Primary and Secondary Prevention of Sudden Cardiac Death: The Role of the Implantable Cardioverter Defibrillator

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Sudden cardiac death (SCD) affects nearly 300,000 people each year in the U.S., and out-of-hospital rates for survival range from only 2% to 25%. A substantial reduction in SCD requires primary prevention through risk-stratification and secondary prevention of sustained ventricular tachycardia (VT-S) and ventricular fibrillation (VF). Because frequent premature ventricular complexes (PVCs) appeared to be associated with an increased risk for SCD in patients with significant ventricular dysfunction, it was thought that suppression of PVCs would prevent SCD. The implantable cardioverter defibrillator (ICD) electrically treats life-threatening VT-S and VF, and it can be implanted readily in the pectoral area. Two randomized, prospective, controlled trials demonstrated conclusively that the ICD is the treatment of choice in the primary prevention of SCD in patients with a previous MI. In addition, three randomized, controlled trials found the ICD to be superior to antiarrhythmic drugs in the secondary prevention of SCD. Physicians should learn to recognize patients who are candidates for the ICD and refer them to an electrophysiologist so that they can get this life-saving therapy.
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Sudden cardiac death (SCD) is a major epidemiologic problem in the United States. It affects nearly 300,000 people each year.[1] Coronary artery disease (CAD) is the most common pathologic finding in victims of SCD.[2] Some patients succumbing to SCD have had an acute ischemic event that precipitated ventricular fibrillation (VF). Alternatively, many patients have no

definable ischemia at the time of the cardiac arrest, but typically have had a previous myocardial infarction (MI) with subsequent left ventricular (LV) dysfunction, often with a left ventricular ejection fraction (LVEF) ≤ 40%.[2]

Survival rates for out-of-hospital cardiac arrest are disappointingly low, ranging from 2% to 25% in the United States.[3] With greater access to the automated external defibrillator, there will likely be a small survival gain, but a substantial reduction in cardiac arrest mortality will come from two sources: better methods to identify and treat potential victims of SCD, and efforts to reduce the incidence of CAD in the population. Although reducing the incidence of CAD is the optimal approach, the more practical immediate approach is the primary prevention of SCD through risk-stratification.

Cardiac arrest survivors who do not have an obvious reversible cause—for example, acute MI—are known to be at high risk for recurrent cardiac arrest and subsequent SCD.[4] Thus, a reduction in SCD will require not only primary prevention but also secondary prevention of sustained ventricular tachycardia (VT-S) and VF. Over two decades of research, including multiple, randomized, prospective trials in both primary and secondary prevention of SCD, have explored both pharmacologic and nonpharmacologic therapies.[2] As will be demonstrated in this review, the implantable cardioverter defibrillator (ICD) has won the day as the most important treatment to reduce SCD.

Primary Prevention of Sudden Cardiac Death

Observations from the past few decades suggested that the presence of frequent premature ventricular complexes (PVCs) appears to be associated with an increased risk of SCD in patients with significant ventricular dysfunction.[2,4–8] In fact, Lown and Wolf[9] developed a classification scheme of varieties of PVCs designating some forms as "warning arrhythmias" that presage the appearance of VF or VT-S. Although other investigators published data describing the shortcomings of this classification to predict patients at risk for SCD, the concept of "warning arrhythmias" has persisted for many years and was the basis of the subsequent PVC suppression hypothesis to prevent SCD.[2]

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The premature ventricular complex suppression hypothesis. The Cardiac Arrhythmia Suppression Trial (CAST) was undertaken to test the validity of the PVC suppression hypothesis. CAST was a randomized, placebo-controlled study that evaluated whether suppression of asymptomatic or minimally symptomatic PVCs after an MI would reduce arrhythmic death.[10] The drugs selected in this study were known to suppress PVCs: encainide, flecainide, and moricizine. Indeed, although these agents did markedly suppress PVCs, the Data Safety Monitoring Board prematurely stopped the study and recommended that encainide and flecainide be discontinued. Importantly, arrhythmic death was found to be more common in patients treated with these drugs (4.5%) than with placebo (1.2%), and the relative risk associated with these drugs was 3.6. Moreover, the total mortality rate was greater with encainide or flecainide than with placebo. Moricizine continued to be studied as a single drug in a subsequent trial, CAST-II, but this trial was also prematurely discontinued because of an increased mortality in patients treated with moricizine compared with placebo in the early phase of the drug's initiation. It was also found that there was no survival benefit in the long-term phase with moricizine.[11]

