The Role of Implantable Cardioverter Defibrillators in Ischemic and Non-Ischemic Cardiomyopathy and Effect on Mortality and Sudden Death

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ABSTRACT

Implantable Cardioverter Defibrillators (ICDs) have evolved from a treatment of last resort to the current and rapidly growing use as a first line therapeutic option. Early clinical trials captured what had only been apparent in observational studies that subsequently paved the way for the utilization of ICDs as secondary prevention in patients who had survived life-threatening arrhythmias. As a result, these randomized clinical trials exhibited a benefit with ICD only in high-risk patients with ischemic cardiomyopathy. However, recent studies have been able to demonstrate a significant role for primary prevention in selected high-risk patients with non-ischemic cardiomyopathy.

INTRODUCTION

Sudden cardiac death (SCD) is among the most common causes of mortality. It is estimated that more than 450,000 deaths are attributed to SCD primarily due to ventricular tachycardia (VT) or ventricular fibrillation (VF), with a survival rate of approximately 5 percent (Zheng et al., 2001; Zipes and Wellens, 1998). Although there has been a reduction in total cardiac mortality, the percentage of deaths from SCD has increased. In fact, SCD accounts for more deaths each year than the total number of deaths from AIDS, breast cancer, lung cancer, and stroke (Josephson et al., 2000). In addition, the risk of sudden death increases dramatically in patients with heart failure (Ellison et al., 2003). Although new medical therapies have helped patients with heart failure live longer, SCD remains a distinctly unpredictable facet of this chronic disease.

In the 1970s, doctors Michael Mirowski and Morton Mower, motivated by the sudden death of a colleague, conceived and developed an implantable device that would detect rhythm abnormalities and deliver defibrillating shocks, the early ICD. They theorized that most of the energy required for external defibrillation wastefully dissipated in surrounding tissues. They believed that a shock delivered directly to the heart would require much less energy, and that a device to deliver it could be made small enough to be implanted in the human body. Mirowski implanted the first device in a human in 1980 and in 1985, the Food and Drug Administration (FDA) approved the use of ICDs, (Mirowski and Mower, 1973; Mirowski et al., 1978; Mirowski et al., 1980).

Initially, attempts at preventing SCD were aimed at suppression of ventricular ectopy, but it was not until the Cardiac Arrhythmia Suppression Trial (CAST) revealed that the treatment of asymptomatic ventricular premature contractions and non-sustained VT with antiarrythmic drugs was not only inappropriate, but also dangerous (Etcht et al., 1991). Over the years ICDs have become a first line therapeutic modality for the secondary prevention of SCD and for primary prevention in selected patients. Recently, however, new studies have paved the way for more inclusive criteria for the use of ICDs as primary prevention. Since only a minority of patients survive an episode of SCD, identifying patients at high risk for SCD is crucial.

This article reviews the early studies that initially led to the use of ICDs as secondary preventative measures and examines their indications as primary preventative measures in both ischemic and non-ischemic cardiomyopathy. Recent studies have examined primary and secondary prevention trials and the potential impact of ICDs in patient survival and sudden cardiac death (Ezekowitz et al., 2003; Lee et al., 2003; Domanski et al., 1999; Buxton et al., 1999). In addition, several significant primary prevention trials have recently been introduced (Hohnloser et al., 2004; Kadish et al., 2004; Bardy et al., 2005). Until now, the role of ICDs in this patient population had remained equivocal; however, these studies have begun to elucidate a more significant role in this patient population.

SECONDARY PREVENTION

Initial uncontrolled studies suggested that ICDs reduced the rate of SCD (Fogoros et al., 1987; Tchou et al., 1988; Kelly et al., 1988; Fogoros et al., 1990). However, in these studies the delivery of a shock by the ICD was understood to surrogate an end point. Such an approach overestimated the benefit of defibrillators, as not all shocks are appropriate and not all arrhythmias lead to sudden death (Winkle et al., 1989). In addition, confidence in conventional antiarrhythmic therapy to prevent sudden death was questioned by many (Etcht et al., 1991; Mason, 1993). Therefore, randomized controlled trials (RCTs) were conducted to evaluate the true effect of implantable defibrillators. Secondary prevention trials enrolled patients with previous history of cardiac arrest or sustained VT and compared ICD therapy with standard therapy (Tables 1 and 2).

