conduction and refractoriness that serve as the substrate for ventricular tachyarrhythmias. It had been estimated that half of the deaths in the post-MI population are due to VT and VF. The relationship between left ventricular systolic dysfunction and deaths due to progressive heart failure and ventricular arrhythmias in patients who have had an MI is well established. Studies dating back to the advent of cardiac imaging were the first to observe the association between reduced ejection fraction and outcome, with the majority of studies concluding that an ejection fraction of ≤40% serves as the threshold for identifying high-risk individuals.

Over the last decade, 6 major trials have evaluated the role of ICDs in the primary prevention of sudden cardiac death in post-MI patients with reduced ejection fraction. A summary of these studies is presented in Table 1. These studies have not only established the utility of ICDs for this purpose but have also demonstrated that the risk of sudden cardiac death in a high-risk cohort treated with current medical therapies is approximately 5% per year and is considerably less than previously estimated. More recently, the Multicenter Automatic Defibrillator Implantation Trial (MADIT) II trial required only prior MI >1 month before enrollment and an ejection fraction ≤30% for study inclusion, given the uncertainties surrounding the long-term predictive value of invasive electrophysiological testing and the near-ubiquitous finding of ambient arrhythmias in the ischemic cardiomyopathy cohort. This study of 1232 patients compared overall mortality in ICD-treated patients versus those treated with conventional medical therapy that included β-adrenergic blockers and ACE inhibitors. Overall mortality was reduced by 31% in patients randomized to receive ICDs during a mean follow-up of 20 months. The mortality benefit resulted entirely from the observed reduction in the risk of arrhythmic death and appeared to be greatest for patients with more remote MIs. The sum of the clinical data suggests that the risk of arrhythmic death has a complex distribution, with an early peak apparently related to acute infarction or pump failure, followed by a gradual increase over time, possibly as the result of long-term electrical remodeling or the development of new ischemia.

The largest study to date demonstrating the superiority of ICDs to medical therapies, including antiarrhythmic therapies, is the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT). This 3-armed study randomized 2521 patients with ischemic or nonischemic cardiomyopathy, an ejection fraction ≤35%, and class II to III congestive heart failure to conventional therapy, conventional therapy plus weight-adjusted amiodarone, or conventional therapy plus a single-zone, single-chamber ICD with backup pacing only. Over a mean follow-up of 45.5 months, survival was no different in the standard therapy arm with and without amiodarone but was 23% lower in the group treated with an ICD. These results were consistent regardless of the cause of heart failure.

Among the central themes of sudden cardiac death prevention has been the understanding that the highest risk of arrhythmic death occurs around the time of an acute MI. The development of coronary care units in the 1960s, the acces-
sibility to rapid external defibrillation, and the associated decline in the rates of post-MI mortality further served as proof-of-concept. However, it has also been recognized that some sustained tachyarhythmias occurring in the immediate peri-MI period may have little long-term prognostic value, especially when they occur in the first few hours of the event.42 With the exception of the Multicenter UnSustained Tachycardia Trial (MUSTT), most ICD studies excluded patients within 3 weeks of an MI. The Defibrillators In Acute Myocardial Infarction Trial (DINAMIT) was designed to test the hypothesis that survivors of recent MI (6 to 40 days) with an ejection fraction of \( \leq 35\% \), and evidence of sympathetic activation as assessed by heart rate variability would derive a survival benefit from ICD implantation. DINAMIT randomized 674 patients to an ICD or standard medical therapies but surprisingly found no difference in overall mortality between the 2 groups during an average follow-up of 30 months. These results occurred despite a 58% reduction in the relative risk of arrhythmic death and were driven mainly by an increase in nonarrhythmic cardiovascular mortality in the ICD arm.38 Although, as the authors suggest, it is possible that VT/VF in this population may serve as a marker for patients at high risk of mechanical cardiovascular mortality from issues such as pump failure, these intriguing findings require further study before final conclusions can be drawn.