What went wrong with CAST and CAST-II? It is certainly possible that fatal arrhythmias were prevented in some patients, but the overall effect of the drugs used in this study was to increase arrhythmic mortality and total mortality. One must remember that antiarrhythmic drugs can also be proarrhythmic, and this action can increase the risk of cardiac arrest and SCD.[12,13] It has been proposed that one of the most important proarrhythmic risks of Class IC antiarrhythmic drugs—for example, flecainide, propafenone, and moricizine—is the interaction of myocardial ischemia with these agents.[14] Although propafenone was not used in CAST, it has drug actions similar to flecainide, and most arrhythmia experts consider it to have a similar risk profile in patients with CAD.

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In my research in this area, I have

always had an additional problem with the PVC suppression hypothesis. The assumption is that PVCs "trigger" VT-S or VF and that by suppressing these triggers one can prevent lethal arrhythmias. This is a very simplistic concept, and one that is not consistent with much of the published data. For example, many episodes of sustained monomorphic VT begin with a mid-cycle PVC that actually has the same appearance as the rest of the arrhythmia, suggesting that it is actually the first beat of tachycardia. Further, VF unrelated to ischemia often is initiated by a run of rapid VT that degenerates to VF, and not by a single PVC. Finally, a lack of knowledge as to why a particular patient at a given point in time develops VF is illustrated in the following often observed paradox: a patient with poor LV function has multiple runs of nonsustained VT throughout the day but never has VT-S or VF, yet a patient with similar LV dysfunction has infrequent PVCs but develops VF and SCD.

Arrhythmia	PVCs; VT-NS	PVCs / VT-NS	VT-S; VF
Heart Disease	Absent	Present	Present
LV Dysfunction	Absent	Absent / Present	Present
Potential Risks for SCD	Minimal	Intermediate	High

Figure 1. *Risk-stratification of sudden cardiac death (SCD) in patients with ventricular arrhythmias. The risk of SCD increases from the lowest risk shown in the left column to the highest risk shown in the right column. The middle column has shades of gray, with the risk worsening from left to right. LV, left ventricle; PVCs, premature ventricular complexes; VF, ventricular fibrillation; VT-NS, nonsustained ventricular tachycardia; VT-S, sustained ventricular tachycardia. Reproduced from Prystowsky EN. Antiarrhythmic therapy for asymptomatic ventricular arrhythmias.* Am J Cardiol. *1998;61(suppl 2):102A–107A, with permission from Excerpta Medica Inc.*

The amiodarone era. Not every antiarrhythmic drug has caused excess mortality in post-myocardial infarction trials. Julian and colleagues[15] randomized 1456 patients to either sotalol or placebo, and the 1-year mortality rate was 18% lower in the sotalol group, although this did not reach statistical significance. This trial went unrecognized for many years. In contrast, numerous investigators worldwide have studied the effects of electrophysiologically guided, as well as empiric, amiodarone therapy to prevent subsequent episodes of VT-S or VF. From these studies there emerged a general impression among many electrophysiologists and arrhythmia specialists that empiric amiodarone was remarkably effective in preventing sustained ventricular tachyarrhythmias. Thus, it is not surprising that several investigators considered empiric amiodarone to be uniquely qualified to reduce SCD after an MI.[16,17]

Two prospective, randomized controlled trials evaluated placebo versus empiric amiodarone therapy in patients after an MI in order to determine whether amiodarone could prevent sudden death and improve overall survival. The European Myocardial Infarction Amiodarone Trial (EMIAT)[16] enrolled 1482 patients with LVEF ≤ 0.4 within 5 to 21 days after they had an MI. EMIAT demonstrated no effect of amiodarone on all-cause mortality. The Canadian Myocardial Infarction Amiodarone Trial (CAMIAT)[17] enrolled 1202 patients with a criterion of >10 PVCs per hour, but no LVEF cutoff was mandated. Data from CAMIAT did demonstrate an 18% reduction in all-cause mortality in the amiodarone group, which, however, did not reach statistical significance. Of note, sudden death was statistically reduced in both of the amiodarone groups in EMIAT (by 35.0%) and CAMIAT (by 48.5%). The results of both trials showed that empiric amiodarone therapy could no longer be recommended for asymptomatic patients after an MI simply to improve overall survival. Recent data on dofetilide, another Class III agent, has also shown no survival advantage in patients after an MI, although it did not increase mortality.[18]