TABLE 1 I SECONDARY PREVENTION TRIALS BASELINE CHARACTERISTICS

Trial	N	Age	Mean LVEF (%)	Follow-ups (Months)	Control Therapy
CASH	288*	58 ± 11	45	57 ± 34	Amiodarone or Metoprolol
CIDS	659	64 ± 9	34	36	Amiodarone
AVID	1016	65 ± 10	32	18 ± 12	Amiodarone

AVID = Antiarrhythmic Versus Implantable Defibrillator; **CASH** = Cardiac Arrest Study Hamburg; **CIDS** = Canadian Implantable Defibrillator Study; **LVEF** = left ventricular ejection fraction; Plus-minus values are means ± standard deviation. * Excludes patients assigned to Propafenone

TABLE 2 I SECONDARY PREVENTION TRIALS EFFECT ON MORTALITY AND SCD

	Overall Mortality (%)			Death Due to Sudden Cardiac Death (%)		
Trial	**Control**	**ICD**	**P**	**Control**	**ICD**	**P**
CASH	44.4	36.4	0.08	33.0	13.0	0.005
CIDS	29.6	25.3	0.14	13.1	9.0	0.094
AVID	24.0	15.8	0.02	10.8	4.7	*

AVID = Antiarrhythmic Versus Implantable Defibrillator; **CASH** = Cardiac Arrest Study Hamburg; **CIDS** = Canadian Implantable Defibrillator Study; **ICD** = implantable cardioverter defibrillator; **SCD** = Sudden Cardiac Death.
*= significant difference, but P value not available

The Cardiac Arrest Survival in Hamburg (CASH) study evaluated the effect of ICDs versus anti-arrhythmic medication (amiodarone, metoprolol, and propafenone) as a secondary measure in survivors of cardiac arrest secondary to documented ventricular arrhythmia (Kuck et al., 2000). The propafenone arm was discontinued early in the study after interim analysis revealed a 61 percent higher mortality rate during follow up (Siebels et al., 1993). The study demonstrated a reduction in total mortality in patients receiving ICD compared to drug therapy (36.4 versus 44.4 percent, P=0.08) and a significant reduction in mortality due to SCD (13 versus 33 percent, P=0.005).

The Canadian Implantable Defibrillator Study (CIDS) trial enrolled patients with resuscitated VF, sustained VT, or unmonitored syncope deemed to be secondary to arrhythmia for treatment with ICD or with amiodarone (Connolly et al., 2000a). After a three-year follow-up, a non-significant 20 percent reduction in the risk of death was observed (10.2 versus 8.3 percent per year, P=0.142), as well as a non-significant reduction in SCD alone.

In a follow-up study, Sheldon and his colleagues analyzed the outcome in order to identify subgroup of patients most likely to benefit from ICD therapy (Sheldon et al., 2000). They identified age, ejection fraction (EF), and New York Heart Association (NYHA) class as independent predictors of risk, and based on these parameters, quartiles of risk were constructed. Patients in the highest risk quartile with at least two risk factors (age greater than 70, left ventricular EF (LVEF) of no more than 35 percent, and NYHA class III or IV) had a significant reduction of death from the ICD compared to amiodarone (14.4 versus 30 percent).

The Antiarrhythmic Drug Versus Defibrillator (AVID) trial randomized patients who were resuscitated from near-fatal VF or sustained VT to either treatment with ICD, or medical treatment with amiodarone. The trial was terminated early when a significant relative reduction in mortality was noted in the ICD group. As expected, the major effect of the ICD was to prevent arrhythmic sudden death (4.7 versus 10.8 percent). A follow up evaluation by the AVID investigators revealed no significant

TABLE 3 | PRIMARY PREVENTION TRIALS IN PATIENTS WITH ISCHEMIC CARDIOMYOPATHY

Trial	N	Age	Mean LVEF (%)	Follow-ups (Months)	Control Therapy
MADIT	196	63 ± 9	26	27	Conventional
MADIT II	1232	64 ± 10	23	20	Conventional
CABG Patch	900	64 ± 9	27	32 ± 16	No ICD
MUSTT	704	67 ± 12	30	39	No EP-guided therapy
DINAMIT	674	62	28	30	Placebo

CABG Patch = Coronary Artery Bypass Graft Patch Trial; **DINAMIT** = Defibrillator in Acute Myocardial Infarction **Trial LVEF** = left ventricular ejection fraction; **MADIT** = Multicenter Automatic Defibrillator Implantation Trial; **MUSTT** = Multicenter Unsustained Tachycardia; Plus-minus values are means ± standard deviation.