**Primary Prevention in Nonischemic Cardiomyopathy**

Although coronary artery disease accounts for \( \approx 80\% \) of the cases of dilated cardiomyopathy, patients with nonischemic dilated cardiomyopathy are also at increased risk of sudden cardiac death by less well-understood mechanisms and have served as the focus of several trials addressing this issue. In the aforementioned SCD-HeFT trial, the beneficial effects of ICD therapy applied equally to patients with ischemic and nonischemic cardiomyopathy.34 Other ICD studies limited to patients with nonischemic dilated cardiomyopathy include the CARDiomyopathy Trial (CAT), the AMIOdarone versus implantable cardioVERTer-defibrillator trial (AMIOVERT), and the DEFibrillator In NonIschemic cardiomyopathy Treatment Evaluation (DEFINITE).43–45 The largest of these trials, DEFINITE, randomized 458 patients with nonischemic dilated cardiomyopathy, ejection fraction \( \leq 35\% \), ambient ventricular arrhythmias, and class I to III heart failure to receive either ICD or standard medical therapy. Throughout a mean follow-up of 29 months, there was a nonsignificant 35% relative risk reduction in all-cause mortality and a highly significant 80% reduction in risk of arrhythmic death.44 A meta-analysis of all primary prevention trials to date that included nonischemic cardiomyopathy patients found a statistically significant 26% overall reduction in total mortality with standard (non–cardiac resynchronization therapy [CRT]) ICD use.21 Recently, the Centers for Medicare and Medicaid Services approved ICD implantation only for patients with nonischemic dilated cardiomyopathy of at least 9 months’ duration, or of 3 months’ duration if the patient was enrolled in the American College of Cardiology/Heart Rhythm Society–sponsored ICD Registry.46–48 Although some nonischemic cardiomyopathies may resolve during this period, the potential benefit must be weighed against the low risk of sudden death in the first months after diagnosis. While an analysis of the DEFINITE data did not reveal any less benefit of ICD therapy in patients with more recent diagnosis

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**TABLE 1. Overview of the Major Randomized Controlled Clinical Trials of ICD Therapy for Primary Prevention of Sudden Cardiac Death in Ischemic Cardiomyopathy**

<table>
<thead>
<tr>
<th>Study</th>
<th>Inclusion Criteria</th>
<th>Number Randomized</th>
<th>Control Group</th>
<th>Primary Point</th>
<th>Main Finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>MADIT I</td>
<td>Prior MI, EF ( \leq 35% ), NSVT, inducible and nonsuppressible VT on EPS, NYHA class I–III</td>
<td>196</td>
<td>Conventional therapy</td>
<td>All-cause mortality</td>
<td>54% RRR in all-cause mortality with ICD ( (P=0.009) ); absolute RR 23%</td>
</tr>
<tr>
<td>CABG-PATCH</td>
<td>EF ( &lt;35% ), abnormal SAECG, elective CABG</td>
<td>900</td>
<td>Conventional therapy</td>
<td>All-cause mortality</td>
<td>No difference in all-cause mortality</td>
</tr>
<tr>
<td>MUSTT</td>
<td>Prior MI, EF ( \leq 40% ), NSVT, inducible VT on EPS</td>
<td>704</td>
<td>EP-guided antiarrhythmic therapy or conventional therapy</td>
<td>Cardiac arrest or death due to arrhythmia</td>
<td>60% RRR in all-cause mortality with ICD ( (P&lt;0.001) ); absolute RR 31%</td>
</tr>
<tr>
<td>MADIT II</td>
<td>Prior MI ( \leq 1 ) month, EF ( \leq 30% ), NYHA class I–III</td>
<td>1232</td>
<td>Conventional therapy</td>
<td>All-cause mortality</td>
<td>31% RRR in all-cause mortality with ICD ( (P=0.016) ); absolute RR 6%</td>
</tr>
<tr>
<td>DINAMIT</td>
<td>Recent (6–40 days) MI, EF ( \leq 35% ), abnormal HRV or elevated average HR on 24-h Holter, NYHA class I–III</td>
<td>674</td>
<td>Conventional therapy</td>
<td>All-cause mortality</td>
<td>No difference in all-cause mortality; 58% RRR from arrhythmia with ICD ( (P=0.009) )</td>
</tr>
<tr>
<td>SCD-HeFT</td>
<td>EF ( \leq 35% ), (ischemic or nonischemic) NYHA class II–III</td>
<td>2521</td>
<td>Conventional therapy ( \pm ) amiodarone</td>
<td>All-cause mortality</td>
<td>23% RRR in all-cause mortality with ICD ( (P=0.007) ); absolute RR 7%</td>
</tr>
</tbody>
</table>