The key randomized, controlled trials of antiarrhythmic drugs in patients who had an MI have taught us two important lessons. First, none of these drugs should be used in asymptomatic patients for the sole purpose of prolonging survival. On the other hand, sotalol, amiodarone, and dofetilide, when used correctly in patients after an MI, appear to be the drugs of choice for patients with arrhythmias that require suppression, and this recommendation has been incorporated into the recent American College of Cardiology/American Heart Association/European Society of Cardiology (ACC/AHA/ESC) Guidelines for the Management of Patients with Atrial Fibrillation.[19]

The implantable cardioverter defibrillator era. The disappointing

results from pharmacologic studies should not deter the clinician from attempting to identify patients at high risk for sudden death. Figure 1 depicts a scheme for stratifying the risk for SCD.[20] Clearly, a nonpharmacologic approach should be sought. One such approach, the implantable cardioverter defibrillator (ICD), is a potent therapy to treat life-threatening VT-S and VF.[2,21]

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Its inventor, Michel Mirowski, MD, actually envisioned the ICD as a prophylactic device for the primary prevention of SCD.[22] Two randomized, prospective, controlled trials have demonstrated conclusively that the ICD is the treatment of choice in the primary prevention of SCD in patients who have had a previous MI.[21,23-25]

Multicenter Automatic Defibrillator Implantation Trial (MADIT). The MADIT study[23] enrolled patients from 30 centers in the United States and 2 centers in Europe. Eligible patients were required to have had the following: an MI at least 3 weeks before entering the study; nonsustained VT of 3 to 30 beats with a rate > 120 per minute; and an LVEF ≤ 35%. Eligible patients underwent electrophysiologic testing, and if VT-S was induced but not suppressed with intravenous procainamide, they were eligible for randomization. Randomization included treatment with an ICD versus "conventional" medical therapy, which unfortunately was not standardized for the trial. However, most patients in the "conventional" group received empiric amiodarone treatment. The mean time from MI to enrollment in MADIT was 27 months, and the mean LVEF was 26%. New York Heart Association Class II and III congestive heart failure was present in 65% of the patients. The study was prematurely terminated after an average follow-up of 27 months because the ICD group had a 56% reduction in mortality compared with that in the conventional group.

Acceptance of the ICD for primary prevention of SCD in patients after an MI did not quickly follow the results of MADIT. In fact, there was much criticism of the trial because it lacked a true "placebo" control group, enrolled a relatively small number of patients (n = 196), and had an apparent significant imbalance in the use of β-adrenergic blockers, with only 8% of the patients in the conventional medical group receiving these agents compared with 26% in the ICD group. Further, of 74% of the patients who were prescribed amiodarone initially, only 45% were still receiving amiodarone at the last patient contact. Despite these drawbacks, subsequent data from the Multicenter Unsustained Tachycardia Trial (MUSTT) supported the observations of MADIT.

Multicenter Unsustained Tachycardia Trial (MUSTT). The MUSTT study[24] was initiated to test the hypothesis that antiarrhythmic therapy guided by electrophysiologic testing could reduce the risk of cardiac arrest and sudden death. Patients enrolled in the trial had CAD, spontaneous nonsustained VT, and an LVEF ≤ 40%.

Prior to the MUSTT study, the standard practice among electrophysiologists was to use serial electrophysiologic-pharmacologic testing to evaluate the effectiveness of antiarrhythmic drug therapy in patients with inducible VT-S or VF.[26] The assumption was that suppression of previously inducible VT-S would prevent recurrent VT-S/VF. Thus, MUSTT tested two major issues concerning programmed ventricular stimulation: 1) whether therapy directed by electrophysiologic testing could reduce mortality, and 2) whether electrophysiologic testing could identify patients at risk for sudden death.

