IMPLANTABLE CARDIOVERTER DEFIBRILLATORS

Implantable cardioverter defibrillators: Uses, abuses, gains and complications

Weiwei Li and Brian Olshansky

Cardiovascular Division, University of Iowa Hospitals and Clinics, Iowa City, Iowa

Address for correspondence:
Brian Olshansky,
Professor of Medicine
Cardiovascular Division
University of Iowa Hospitals and Clinics
200 Hawkins Drive, 4426a JCP
Iowa City
Iowa
52242
USA

Email:
brian-olshansky@uiowa.edu

ABSTRACT

Sudden cardiac death (SCD) due to a ventricular arrhythmia is one of the most common causes of death, yet its management continues to be a challenge. Controlled clinical trials have provided evidence that implantable cardioverter defibrillators (ICDs) are effective in reducing the risk of SCD in selected patients with ischaemic or non-ischaemic cardiomyopathy and/or ventricular arrhythmias. As increasing numbers of patients become eligible for ICDs, deciding whom should receive these becomes more complex, especially in patients with borderline risk factors and those with co-morbidities in whom the risk of death from non-arrhythmic cardiovascular cause is higher. What type of ICD a patient should receive remains a challenge. While ICD shocks themselves can affect outcomes adversely, no other therapy has proven more effective to date. Risks of implantation include infection, lead dislodgement and perforation. An ongoing challenge which also needs to be addressed includes whom will be footing the bill for device implants. More data is required to determine which patient population will benefit the most from ICD implants.

SAHeart 2010; 7:154-164

INTRODUCTION

Sudden cardiac death (SCD) is one of the most common causes of death.[1] The annual risk of SCD is 0.1-0.2% per year in the United States and many other developed countries. Despite advances in cardiovascular care, SCD remains a continuing and challenging problem. Similarly, in South Africa, challenges remain regarding the treatment to reduce the risk of SCD. When a life threatening arrhythmia occurs, adequate resuscitation measures are rarely available.[2]

Ventricular tachycardia (VT) or ventricular fibrillation (VF) is a major cause of SCD. Within a few minutes of ventricular fibrillation, poor cerebrovascular perfusion leads to incorrectable hypoxic encephalopathy. Resuscitation efforts are generally futile. The short-term outcomes of out-of-hospital cardiac arrest were evaluated by Stein et al. Five hundred and one adult cardiac arrest cases in Johannesburg, South Africa were reviewed. Of 153 of the 205 cases with a presumed cardiac cause for cardiac arrest, the median response time was 9 minutes and, by that time, only 23% were found to have a shockable rhythm. Only 36 of the resuscitated cases had return of spontaneous circulation. This was likely due to length of response time.[2]

Rapid defibrillation, only when occurring within seconds to minutes from the onset of ventricular arrhythmia, can terminate it and prevent an otherwise certain death. ICDs however, can detect VT and VF and defibrillate rapidly to return the rhythm to normal within seconds. Therefore, an ICD implant may conceivably prevent SCD and improve long-term survival in patients at risk for life threatening ventricular arrhythmias.

However, many issues remain about ICDs and tachycardia termination in patients at high risk for SCD. Not all SCD is due to VT or VF even if these arrhythmias occur at end of life. In high-risk post-myocardial infarction patients, only half of SCDs are due to ventricular tachyarrhythmias as determined by recordings using an implantable loop recorder.[3] A haemodynamic death may end in fibrillation. Defibrillation will therefore not necessarily make a difference. Furthermore, individuals at high risk may have multiple co-morbidities that place them at high risk for death irrespective of

their arrhythmias. Treatment of VT or VF will not necessarily prolong long term survival in them. For this reason, they may not be candidates for ICDs based on present data. Not all patients who receive ICDs require them. When an ICD is implanted, an inappropriate shock for a non-life threatening arrhythmia may result. There can be other complications of ICD implants.

This manuscript will address critical issues regarding ICD use in high-risk populations in an attempt to address ICD uses, abuses, gains and complications.

WHO IS AT RISK FOR SCD?

Determining who is at risk for SCD and likely to benefit from an ICD is quite complex. Everyone has some risk for SCD.[4] Several important factors must be considered for an ICD to have a major impact in outcomes:

- The risk of SCD due to VT or VF exceeds the risk of mortality from other causes;
- The number of patients needed to treat to save one life needs to be lower than the potential adverse effects and complications from an ICD; and
- Costs must be factored into the therapy benefits.