EF indicates ejection fraction; NSVT, nonsustained VT; EPS, electrophysiological study; NYHA, New York Heart Association; RRR, relative risk reduction; RR, risk reduction; CABG, coronary artery bypass grafting; SAECG, signal-averaged ECG; HRV, heart rate variability; and HR, heart rate.
of dilated cardiomyopathy, a watch-and-wait approach in the first few months after diagnosis would likely result in only a small number of events, provided care is taken to monitor patients closely during this time.

The myriad of clinical trials and subgroup analyses examining the role of ICD therapy for primary prophylaxis of sudden death in patients with cardiomyopathy may still leave some practicing physicians with 2 simple questions: Who should get a prophylactic ICD, and when should it be implanted? Table 2 shows a compilation of current indications. Clinical judgment must also be applied, because competing comorbidities that impact duration and/or quality of life, very advanced age, and psychological factors may limit the potential benefit of ICDs even in those patients who meet these broad implantation indications.

**Primary Prevention of Sudden Death in Other Diseases**

A number of diseases other than dilated cardiomyopathy have been associated with an increased incidence of sudden cardiac death. These include inherited diseases of ion channels, such as LQTS, Brugada syndrome, and catecholaminergic VT. In addition, other structural heart diseases, such as right ventricular dysplasia, hypertrophic cardiomyopathy, and certain types of congenital heart disease, may be associated with increased risk of sudden death. The frequency of these conditions is not as high as that of ischemic or nonischemic dilated cardiomyopathy, which makes prospective randomized, controlled trials difficult to perform. Nonrandomized observational studies suggest subgroups of high-risk patients may benefit from ICD therapy.

In the absence of large-scale trials for most of these conditions, risk-stratification algorithms based on retrospective studies have been created in an attempt to help select appropriate patients for ICD therapy. In addition, there are disease-specific markers, such as the length of the QT interval in the inherited LQTS, the presence of persistent rather than intermittent right precordial ST elevation in Brugada syndrome, and the degree of left ventricular hypertrophy in patients with hypertrophic cardiomyopathy, that appear to portend an increased risk of sudden death and may make aggressive use of the ICD for the primary prevention of sudden death appropriate.

**Cost-Effectiveness of ICD Therapy**

Data strongly support the use of ICDs to prevent sudden cardiac death in specific groups of high-risk patients, but as the broadening inclusion criteria encompass expanding numbers of potential implants, the issue of cost has generated a great deal of interest. For the AVID study, charges for hospitalization, surgical procedures, and antiarrhythmic drugs were collected for 1008 patients. Analysis of these data found that at 3 years of follow-up, survival for patients with ICDs was 0.21 years longer than for patients treated with antiarrhythmic drugs at an incremental cost of $14 101, yielding a cost-effectiveness ratio of $66 677 per year of life saved. Three major primary prophylaxis trials that examined patients with ischemic cardiomyopathy have published cost-effectiveness analyses. MADIT-II found that during the 3.5-year study period, the incremental cost-effectiveness of ICD therapy was $235 000 per year of life saved, although these results may be biased against the ICD given the short follow-up period and the high up-front costs of ICD therapy. A 12-year projection of cost-effectiveness from MADIT-II found that the ratio ranged from $78 600 to $114 000. Most recently, the SCD-HeFT investigators released their cost-effectiveness data and concluded that compared with medical therapy alone, ICD therapy cost $38 389 per year of life saved and $41 530 per quality-adjusted life-year saved. The favorable cost-effectiveness from SCD-HeFT is based on a projected 10-year survival, which is twice the actual follow-up; with shorter time horizons, costs escalate markedly.