A total of 85 centers in the United States and Canada participated in MUSTT. Nonsustained VT had to occur at least 4 days after an MI or a revascularization procedure and within 6 months of enrollment in the study, and exercise-induced ischemia required treatment before a patient could be enrolled in the trial. Randomization was possible if sustained monomorphic VT was induced with ≤3 extrastimuli, or sustained polymorphic VT was initiated with ≤2 extrastimuli. The randomized patients were given either no specific antiarrhythmic treatment—ie, a true control group—or underwent electrophysiologic-guided therapy. The selection of antiarrhythmic agents for serial electrophysiologic-pharmacologic testing was randomized, and an ICD could be implanted if the drugs proved ineffective.

Inducible sustained VT occurred in 767 of 2202 patients (35%), and 704 patients agreed to randomization. Nonrandomized patients were followed in a registry. There were 353 patients assigned to the control group with no antiarrhythmic therapy, and 351 received electrophysiologically guided therapy. The mean time from myocardial infarction to enrollment in MUSTT was 39 months, and the mean LVEF was

30%. New York Heart Association Class II or III congestive heart failure was present in 64% of the patients. Importantly, 40% of the patients received β-adrenergic blockers at discharge. Patients assigned to the control group with no antiarrhythmic therapy actually had greater β-adrenergic blocker use: 51% compared with 29% in the electrophysiologically guided treatment group. Of the 351 patients who were electrophysiologically guided, 45% were discharged after receiving an antiarrhythmic drug compared with 46% of those who were given an ICD.

The median follow-up duration was 39 months. The overall mortality rates after 2 and 5 years, respectively, were 22% and 42% for patients randomized to electrophysiologically guided therapy compared with 28% and 48% for patients in the control group ($P = .06$). The arrhythmic death or cardiac arrest endpoint at 2 and 5 years, respectively, was 12% and 25% for patients randomized to electrophysiologically guided therapy compared with 18% and 32% for the control group ($P = .04$).

A subsequent analysis of the treatment group demonstrated that the ICD was responsible for the lower rates of arrhythmic deaths and total mortality. The 5-year rate of cardiac arrest or arrhythmic death was 9% for those who had received an ICD compared with 37% for those treated with antiarrhythmic drugs. The overall 5-year mortality rate was 24% for the ICD-treated patients compared with 55% for those receiving antiarrhythmic drugs. A subsequent analysis showed no difference among the antiarrhythmic drugs in their ability to prolong survival.[27]

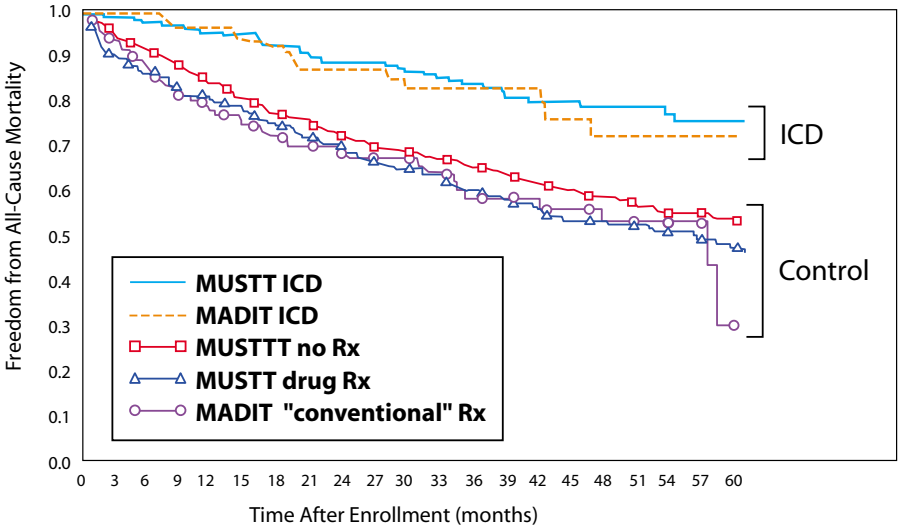

Figure 2. *Kaplan-Meier survival curves for all-cause mortality in the Multicenter Unsustained Tachycardia Trial (MUSTT) and Multicenter Automatic Defibrillator Implantation Trial (MADIT) studies. ICD, implantable cardioverter defibrillator; Rx, treatment. Reproduced from Prystowsky EN. Screening and therapy for patients with nonsustained ventricular tachycardia.* Am J Cardiol. *2000;86(suppl):34K–39K, with permission from Excerpta Medica Inc.*