To address some of these issues, the risk of SCD per year and the chance of dying from other causes need to be considered. Myerberg has considered how the risk of SCD can be transcribed into a decision analysis approach:[5] In the overall population, the risk of SCD due to VF is very small but the total events per year are great due to the size of the population. Alternatively, patients who had recent myocardial infarction with severe ventricular dysfunction have a high rate of SCD. However, the total number of events was small because of the smaller denominator pool in this group. Furthermore, these patients may have a high rate of death from other causes even if the arrhythmic risk were improved. In the middle risk group are patients with heart failure and an impaired left ventricular ejection fraction (LVEF). The risk of SCD of this patient group is moderate in the range of 10-20% per year.[5] This group represents a large population. Therefore, the total events per year are modest or large. Not all patients with heart failure and impaired LVEF will utilise the ICD. In fact, many of these patients will die from non-arrhythmic cardiovascular death or other causes.[6,7] Question remains how to predict who benefits most from an ICD.

All patients with heart disease, such as coronary artery disease, valvular heart disease, cardiomyopathy, congestive heart failure and non-sustained ventricular tachycardia (NSVT) are at higher risk for death than those without heart disease. Even those with normal LVEF but diastolic dysfunction may have some risk.[8] Patients who have had cardiac arrest and have been resuscitated represent a small selected population who are believed to carry an even higher risk of SCD.

WHAT ARE THE RISK PREDICTORS?

Amongst several predictors of SCD due to VF, two have stood the test of time: LVEF and heart failure as determined by functional class. These predictors are modulated by other factors, such as, the underlying cardiovascular condition; coronary artery disease; valvular disease; and cardiomyopathy. They are also modulated by co-morbidities, age and concurrent medications. LVEF is not a linear predictor of risk. The risk of SCD increases rapidly when the LVEF is <35-40%.[9]

Various other non-invasive markers have been considered in the past. In a study of 416 post-myocardial infarction patients heart rate variability, abnormal signal averaged electrocardiography, frequent ventricular ectopy, poor LVEF and impaired Killip class were found to predict SCD. Killip class and LVEF were the least predictive (even though they are often used now). For those patients who had a positive heart rate variability and a positive signal averaged electrocardiogram, the relative risk for arrhythmic events was 18.5 times greater ($p < 0.0000$).[10]

Recently, microvolt T-wave alternans has been advocated as a methodology to reduce the number of ICD implants.[11] The Alternans Before Cardioverter Defibrillator (ABCD) trial indicated that a positive microvolt T-wave alternans test can predict who is at greatest risk. Other data dispute this finding.[12,13] Microvolt T-wave alternans testing has not been incorporated into current risk stratification strategies.

Electrophysiological testing has been used to predict risk. However, it is insensitive and non-specific, even for patients with coronary artery disease. The Multicentre Unsustained Tachycardia Trial (MUSTT) included patients with ischaemic heart disease, NSVT and LVEF ≤40%. The five-year SCD risk was 25% for those receiving

electrophysiologically-guided therapy versus 32% for those assigned to no anti-arrhythmic therapy (p <0.001). Additionally, the five year mortality was 42% and 48% respectively (p =0.005).[14] While the differences were statistically significant, the clinical relevance of this difference is questionable. Electrophysiological testing is no longer considered a risk stratification strategy for determining the need for an ICD.[15]

There are many non-specific predictors of SCD including an elevated high sensitivity CRP; positive family history of sudden death; male sex; reduced water intake; abstaining from alcohol; times around holidays; and a lack of religious belief.[16-19] While men appear to be at high risk for SCD, dogs as pets appear to modulate this risk substantially.[20] One could even draw a geographic map of where the risk for SCD is greatest and then only target individuals who live in that area. This information highlights the absurdity of trying to define risk for sudden cardiac death using non-specific predictors.