Overall, these studies support the assertion that the cost of ICD therapy in patients who meet the inclusion criteria of the aforementioned trials may fall within the acceptable range from a societal vantage point under certain assumptions. Given the up-front costs of the ICD combined with the potential for a greater accrual in survival over time, the cost-benefit ratio of ICD therapy may be even more attractive than reported from randomized trials. Furthermore, efforts to better risk-stratify patients for primary prophylaxis would, if successful, reduce the number needed to treat and favorably impact the cost-effectiveness of ICD therapy.

As previously stated, there are no randomized trials to date that evaluated the use of ICDs for the treatment of LQTS or hypertrophic cardiomyopathy. Thus, cost-effectiveness data can only be derived by analytical models. One such analysis found that ICD therapy is highly cost-effective for the treatment of patients with LQTS or hypertrophic cardiomyopathy when used for primary prophylaxis in high-risk patients or for secondary prevention, driven mainly by the cost savings of added years of gained productivity in these generally young, otherwise healthy individuals.

**Quality of Life With ICD Therapy**

For the 3 published randomized, controlled studies of ICD implantation that evaluated health-related quality of life, the findings are inconclusive. However, research reviews have concluded that the ICD is at least equal to, if not better than, antiarrhythmic medications with regard to most indicators of health-related quality of life. In addition, a meta-analysis concluded that virtually all of the psychological burden or health-related quality-of-life decrement associated with the ICD population is attributable to the presence of ventricular tachyarrhythmias and not to the ICD and suggested that some of the smaller individual studies may have overestimated the negative psychological effects directly attributable to the device.

The experience of shock remains a distinguishing characteristic of ICD patients over and above device implantation itself. Nonetheless, the changes in the mental-emotional scales seen with a single shock are often small and unlikely to reach the threshold for a clinically observable change. The clinical experience of psychological distress secondary to ICD shock may be more likely after the additive effects of multiple shocks, which result in obvious decrements in quality of life. Data from randomized controlled trials in the secondary prevention population indicate that even 1 shock is associated with reduced quality of life. Other studies,
<table>
<thead>
<tr>
<th>Recommendation Class</th>
<th>Prevention Type</th>
<th>Inclusion Criteria</th>
</tr>
</thead>
</table>
| I (therapy recommended) | Primary | Patients with ischemic heart disease who:  
- Are at least 40 days post-MI  
- Are >3 mo postrevascularization  
- Have an EF ≤30%  
- Have NYHA class II or III symptoms  
- Are undergoing optimal medical therapy  
- Have an expected survival with good functional status of >1 y |
| I (therapy recommended) | Secondary | Patients with nonischemic cardiomyopathy who:  
- Have EF ≤30%  
- Have NYHA class II or III symptoms  
- Are undergoing optimal medical therapy  
- Have an expected survival with good functional status of >1 y |
| IIa (therapy reasonable) | Primary | Patients with current or prior symptoms of heart failure and reduced LVEF who have a history of cardiac arrest, VF, or hemodynamically destabilizing VT  
- Cardiac arrest due to VF or VT not due to a transient or reversible cause  
- Spontaneous sustained VT in association with structural heart disease  
- Syncope of undetermined origin with clinically relevant, hemodynamically significant sustained VT or VF induced at EPS when drug therapy is ineffective, not tolerated, or not preferred |
| IIb (therapy might be considered) | Primary | Documented familial or inherited conditions with a high risk of life-threatening VT, such as LQTS, hypertrophic cardiomyopathy, or Brugada syndrome  
- Patients without heart failure who:  
  - Have EF 30% to 35% of any origin  
  - Have NYHA class II or III symptoms and who:  
    - Are at least 40 days post-MI  
    - Are >3 mo postrevascularization  
    - Are taking chronic optimal therapy  
    - Have expected survival with good functional status >1 year  
  - Have ischemic cardiomyopathy who:  
    - Are at least 40 days post-MI  
    - Are >3 mo postrevascularization  
    - Have an EF ≤30%  
    - Are NYHA class I  
    - Are taking chronic optimal therapy  
    - Have an expected survival with good functional status of >1 y |
| IIb (therapy might be considered) | Secondary | Cardiac arrest presumed to be due to VF when EPS is precluded by other medical conditions  
- Severe symptoms attributable to ventricular tachyarrhythmias in patients awaiting cardiac transplantation |
| III (contraindicated) | Primary and secondary |  
- Syncope of undetermined cause in a patient without inducible ventricular tachyarrhythmias and without structural heart disease  
- Incessant VT or VF  
- VF or VT resulting from arrhythmias amenable to surgical or catheter ablation  
- Significant psychiatric illnesses that may be aggravated by device implantation or may preclude systematic follow-up  
- Terminal illnesses with projected life expectancy <6 mo  
- Patients with coronary artery disease with LV dysfunction and prolonged QRS duration in the absence of spontaneous or inducible sustained or nonsustained VT who are undergoing coronary bypass surgery  
- NYHA class IV drug-refractory congestive heart failure in patients who are not candidates for cardiac transplantation or CRT  
- VF or VT resulting from arrhythmias amenable to surgical or catheter ablation |