Figure 2 shows a composite of the Kaplan-Meier survival curves for all-cause mortality in the MUSTT and MADIT studies.[22] Although there were some differences in trial design and issues such as β-adrenergic blocker use, it is remarkable how similar the survival curves are from these two trials. In the MUSTT and MADIT types of patients, treatment with the ICD resulted in an approximately 50% lower overall mortality rate than the rates resulting from conventional therapy in the MADIT trial and from electrophysiologically guided antiarrhythmic drug treatment or no antiarrhythmic therapy in the MUSTT study. These two randomized, prospective, controlled trials present strong evidence that patients with characteristics of the subjects in the MUSTT and MADIT trials should be sought out and undergo electrophysiologic testing, and if inducible sustained VT occurs, an ICD should be implanted. Indeed, the electrophysiologic testing and subsequent implantation of an ICD in U.S. Vice President Dick Cheney was based at least in part on the data from these trials.

The overall 5-year mortality rate was 24% for the ICD-treated patients compared with 55% for those receiving antiarrhythmic drugs.

Is electrophysiologic testing necessary? Both the MUSTT and MADIT studies employed electrophysiologic testing to stratify risk in patients with significant LV dysfunction after an MI. However, it is not clear whether electrophysiologic testing adds anything to risk-stratification in such patients. A subgroup analysis of the MUSTT registry patients was performed that addressed this question.[28] A comparison was made between patients who had sustained VT initiated but were randomized to no specific antiarrhythmic therapy and patients in the registry. Preliminary data show that combinations of clinical vari-

ables in the noninducible, nonrandomized group were associated with mortalities equal to and at times greater than those in patients with inducible VT-S who were given no specific antiarrhythmic treatment. In fact, an analysis of only those patients with LVEF < 30% demonstrated no significant difference in the 5-year mortality curves between patients with inducible VT-S and those in the registry group. Therefore, it is conceivable that the mere presence of substantial LV dysfunction is a strong enough risk stratifier for ICD implantation. However, this concept requires supportive data, possibly from the Sudden Cardiac Death Heart Failure Trial (SCD HeFT) or MADIT-II.[21]

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Secondary Prevention of Sudden Cardiac Death

Secondary prevention of SCD applies to those patients who have been fortunate enough to have survived a cardiac arrest or an episode of hemodynamically significant sustained VT. As mentioned earlier, patients who have survived a cardiac arrest not related to an obvious reversible cause are at high risk for a subsequent event.[4] It is imperative to treat these patients aggressively with specific antiarrhythmic therapy to prevent SCD.

Serial electrophysiologic-pharmacologic testing. The initial approach to preventing secondary SCD was based on a concept of the suppression of "triggers" that presumably initiate lethal ventricular arrhythmias. The major proponent of this approach was Dr. Lown, and Graboys and colleagues[29] from his group reported their noninvasive approach to the treatment of patients with malignant ventricular arrhythmias. In essence, Lown proposed that the frequent and complex forms of nonsustained ventricular arrhythmias were the "triggers" for VT-S or VF. From this assumption it followed that adequate suppression of these nonsustained arrhythmias would prevent sudden death. Indeed, these investigators demonstrated an impressive survival rate in patients who underwent their elaborate system of noninvasive monitoring of ventricular arrhythmia suppression.[29] However, most patients with VT-S or cardiac-arrest survivors do not have frequent spontaneous ventricular arrhythmias.[4,30] Thus, in our own experience, this approach could not be applied to the majority of patients with life-threatening ventricular arrhythmias.