TABLE 4 | PRIMARY PREVENTION TRIALS IN PATIENTS WITH ISCHEMIC CARDIOMYOPATHY AND EFFECT ON MORTALITY AND SCD

	Overall Mortality (%)			Death due to SCD (%)		
Trial	**Control**	**ICD**	**P**	**Control**	**ICD**	**P**
MADIT	38.6	15.8	0.009	12.9	3.2	*
MADIT II	19.8	14.2	0.016	9.9	3.8	<0.01
CABG Patch	21.3	22.2	0.64	6.2	3.4	†
MUSTT	48.0	42.0	0.06	See Table 5		
DINAMIT	17.0	18.7	0.66	8.5	3.6	0.009

CABG Patch = Coronary Artery Bypass Graft Patch Trial; **DINAMIT** = Defibrillator in Acute Myocardial Infarction Trial; **ICD** = implantable cardioverter defibrillator; **MADIT** = Multicenter Automatic Defibrillator Implantation Trial; **MUSTT** = Multicenter Unsustained Tachycardia; **SCD** = Sudden Cardiac Death.
*= Significant difference, P value not available
†= Non-significant difference, P value not available

improvement in survival in patients treated with ICD therapy, with LVEF of greater than 35 percent (83.4 versus 82.7 percent at two years). However, in those with an LVEF between 20-34 percent, survival was significantly improved (Domanski et al., 1999).

In a meta-analyses Connolly and colleagues combined all three trials described above and revealed a significant 28 percent relative risk reduction in all cause mortality (Connolly et al., 2000b). SCD alone decreased by 50 percent. Furthermore, over a follow-up of six years, the ICD extended survival by 4.4 months. The analysis also confirmed previous findings; patients with EFs of greater than 35 percent received less benefit (P=0.011). Finally, patients treated with ICDs implanted before July 1st 1991, the "epicardial era," received significantly less benefit than endocardial systems.

PRIMARY PREVENTION

Primary prevention trials enrolled participants who were high-risk for fatal ventricular arrhythmias. While initial studies focused on patients with ischemic cardiomyopathy, recent trials have addressed and extended the concentration to patients with non-ischemic cardiomyopathy.

Ischemic (Tables 3 and 4)

The Multicenter Automatic Defibrillator Implantation Trial (MADIT) enrolled patients with a prior history of coronary artery disease, NYHA class I-III, EF of less than 35 percent, a documented episode of asymptomatic unsustained VT, and inducible non-suppressible VT on

electrophysiologic study (Moss et al., 1996). They were randomized to receive either an ICD or managed with conventional medical therapy at the discretion of individual physicians. However, 74 percent of patients in the conventional treatment group received amiodarone. After an average follow-up of 27 months, 15 deaths occurred in the ICD group and 39 in the conventional group, for a relative reduction of 54 percent (P=0.009). However, the limited number of patients enrolled and the stringent inclusion criteria limit the study's generalizability. Furthermore, since the study required enrolling patients with inducible sustained VT not responsive to antiarrhythmic therapy, it favored high-risk patients who would be less likely to be well managed with pharmaceutical therapy. Nevertheless, examination of such discrepancy by the authors did not reveal any significant interaction.

In addressing these criticisms, the second Multicenter Automatic Defibrillator Implantation Trial (MADIT II) enrolled patients with a prior history of a myocardial infarction and an EF of less than 30 percent. Unlike the original study, the MADIT II did not require the presence of spontaneous or inducible arrhythmia or electrophysiologic studies (Moss et al., 2002). The patients were randomized to either conventional therapy or prophylactic ICD; however, the study was prematurely terminated after a follow-up of 20 months because the ICD significantly reduced all-cause mortality (19.8 versus 14.2, P=0.016). Follow-up analysis revealed that the survival benefit was entirely due to a reduction in sudden death (3.8 versus 10 percent) (Greenberg et al., 2004).