EF indicates ejection fraction; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction; EPS, electrophysiological study; and LV, left ventricular.
Risk Stratification for ICD Therapy

In certain populations, the cost-effectiveness of ICD therapy appears to be marginal. Currently, ejection fraction is the primary factor used to select patients for ICD therapy. A number of other diagnostic tests that examine both fixed and transient factors that may predispose to sudden death could potentially improve patient selection for ICD therapy and thus improve both clinical benefit and cost-effectiveness. These tests include the signal-averaged ECG, heart rate variability, T-wave alternans, heart rate turbulence, and electrophysiological testing. For most of these tests, some studies suggest substantial benefit in predictive testing, whereas others have failed to demonstrate that such a benefit can be translated routinely in a clinical setting. For example, the MUSTT study suggested that electrophysiological testing may have moderate accuracy in determining which patients are at risk for sudden death, although substantial risks remain even in patients without inducible tachyarrhythmias. In contrast, a retrospective analysis of the MADIT II data did not suggest such benefit. In a small study, T-wave alternans was found to have a very high negative predictive value for predicting ventricular arrhythmias. One prospective study, Alternans Before Cardioverter Defibrillator (ABCD), suggested that T-wave alternans had predictive accuracy similar to electrophysiological testing but clearly a lower positive and negative predictive value than was apparent in the single-center study. Another prospective study, however, was unable to show that T-wave alternans was useful for risk-stratifying patients for arrhythmia vulnerability. Although utilizing additional risk-stratification techniques to select patients for ICD therapies is attractive and potentially important, currently available data are not adequate to routinely recommend additional risk-stratification techniques for selection of patients for ICD therapy. In patients who fall into “borderline” areas, such as those with ejection fractions of 30% to 40% or those with class 1 heart failure, additional risk-stratification techniques may be useful when applied on an individual basis.

Device Selection, Programming, and Testing

ICDs can be divided into 3 categories: single-chamber, dual chamber, and biventricular (CRT). The majority of ICDs implanted in the United States are dual-chamber ICDs, despite the fact that most of these patients have no pacing indications and despite the higher costs and complications associated with atrial lead placement. This contradiction is driven mainly by the anticipated reduction in inappropriate therapies due to enhanced discrimination of supraventricular tachyarrhythmias, concerns about the future development of pacing indications from medical therapies used in heart failure regimens, and the clear advantage of having an atrial electromgram present for the retrospective diagnosis of treated arrhythmias. However, all but 1 study failed to demonstrate a reduction in inappropriate shocks in dual-chamber systems, whereas unnecessary right ventricular pacing from such systems has been associated with worsening heart failure.