The introduction of serial electrophysiologic-pharmacologic testing provided a new method to evaluate the apparent efficacy of antiarrhythmic drugs to suppress future VT-S or VF.[26,31] This method does not rely on the suppression of ambient, nonsustained ventricular triggers, but attempts to evaluate the heart's ability to support a sustained ventricular tachyarrhythmia in the presence of antiarrhythmic drugs. Patients undergoing a baseline electrophysiologic test with the introduction of multiple premature extrastimuli have VT-S initiated, and a repeat electrophysiologic study is performed with the patient taking an antiarrhythmic drug. This process is repeated until an agent is found that prevents the induction of a VT-S, or the VT-S is slow enough to be hemodynamically stable. The electrophysiology community embraced this concept wholeheartedly, setting up a battleground between the electrophysiologist armed with electrode catheters and the "arrhythmologist" employing electrocardiographic monitoring and treadmill testing.

The noninvasive and invasive approaches to monitoring drug efficacy subsequently underwent prospective evaluation. Mitchell and colleagues[32] performed a randomized clinical trial of 57 patients with VT or VF and showed that an invasive approach yielded a substantial advantage for patients to remain event-free at 1 and 2 years. A second trial randomized 486 (23%) of 2103 enrolled patients to either serial electrophysiologic-pharmacologic testing or noninvasive monitoring to guide therapy.[33] Importantly, during the follow-up there was an inordinately high recurrence rate of ventricular tachyarrhythmias in patients who were predicted to have drug efficacy by either technique. Thus, both noninvasive and invasive methods appeared to have poor predictability for drug success in these high-risk patients. In a different group of patients, in the MUSTT study, which evaluated primary prevention of SCD, suppression of inducible VT-S fared no better than no specific antiarrhythmic drug therapy did to reduce mortality.[24]

Implantable cardioverter defibrillator. The first ICD was implanted in 1980, and the ICD was approved by the U.S. Food and Drug Administration for use in 1985.[2] Since its first use, the ICD has demonstrated an outstanding and unparalleled effectiveness in preventing SCD by electrically treating VT-S or VF.[34,35] Winkle and associates[35] reported a sudden-death survival rate of 99% at 1 year and an overall

survival rate of 92% at 1 year in patients with documented life-threatening VT/VF.

An analysis of telemetry data from ICDs revealed that the majority of VF episodes are preceded by rapid VT-S. This has enabled various therapies to be programmed into the modern ICDs—for example, antitachycardia pacing and low- or high-energy shocks. The newest generation of ICDs is easily implanted in the pectoral area using a method similar to the one in which permanent pacemakers are implanted. The relatively benign procedure of implanting an ICD was vividly demonstrated when one was implanted in Vice President Cheney, and he was discharged on the same day.

A question remained, however, as to whether the ICD actually improved survival compared with antiarrhythmic drugs in these patients, who often have significant LV dysfunction. The Antiarrhythmics Versus Implantable Defibrillators (AVID) trial evaluated this question.[36] Eligible patients either had survived a cardiac arrest, had VT-S with syncope, or had VT-S and an LVEF ≤ 40% and either hypotension, chest pain, or presyncope during ventricular tachycardia. The mean LVEF of the overall population was 31%, and over half the patients had congestive heart failure. Enrollment included 455 patients with VF and 561 with VT-S. Patients were randomized to receive an ICD or either amiodarone or sotalol, although so few received sotalol that this essentially became an amiodarone versus ICD trial. AVID was terminated prematurely because the overall survival rate in the ICD group was clearly better than that in the drug group. The death rates decreased by 39%, 27%, and 31% at 1, 2, and 3 years, respectively, for those patients who received an ICD. The survival benefit was most prominent in patients with an LVEF of ≤35%, and in patients with a higher LVEF, the survival was not statistically different between amiodarone and the ICD. Thus, AVID firmly established the superiority of the ICD compared with amiodarone in the survival of patients with previous cardiac arrest or hypotensive VT-S, in particular those with an LVEF ≤ 35%.