THE GOAL OF IDEAL THERAPY IS TO PREVENT SCD

The goal of an ideal therapy is to prevent SCD and improve survival including maintaining quality-of-life and individual autonomy. An ideal therapy would also be highly effective, low risk and low cost. Several time-honoured and well-tested therapies can improve survival in patients with cardiovascular disease especially when cardiomyopathy is present. These include beta-adrenergic blocking drugs;[21] angiotensin converter inhibitors; aldosterone antagonists; and statins in selected patients.[22] These therapies and changing demographics have had a major impact. Today, the risk of SCD is much less than years past.[23,24] Other therapies, including diuretics, digitalis and nitrates used to treat cardiovascular conditions have not been shown to improve long-term survival in the general population.

Anti-arrhythmic drugs were once considered the mainstay of therapy to prevent SCD in patients at risk. Anti-arrhythmic drugs can suppress arrhythmias but they can also be pro-arrhythmic and therefore increase the risk of SCD.[25] Specific drugs that are potentially dangerous in patients with structural heart disease include the Class I drugs: procainamide; quinidine; mexiletine; propafenone; flecainide; encainide; and moricizine. Based on the Cardiac Arrhythmia Suppression Trial (CAST) I and II and many other trials,[25,26] these drugs can substantially increase the risk of SCD even though they may suppress ventricular arrhythmias. Class III drugs may be safer but no data support their use as life saving agents.[27-29] Amiodarone, whose stated indication is to treat life-threatening ventricular arrhythmias, has not been shown to decrease the risk for SCD in patients at risk. Amiodarone has been extensively tested in various populations and has not been convincingly associated with improved long-term outcome yet.[30-32]

ICDs TREAT VF, REDUCE SCD, IMPROVE SURVIVAL AND SAVE LIVES

ICDs have been shown in many well-controlled studies to improve outcomes including total mortality in patients at risk for SCD. Based on these studies, several guidelines have been written recommending when an ICD should be considered.[33,34] The Anti-arrhythmics Versus Implantable Defibrillators (AVID) trial and the Canadian Implantable Defibrillator Study (CIDS) are large multicentre trials focusing on the utility of ICDs for secondary prevention.[35,36] In the AVID trial, the relative benefit included a 39% reduction in total mortality at one year. The absolute benefit included a 9% reduction in mortality at one year.[35] The cost per life year saved was $100 000.[37] There was additional survival of 2.8 months (p <0.02). Despite the relative risk reduction compared with anti-arrhythmic drugs (particularly, amiodarone), the additional gain in life (measured in days) was rather inconsequential. This raises questions to the value of the therapy. The other major secondary prevention trial, the CIDS trial, was inconclusive.[36]

Most importantly, there have been a large number of trials focusing on the utility of ICDs for primary prevention in patients with ischaemic cardiomyopathy and non-ischaemic cardiomyopathy. While many studies have shown the benefit of ICDs in select populations,[14,35,38-41] not all of these studies have demonstrated benefit.[42,43] Some of these studies demonstrate benefit but did not reach statistical significance.[44,45] Other studies are negative and have not shown the benefit in high risk populations.[43]

The Multicentre Automatic Defibrillator Implantation Trial (MADIT II) compared defibrillator against "conventional" therapy in patients with ischaemic heart disease and poor ejection fraction (LVEF

≤30%).[41] The number requiring treatment, the cost per life year saved, and the reduction in total mortality, was much more in line with what was expected of a primary prevention trial. These data were supported by the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT), which included a diverse population of patients with ischaemic and non-ischaemic cardiomyopathy who were treated for congestive heart failure.[38] The SCD-HeFT population had LVEF ≤35% and NYHA functional Class II-III heart failure. Patients were randomised to placebo, amiodarone or ICD therapy and followed up over the long term. There was a 23% relative risk reduction in ICD therapy group (p =0.007) (Figure 1). However, the majority of heart failure patients with high risk are dying of end stage heart failure in the hospital instead of SCD.[7]

Further analysis of this trial has demonstrated that patients with renal insufficiency, who cannot walk more than 900 feet on a six minute walk test, with atrial fibrillation or syncope[46] do not benefit as much from an ICD and may be at risk of death regardless. In addition, patients with NYHA functional Class III congestive heart failure did not seem to achieve benefit. These data highlight the fact that patients with multiple co-morbidities and those who are "sicker" may not benefit from an ICD. Recent analysis of the SCD-HeFT data further highlights this. The study shows that a composite of co-morbid factors can identify subsets of heart failure patients in SCD-HeFT in whom an ICD therapy was of no benefit.[47] Data from the Inhibition of Unnecessary RV Pacing with AV Search Hysteresis in ICDs (INTRINSIC RV) study corroborate these findings.[48]