Long-term follow-up of patients randomized to single- or dual-chamber ICDs showed no difference in mortality or arrhythmogenic morbidity. Whether dual-chamber devices designed with algorithms to provide atrial rate support with minimal ventricular pacing provide clinically relevant benefits remains to be determined, although it appears that such an approach is superior to standard programming. Until such evidence is available, it appears justified to recommend a single-chamber ICD programmed to backup VVI pacing at 40 bpm in individuals who do not have any pacing indication or prior history of atrial tachyarrhythmias. Patients who receive a dual-chamber device should have efforts made to minimize unnecessary right ventricular pacing by extending the atrioventricular delay to physiologically acceptable parameters or by the use of specifically designed algorithms.

There are no guidelines concerning device programming for the treatment of ventricular tachyarrhythmias, because therapies must be tailored to each individual’s clinical circumstances. Randomized trials of device therapy have generally included single-zone programming for shocks to be delivered for rates exceeding ≤180 bpm. Although concerns have been voiced about the possibility that rapid antitachycardia pacing designed to pace-terminate VT may actually accelerate the arrhythmia, reports have demonstrated that antitachycardia pacing designed to pace-terminate VT may actually accelerate the arrhythmia, reports have demonstrated that antitachycardia pacing designed to pace-terminate VT may actually accelerate the arrhythmia. A randomized study compared a single empirical attempt at antitachycardia pacing versus shock for fast VT at 188 to 250 bpm and found an 81% efficacy rate of antitachycardia pacing and no difference in acceleration, episode duration, or sudden death between the 2 groups.

As with device programming, there are no guidelines concerning the testing of defibrillation thresholds either at the time of implantation or routinely during follow-up. Although device evaluation at implantation appears reasonable, it also exposes the patient to some risk, possible discomfort, and longer procedure times. A 10-J safety margin has been the traditional “standard of care,” but this number was derived before the introduction of current technologies designed to enhance the efficacy of defibrillation, and there is evidence that lower margins may be acceptable. Although the recently published SCD-HeFT trial did not perform routine defibrillation threshold testing during implantation, an observational study found that 9% of patients with standard-output devices and 3% to 4% of patients with high-output devices had a <10-J safety margin at implantation. Because nearly all of these patients received successful system modification at the time of implantation, the clinical outcomes of patients with <10-J safety margins are unknown. Additional study is needed before any evidence-based conclusions can be drawn on this issue. In the interim, device-based testing of defibrillation thresholds is reasonable, and an 8- to 10-J difference
between the maximum delivered energy of the device and the energy required to terminate VF should be used to define an adequate safety margin.

Routine follow-up testing has also evolved over time. The ability to assess shocking-lead impedance and other parameters has enabled practitioners to evaluate lead integrity without delivering therapy. Because the diagnostic yield of long-term assessment of defibrillation thresholds in the modern ICD era is uncertain, it appears reasonable that the need for and timing of such testing should be at the discretion of the treating physician. The addition of medical therapies, the development of conditions known to affect defibrillation thresholds, changes in clinical status, or concerns about the efficacy of therapy should elicit additional consideration for defibrillation threshold testing.