Two other randomized controlled trials have evaluated the ICD versus antiarrhythmic drug therapy. The Cardiac Arrest Study Hamburg (CASH) trial randomized survivors of cardiac arrest secondary to documented ventricular arrhythmias to receive an ICD or drug treatment.[37] The initial therapies were amiodarone, metoprolol, and propafenone. Propafenone was discontinued because of safety concerns, and the final study analyzed treatment with the ICD versus only amiodarone and metoprolol. Amiodarone was given empirically and was not guided by electrophys-

Main Points

- A substantial reduction in sudden cardiac death (SCD) requires primary prevention through risk-stratification and secondary prevention of sustained ventricular tachycardia (VT-S) and ventricular fibrillation (VF).
- The premature ventricular complex (PVC) suppression hypothesis postulated that because frequent PVCs appeared to be associated with an increased risk for SCD in patients with significant ventricular dysfunction, suppression of PVCs would prevent SCD.
- The Cardiac Arrhythmia Suppression Trial (CAST), using three drugs known to suppress PVCs, was prematurely stopped when two of the drugs—encainide and flecainide—induced arrhythmic death and total mortality more frequently than placebo did. The third drug, moricizine, was also discontinued in a subsequent CAST II trial when it demonstrated a higher mortality rate than placebo did.
- Studies suggested that empiric amiodarone therapy might be remarkably effective in preventing VT-S, but two large trials of patients with a previous myocardial infarction (MI) showed that amiodarone therapy did not improve overall survival.
- The implantable cardioverter defibrillator (ICD) is a potent therapy to prevent SCD by electrically treating life-threatening VT-S and VF, and it can be implanted easily in the pectoral area.
- Two randomized, prospective, controlled trials—Multicenter Automatic Defibrillator Implantation (MADIT) and Multicenter Unsustained Tachycardia Trial (MUSIT)—demonstrated conclusively that the ICD is the treatment of choice in the primary prevention of SCD in patients with a previous MI.
- Three randomized, controlled trials—Antiarrhythmics Versus Implantable Defibrillators (AVID), the Cardiac Arrest Study Hamburg (CASH), and the Canadian Implantable Defibrillator Study (CIDS)—found the ICD to be superior to antiarrhythmic drugs in the secondary prevention of SCD.

iologic testing. The primary endpoint was all-cause mortality, and a total of 288 patients remained in the study after propafenone was discontinued. During the follow-up, therapy with an ICD was associated with a 23% lower rate of all-cause mortality than that for amiodarone/metoprolol, although this did not reach statistical significance.

The Canadian Implantable Defibrillator Study (CIDS) was another randomized trial that compared the ICD with amiodarone.[38] Similar to the results in the CASH trial, the all-cause mortality rate in those patients who received an ICD was 19.7% lower than the rate with amiodarone, but this difference, too, did not reach statistical significance. Thus, both the CASH and CIDS trials provide further support to the superiority of the ICD over amiodarone in the secondary prevention of SCD.

Indications for ICD Therapy

Indications for ICD therapy have been codified by the American College of Cardiology, the American Heart Association, and the North American Society of Pacing and Electrophysiology.[2,39] A Class I indication conveys general agreement that an ICD is warranted, whereas Class II A and B indications are more controversial, yet still appropriate. Class I indications for an ICD include cardiac arrest caused by VF or VT without a transient or reversible cause; spontaneous VT-S; syncope of undetermined origin, with clinically relevant, hemodynamically significant VT-S or VF induced at electrophysiologic testing when prior drug therapy is ineffective, not tolerated, or not preferred; and nonsustained VT with CAD, prior LV dysfunction, and inducible VF or VT-S at electrophysiologic testing that is not suppressible by a Class I antiarrhythmic drug. Of note, it is no longer necessary to prove the ineffectiveness of drug therapy in this latter situation, and after the results of the MUSTT study, we do not offer drug therapy as a primary prevention of SCD to these patients.

Conclusions

Numerous investigators from around the world have evaluated therapies to prevent primary and secondary SCD, and they have brought about a remarkable transformation in our understanding of the prevention of SCD. Randomized, prospective, controlled trials have shown that the ICD is superior to other treatments in preventing primary and secondary SCD. Cardiology societies in both the United States and Europe have published similar indications for the ICD. It is important for physicians to recognize patients who are candidates for the ICD and to refer them to an electrophysiologist so that they can get this life-saving therapy. Adjunctive drug therapy with β-adrenergic blockers, angiotensin-converting enzyme inhibitors, and statins should be given as needed. Although these therapies will undoubtedly reduce the incidence of SCD, dramatic breakthroughs will likely have to await advances in molecular biology. ■

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