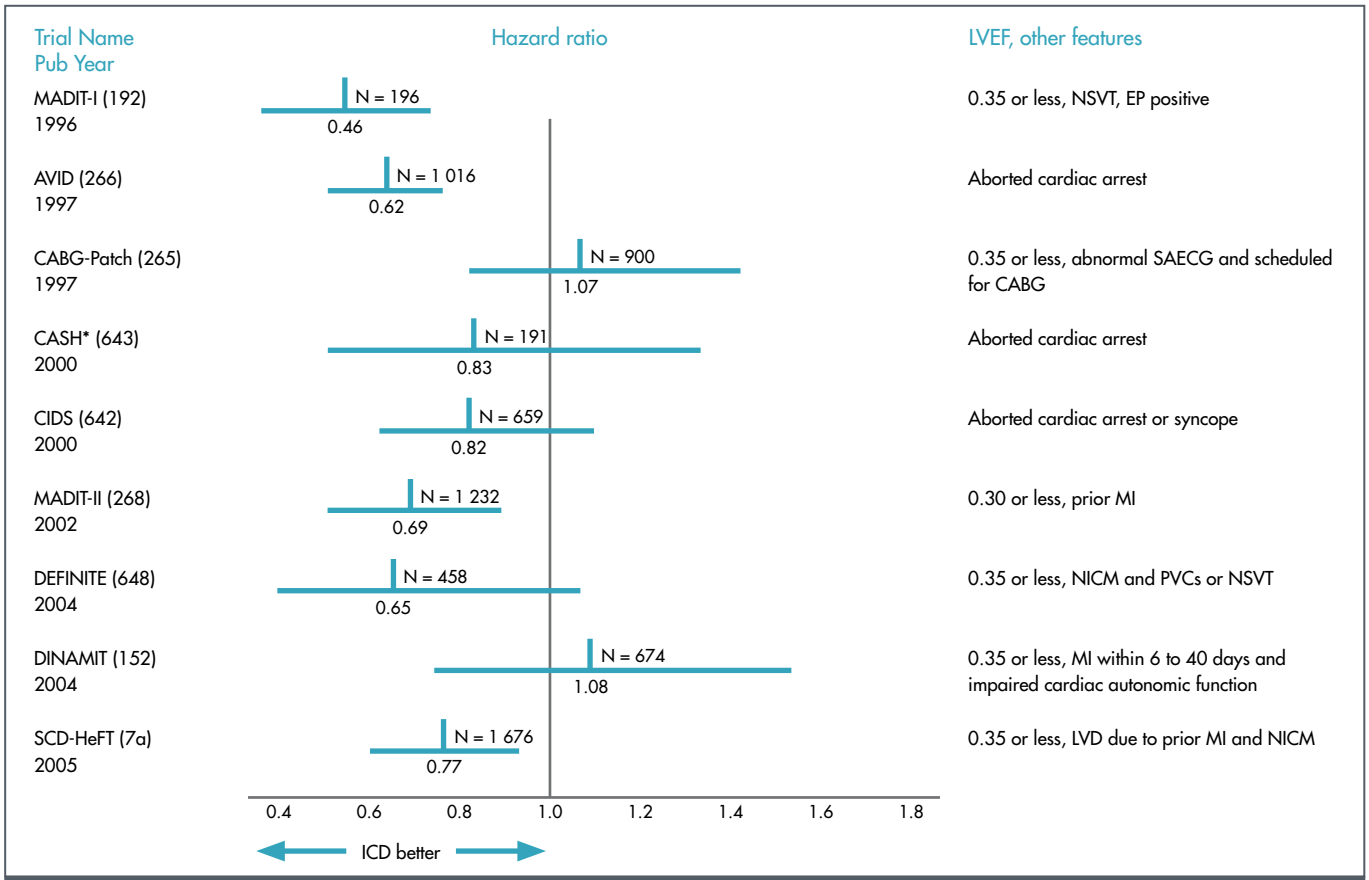

FIGURE 1: Major clinical trials of device therapy for primary and secondary prevention of sudden cardiac death (Zipes DP, Camm AJ, Borggrefe M, et al. ACC/AHA/ESC 2006 Guidelines for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death: A report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death). J Am Coll Cardiol. Sep 5 2006;48(5):e247-346.)