Who Should Implant ICDs, and What Are the Risks?
The broadened indications for ICD therapy and the development of CRT created widespread concern for a future mismatch between implant demand and the number of implanting physicians. Also recognized, however, was the need to set and maintain high standards for device implanters, particularly in view of the unique challenges associated with device placement, programming, and follow-up for ICDs. As a result of these dual concerns, the Heart Rhythm Society issued guidelines for clinical competency for ICD implanters. The Recommendations for Training in Adult Cardiovascular Medicine Core Cardiology Training II (COCATS2) set forth the requirements for physicians currently in cardiovascular training programs. These include didactic training, 50 primary pacemaker implantations, 20 pacemaker system revisions or replacements, 100 pacemaker follow-up visits, and a minimum of 50 ICD follow-up visits. For physicians highly experienced in pacemaker placement (ie, >35 implantations per year with a minimum of 100 implantations over the preceding 3 years) who wish to implant ICDs for primary prophylaxis only or CRT devices, recommendations have also been outlined. These include the completion of didactic training not provided directly by industry, 10 proctored ICD implantations and 5 revisions, 5 proctored CRT implantations, monitoring patient outcomes and complication rates, and an established method of patient follow-up. Maintenance of competence is also required and should consist of 10 ICD and CRT procedures per year and 20 patients per year in follow-up.

The advent of transvenous leads and downsized generators has markedly changed the complexity of ICD implantation. Compared with the era of epicardial leads that required thoracotomy and abdominal generator implants, the current generation allows for very high implantation success rates, reduced operative times, and a substantial shift in the rate and types of complications. Despite these advances, ICD implantation still carries risks both in the perioperative period and long-term. In a case series of 3344 patients from the European Registry of Implantable Defibrillators, the most common complications in the first 3 months after implantation were pocket hematoma in 1.9% and lead dislodgement in 1.4%. Infections were noted in 0.3%, and 1.6% complained of chronic pain in the generator pocket. An analysis of more than 23 000 Medicare patients who underwent ICD implantation demonstrated an overall complication rate of 11%, which was dominated by mechanical complications of the ICD system such as lead dislodgement (4.8%), hematoma/hemorrhage (2.5%), infection (1.4%), and pneumothorax (1.0%). Pericardial effusion/tamponade occurred in 0.3% of patients, and overall mortality in that study was 0.9%, one third of which occurred in patients with 1 or more complications.

Complication types and rates may be affected by numerous variables, including operator experience, access approach, the number of leads implanted, patient comorbidities, and medical therapies, including antiplatelet agents, anticoagulants, and steroids. A national ICD registry established by the Centers for Medicare and Medicaid Services will better define the outcomes of ICD recipients in clinical practice.

Device Recalls
Device malfunctions have recently gained national attention. As with all man-made devices at this level of complexity, complete elimination of malfunctions is unlikely to ever be achieved. Furthermore, those failures that do occur must be kept in the context of the thousands of lives saved and the countless others improved during the vast majority of times that these devices function appropriately. Despite the remarkable strides made in device technology, recent events have raised important questions about current systems for postmarket surveillance, analyses of device performance, and communication of such performance to physicians and patients. Studies have demonstrated that device advisories are not uncommon, can affect hundreds of thousands of devices, and can be associated with significant cost, potential morbidity, and mortality. A recent survey of pacemaker and ICD registries found that the ICD malfunction rate was ~20-fold higher than that of pacemaker malfunction, and although malfunction rates for the latter declined significantly over a 21-year period, ICD malfunctions actually increased in more recent years.

These concerns have resulted in specific recommendations made by the Heart Rhythm Society to device manufacturers, the Food and Drug Administration (FDA), Congress, the Centers for Medicare and Medicaid Services, and physicians. The document sets forth standards for independent performance review, terminology, and physician notification and requests the inclusion of performance data and data on adverse device events in a national registry, among other important recommendations. The ultimate goal of this effort is to “enhance and strengthen knowledge, confidence, and trust in cardiac rhythm management devices through: (1) greater transparency in post-market surveillance, analysis, and reporting; (2) enhanced systems to increase the return of devices to manufacturers and to improve the analysis and reporting of device performance and malfunction information; and (3) cooperation among industry, the FDA, and physicians in an effort to prevent injuries and deaths due to device malfunction.” Whether these efforts result in a substantial improvement in device reliability and the methods
by which malfunctions are dealt with will require further study.