Unlike in MADIT I, where the benefit was evident after the first month of ICD use, in MADIT II divergence did not appear until after nine months. Moss and colleagues attributed this difference to the lower mortality rate in the conventional-therapy group in the MADIT II study, and the absence of the stringent criteria used in the original study, the lower EF eligibility, and the use of more optimal medical management (Moss et al., 2002). Subsequently, such results led to the FDA approval of ICD implantation for primary prevention.

The Coronary Artery Bypass Graft (CABG) Patch Trial evaluated the role of ICD in reducing the overall long-term mortality in patients undergoing surgical revascularization for severe coronary heart disease, with EF below 36 percent, and abnormalities on signal-averaged electrocardiogram (Bigger, 1997). The trial randomized patients at the time of the CABG procedure to either implantation of an epicardial defibrillator or a control group. After a follow-up of 32 months, the study was terminated when no benefit was evident during interim analysis.

Bigger and colleagues attempted to resolve the lack of significance in the CABG Patch Trial. They examined the cause of death in the trial, and demonstrated that only 54 deaths (27%) occurred out of hospital, with majority of deaths occurring in the hospital prior to discharge early in the postoperative period. In the CABG Patch Trial, ICD therapy reduced arrhythmic death by 45 percent without significant effect on nonarrhythmic deaths, and since 71 percent of the deaths were nonarrhythmic, total mortality was not significantly reduced (Bigger, 1999). In addition, the CABG Patch Trial used ICDs with an epicardial-lead system which might be less effective (Domanski et al., 1999).

The Multicenter Unsustained Tachycardia Trial (MUSTT) (Buxton et al., 1999) evaluated the role of antiarrhythmic therapy guided by electrophysiologic testing (Buxton et al., 1999). Patients with inducible VT were randomly assigned to either no therapy or antiarrhythmic therapy guided by serial electrophysiological studies. Patients would receive a defibrillator only if one or more of the trial drugs were tried and were found to be unsuccessful. After five years, a significant benefit was demonstrated with electrophysiologically guided (EPG) therapy with 25 percent of patients in the EPG guided therapy and 32 percent of patient without antiarrhythmic therapy reaching primary end point of cardiac arrest or death from arrhythmia (RR 0.73; P=0.04) (Table 5). The five-year estimates of overall mortality showed trends of 42 and 48 percent, respectively (P=0.06). Nevertheless, the reduction in overall mortality and SCD in the EPG guided group were largely attributed to ICD therapy; at five years, SCD occurred in 9 percent of patients with EPG guidance and ICD therapy versus 37 percent of patients with EPG therapy without ICD (Table 5). Similar results were demonstrated for overall mortality, with 24 percent and 55 percent, respectively. However, due to its atypical inclusion criteria, some have suggested that the MUSTT study may be better described as a test of an electrophysiologically guided treatment strategy since the investigators prescribed ICDs based on EPG studies and not in a randomized fashion (DiMarco, 2003).

The majority of patients evaluated in the studies of primary prevention trials included patients who had experienced a myocardial infarction (MI) more than six months prior to enrollment. Since the mortality rates remain high, and a significant cause of mortality post MI is attributed to arrhythmia, the Defibrillator in Acute Myocardial Infarction Trial (DINAMIT) set out to assess the benefit of prophylactic ICDs in this patient population (Hohnloser et al., 2004). This study randomized patients within 40 days of a MI to ICD implantation with optimal medical therapy (OMT) and compared all-cause mortality to OMT alone.