**Future Directions**

Three major issues that are part of a forward look at ICD therapy include: (1) improved risk stratification of patients who currently have indications for ICD implantation; (2) development of risk-stratification techniques for the larger but lower-risk populations who do not currently have indications for ICD therapy; and (3) technological advances in device therapy itself. Although the multicenter trials described above have dramatically increased our knowledge about which patients are appropriate for ICD therapy, significant questions remain. The absolute mortality benefit for patients in primary prophylaxis studies is relatively low, which results in estimates that 18 devices need to be implanted to save 1 life in a patient with ischemic cardiomyopathy and 25 devices to save 1 life for patients with nonischemic cardiomyopathy.21 Thus, most patients implanted with an ICD will never receive lifesaving therapy from the device. Better risk-stratification techniques could spare these individuals from exposure to the risks of implantation and improve the cost-effectiveness of ICD therapy. A comprehensive prospective, observational analysis of risk-stratification techniques is currently under way. This study, being performed in patients with coronary disease who qualify for primary prevention ICDs, should help evaluate the ability of current techniques to predict arrhythmic events. In addition, insights gleaned from the ongoing ICD registry may allow for the identification of clinical variables that predict ICD benefit. These may include ejection fraction, time since infarct, and heart failure class. If a high predictive value can be achieved by a single measure or a combination of clinical variables and stratification techniques, a randomized trial using this approach may be appropriate. Similar studies should be performed on patients with nonischemic cardiomyopathy. Because total mortality should remain the end point for these studies, it may require more than 5 years for these issues to be resolved. In the interim, clinicians will be forced to use available trial data and make the best case-by-case decisions that they can.

Although the absolute number of patients who experience sudden cardiac death in the population with known but less extensive degrees of structural heart disease is large, the relative risk is small. Thus, identifying those patients who currently have no indications for ICD therapy but who may benefit from its use is an important but challenging issue. Trials using existing risk-stratification techniques alone are unlikely to provide the necessary predictive value in patients at lower risk of events. A study is currently under way comparing ICD versus standard medical therapy in patients with ejection fractions above 30% to 35% but with large infarcts on cardiac magnetic resonance imaging. The hypotheses of this study are that patients with large areas of scar are at risk for sudden death even if left ventricular ejection fraction is preserved and that ICD therapy can reduce this risk. This study and other proposed studies like it have the potential for determining whether myocardial scar, recurrent ischemia, or other factors contribute to sudden death in patients with relatively preserved ventricular function. Although it is still unclear whether ICD therapy in this population can be cost-effective, the large public health nature of the problem suggests that further studies are appropriate.

The last decade has resulted in amazing improvements in the technological aspects of ICDs although problems with device reliability remain. ICD manufacturers should first focus on device reliability and on improved communication with physicians and patients. However, technological improvements that will result in significant patient benefit continue to be made. A leadless ICD system may one day simplify device implantation and eliminate lead-related complications. Remote monitoring of ICD therapy is now provided by a number of manufacturers, which allows patients who live far away from providers to still have their devices evaluated and those who have symptoms or shocks to have remote interrogation that can be useful in management. ICDs have already become cardiac management devices rather than simply defibrillators. They include sophisticated pacing algorithms, atrial antitachycardia pacing, heart failure monitoring, and other refinements. These trends are likely to continue, and automatic adjustments in ICD therapy and heart failure therapy based on physiological monitoring will be further refined. ICD size should continue to decrease, and battery life should continue to improve. Advances in ICD technology must be balanced with encouragements to limit the cost of this therapy. These developments may result in increasing adoption rates for established indications, as well as expansion of the use of ICDs to new populations, both of which will result in significant improvements in public health.

**Conclusions**

The ICD represents a true revolution in the treatment of ventricular arrhythmias over the last 25 years; however, the risk/benefit ratio of devices and cost-effectiveness in some populations remains marginal. Nonetheless, current therapies and future advances should allow the ICD to continue to produce transformational changes in cardiac care.

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**References**


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