The study enrolled patients with a history of recent MI, within 6 to 40 days, with EF of less than 35 percent and impaired cardiac autonomic function. After an average follow up of 30 months there was no difference in overall mortality between the two treatment groups (P=0.66). Although the study revealed a significant

TABLE 5 I RESULTS OF THE MUSTT TRIAL

Effect of EPG therapy			
	No Treatment	**EPG guided treatment**	**Relative risk of event with EPG therapy (95% CI)**
Death due to arrhythmia	32%	25%	0.73; (0.53-0.99); P=0.04
Overall Mortality	48%	42%	0.80; (0.64-1.01); P=0.06
Effect of ICD therapy			
	EPG without ICD	**EPG with ICD**	
Death due to arrhythmia	37%	9%	P<0.001
Overall Mortality	55%	24%	P<0.001

CI = confidence interval; **EPG** = Electrophysiologically guided; **ICD** = implantable cardioverter defibrillator; **MUSTT** = Multicenter Unsustained Tachycardia

TABLE 6 I PRIMARY PREVENTION TRIALS IN PATIENTS WITH NON-ISCHEMIC CARDIOMYOPATHY

Trial	N	Age	Mean LVEF (%)	Follow-ups (Months)	Control Therapy
CAT	104	52	24	66 ± 26	No ICD
AMIOVIRT	103	59	23	24 ± 16	Amiodarone
DEFINITE	458	58	21	29 ± 14	Medical Therapy
SCD-HeFT	2521	60	25	45.5	Placebo

AMIOVIRT = Amiodarone Versus Implantable Cardioverter-Defibrillator Randomized Trial; **CAT** = Cardiomyopathy Trial; **DEFINITE** = Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation; **ICD** = implantable cardioverter defibrillator; **LVEF** = left ventricular ejection fraction; **SCD-HeFT** = Sudden Cardiac Death-Heart Failure Trial Plus-minus values are means ± standard deviation.

reduction in SCD (P=0.009), this was offset by an increase in non-arrhythmic death (P=0.02). Therefore, it seems that ICD therapy changed the risk of death from arrhythmic to non-arrhythmic causes.

Non-Ischemic (Tables 6 and 7)

Although primary ischemic cardiomyopathy prevention trials had fueled a dramatic growth in the use of ICDs by the turn of the century, scarce data was available for benefits of ICD application in heart failure patients with non-ischemic cardiomyopathy (Josephson and Wellens, 2004) (Tables 6 and 7).

The Cardiomyopathy Trial (CAT) was one of the first trials to evaluate the role of ICD therapy in patients with non-ischemic cardiomyopathy (Bansch et al., 2002). It randomly assigned patients with recent onset dilated cardiomyopathy (DCM) of non-ischemic etiology and EF of less than 30 percent to either an ICD or a control group. The trial was terminated early after inclusion of only 104 patients because the all-cause mortality rate after one year was much lower than the expected 30 percent in the control group. As such, no significant mortality benefit was evident after one, two, and four-year follow-ups. Accordingly, the investigators argued that even if the study had continued to collect over 1,300 patients, it would have less than 50 percent power

TABLE 7 | PRIMARY PREVENTION TRIALS IN PATIENTS WITH NON-ISCHEMIC CARDIOMYOPATHY AND EFFECT ON MORTALITY AND SCD

	Overall Mortality (%)			Death Due to SCD (%)		
Trial	**Control**	**ICD**	**P**	**Control**	**ICD**	**P**
CAT	31.4	26.0	0.554	N/A	N/A	N/A
AMIOVIRT	13.5	11.8	0.8	3.8	2.0	0.7
DEFINITE	14.1	7.9	0.08	6.1	1.3	0.006
SCD-HeFT	28	23	0.007	N/A	N/A	N/A

AMIOVIRT = Amiodarone Versus Implantable Cardioverter-Defibrillator Randomized Trial; **CAT** = Cardiomyopathy Trial; **DEFINITE** = Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation; **ICD** = implantable cardioverter defibrillator; **N/A** = Data Not Available; **SCD-HeFT** = Sudden Cardiac Death-Heart Failure Trial. **SCD** = Sudden Cardiac Death. Plus-minus values are means ± standard deviation.

to show the expected difference of six percent between the two groups.

Of note, CAT was a multicenter study with a very poor enrollment rate. It took over six years to enroll 104 patients among 15 centers combined. In addition, the number and clinical characteristics of screened yet not enrolled patients in the trial and their outcomes remain unknown. Moreover, the trial limited its inclusion to patients with recently diagnosed cardiomyopathy.

Similarly, the Amiodarone Versus Implantable Cardioverter-Defibrillator Randomized Trial (AMIOVIRT) examined the impact of ICD therapy versus amiodarone in non-ischemic DCM patients with EF less than 35 percent (Strickberger et al., 2003). However, unlike the previous studies which included only newly diagnosed DCM, AMIOVIRT included patients with established DCM. The study also included patients with asymptomatic non-sustained VT as part of its inclusion criteria. However, the study was stopped prematurely due to a lack of benefit at one or three year follow-up. Similar to the CAT study, AMIOVIRT was hindered by its small sample size and mortality rates which fell well below their original estimate. Hence, the AMIOVIRT authors argued that with the observed mortality rates, over 12,000 patients would have been required to achieve a power of 80 percent. However, others argue that the discrepancy between previously reported mortality rates and the remarkably low observed mortality rates in these two trials may be due to differences in patient selection and medication usage (Grimm, 2003).

The Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation (DEFINITE) randomized patients with non-ischemic DCM, an EF of less than 36 percent, and premature ventricular complexes or non-sustained VT (Kadish et al., 2004). It found a trend toward a reduction in mortality (P=0.08) and a significant benefit in SCD (P=0.006) with ICD compared to optimal medical therapy. The all cause mortality rate in the control group was 14.1 percent; however, only about one third of the deaths were due to sudden death, well below the originally anticipated 50 percent. Consequently, the trial was underpowered to demonstrate a significant difference in all cause mortality. The investigators attributed the low mortality rate to the fact that eighty-five percent of patients in the DEFINITE trial were treated with ACE inhibitors and beta-blockers, a higher compliance rate than previous trials (Moss et al., 1996; Moss et al., 2002). The lower than expected number of SCD due to arrhythmia may have been due to the high use of beta-blockers and ACE inhibitors (Waagstein et al., 1997; Heidenreich et al., 1997; Poole-Wilson et al., 2003).

Recently, the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT), a large, multicenter, randomized trial of patients with either ischemic or non-ischemic heart failure, NYHA Class II or III, and EF less than 35 percent, compared the placebo, amiodarone, and single-lead ICD in addition to conventional therapy (Bardy et al., 2005). After a five year follow up, the study revealed therapy with ICD significantly decreased the relative risk of death by 23 percent as compared to placebo, regardless of heart failure etiology (P=0.007). In addition, the sub-group analysis revealed that ICD therapy had a significant benefit in patients in NYHA class II, but not in NYHA class III heart failure. In contrast, amiodarone therapy had no benefit in patients in NYHA class II, and even decreased survival among patients in NYHA class III heart failure.

In comparison to the AMIOVIRT and DEFINITE, which failed to exhibit a mortality benefit in patients with non-ischemic cardiomyopathy, this larger study did not require the presence of non-sustained VT as entry criteria. In addition, although the mortality benefit was smaller than previous studies, the authors attribute this

TABLE 8 | INDICATIONS FOR IMPLANTABLE CARDIOVERTER DEFIBRILLATORS THERAPY*

CLASS I:

1. Cardiac arrest due to VF or VT, not due to transient or reversible cause.
2. Spontaneous sustained VT in association with structural heart disease.
3. Syncope of undetermined origin with clinically relevant, hemodynamically significant sustained VT or VF induced at electrophysiological study when drug therapy is ineffective not tolerated, or not preferred.
4. Non-sustained VT with coronary artery disease, prior MI, LV dysfunction, and inducible VF or sustained VT at electrophysiological study that is not suppressible by a class I antiarrhythmic drug.

CLASS IIA:

1. Patients with LVEF of 30 percent, at least one month post MI and three months post coronary revascularization surgery.

CLASS IIB:

1. Cardiac arrest presumed to be due to VF when electrophysiological testing is precluded by other medical conditions.
2. Severe symptoms (eg, syncope) attributable to ventricular tachyarrhythmias in patients waiting cardiac transplantation.
3. Familial or inherited conditions with a high risk for life-threatening ventricular tachyarrhythmias such as the long QT syndrome or hypertrophic cardiomyopathy.
4. Nonsustained VT with coronary artery disease, prior MI, LV dysfunction, and inducible sustained VT or VF at electrophysiological study.
5. Recurrent syncope of undetermined etiology in the presence of ventricular dysfunction and inducible ventricular arrhythmias when other causes of syncope have been excluded.
6. Syncope of unexplained etiology or family history of unexplained sudden cardiac death in association with typical or atypical right bundle-branch block and ST-segment elevations (Brugada syndrome).
7. Syncope in patients with advanced structural heart disease in which thorough invasive and noninvasive investigation has failed to define a cause.

CLASS III:

1. Syncope of undetermined cause in a patient without inducible ventricular tachyarrhythmias and without structural heart disease.
2. Incessant ventricular tachyarrhythmias.
3. Ventricular tachyarrhythmias arising from rhythm disturbances that are amenable to surgical or catheter ablation.
4. Ventricular tachyarrhythmias due to a transient or reversible disorder when correction of the disorder is considered feasible and likely to substantially reduce the risk of recurrent arrhythmia.
5. Significant psychiatric illnesses that may be aggravated by device implantation or may preclude systematic follow-up.
6. Terminal illnesses with projected life expectancy more than 6 months.
7. Patients with coronary artery disease, left ventricular dysfunctional, and prolonged QRS duration without spontaneous or inducible-ventricular tachycardia undergoing coronary artery bypass surgery.
8. Patients with class IV heart failure who are not candidates for cardiac transplantation.

EF = Ejection fraction, **LVEF** = Left Ventricular Ejection Fraction, **MI** = Myocardial Infarction, **VF** = Ventricular Fibrillation, **VT** = Ventricular Tachycardia

*Adapted and modified from Gregoratos et al., 2002.

discrepancy to the higher compliance with optimal medical therapy. Nevertheless, this study is by far the largest trial to date to that assesses the application of ICD therapy in primary prevention for patients with non-ischemic cardiomyopathy.

CONCLUSION

There have been dramatic advances in the treatment of patients with ventricular arrhythmias. Over the last quarter of century, ICD therapy has proven to be a highly effective treatment in reducing the risk of arrhythmic death when used as either a primary or secondary preventative measure. There seems to be little doubt that ICD therapy should be routinely considered in some patients, such as those with advanced ischemic cardiomyopathy who are resuscitated after ventricular fibrillation. However the debate for the role of ICD in primary prevention is ongoing. As indications for ICD therapy begin to expand rapidly, it is clear that stringent proven methods for risk stratification are vital.

In 2002, the American College of Cardiology updated its recommendations in accordance with published trials (Table 8) (Greegoratos et al., 2002). However, in light of new data from recent trials that have demonstrated a role for ICD therapy in selected patients with non-ischemic cardiomyopathy, it is clear that current recommendations have to be revisited, revised, and made more comprehensive to include patients with non-ischemic cardiomyopathy with poor left ventricular function. However, additional research is required to further identify appropriate patient characteristics.

Also in light of the new data from latest trials, the Center for Medicare and Medicaid Services expanded its previous 2003 guidelines, which were based on the MADIT II criteria, to include prophylactic use of ICD in high risk patients with ischemic or non-ischemic cardiomyopathy and EF of less than 30 percent. If clinical trials prove to be right, such expansion will enable an even greater number of individuals with heart failure to benefit from ICD therapy. Furthermore, recent trials that included cardiac resynchronization therapy in conjunction with ICD therapy in patients with severe heart failure have had promising results (Bristow et al., 2004; Young et al., 2003; Higgins et al., 2003).

Further large randomized controlled trials are needed to fully recognize the potential of such therapies. Although it is clear that ICDs can convert malignant ventricular arrhythmias to sinus rhythm, such benefits are associated with a large cost to society, as each device implantation and follow-up would add billions of dollars to Medicare costs alone (Morgan, 2002; Owen et al., 2002; Weiss and Saynina, 2002; Exner et al., 2001). A discussion of cost-effectiveness analysis and affect on quality of life were beyond the scope of this review. However, these considerations are vital and continued debate and research will determine how far individuals and society are willing to implement such therapies.

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