MADIT-I: Multicentre Automatic Defibrillator Implantation Trial I, AVID: Anti-arrhythmics Versus Implantable Defibrillators, CABG-Patch: Coronary Artery Bypass Graft (CABG) Patch Trial, CASH: Cardiac Arrest Study Hamburg, CIDS: Canadian Implantable Defibrillator Study, MADIT-II: Multicentre Automatic Defibrillator Implantation Trial II, DEFINITE: The Defibrillators in Non-ischaemic Cardiomyopathy Treatment Evaluation, DINAMIT: Defibrillator in Acute Myocardial Infarction Trial, SCD-HeFT: Sudden Cardiac Death in Heart Failure Trial, LVEF: Left ventricular ejection fraction, NSVT: Non-sustained ventricular tachycardia, EP: Electrophysiology, SAECG: Signal Averaged Electrocardiogram, MI: Myocardial infarction, PVC: Premature ventricular complex, NICM: Non-ischaemic cardiomyopathy, LVD: Left ventricular dysfunction.

THE EXPERTS DISAGREE ON A CURRENT RECOMMENDATION

Approximately 14 years ago, Stevenson and Ridker published an article in JAMA[49] stating that ICDs may benefit 1 in 14 if the LVEF is ≤40% after myocardial infarction. While the number needed to treat to save one life appears to be in line with what we would expect, these investigators felt that the risk of SCD is so low that "routine referral to an arrhythmia specialist is not warranted". Actually, the number needed to treat for one life saved is one of the best deals we have in cardiology.

In the United States, the Combined Medicare Medicaid Services have developed a "decision summary" in which they include the criteria for ICD implantation.[50] For primary prevention, they include patients with ischaemic or non-ischaemic cardiomyopathy with NYHA II-III heart failure and LVEF ≤35%; no myocardial infarction within 40 days; no bypass surgery or revascularisation within three months; and no acute diagnosis of dilated cardiomyopathy within three months. Furthermore, ICDs are considered "reasonable and necessary" if there is ischaemic or non-ischaemic cardiomyopathy and LVEF ≤30% without heart failure symptoms on proper medical management. For secondary prevention, patients who have had prior VT or VF that is otherwise unexplained are ICD candidates. Other potential conditions include hypertrophic cardiomyopathy; right ventricular cardiomyopathy; long QT interval syndrome; catecholamine-induced polymorphic ventricular tachycardia; and idiopathic ventricular fibrillation among others (Table 1). Unfortunately, the definition of high risk remains uncertain for many of these diseases and the best way to determine who should receive an ICD remains a matter of discussion.[33]

Another concern is for people with borderline risk, for example, patients with diastolic heart failure or with only mild ventricular dysfunction. These patients remain at high risk but may not be as high as patients with severely impaired ventricular function. We have not yet defined which patient with valvular heart disease should have ICDs. There are little data concerning patients with mild QT prolongation or mild left ventricular hypertrophy. Furthermore, limited data is available regarding patients with mild ventricular dysfunction and syncope or patients with a positive family history of sudden death.

CONCERNS ABOUT ICDs

As more data become available through registries and randomised controlled clinical trials, concerns have arisen, including differences in implantation rates based on race and gender; recalls of both ICDs and leads; and inappropriate shocks for sinus tachycardia, NSVT or atrial fibrillation. A procedure complication is an important issue, especially when it comes to revising systems or placing new pulse generators. There are restrictions for patients who receive ICDs. In the United States, for example, individuals with ICDs cannot drive commercially.

Race and gender versus ICD implantation

Data regarding race and gender equipoise remains a concern. In a recent report looking at the "Get with the guidelines" programme for the American Heart Association, of those eligible for an ICD less than 40% actually received one.[51] Compared with white men, black men were less likely and white women were even less likely to receive ICDs when exhibiting the required indications. The group least likely to receive an ICD despite required indications was black women with 44% less chance compared with white men.

Based on a study that compared ICD recipients in Medicare Database to a heart failure cohort without ICDs,[52] there was no clear-cut benefit in an ICD implant for primary prevention. While these populations may not be entirely comparable, it raises issues about the need for ICDs in this population. For secondary prevention, there appeared to be a benefit of receiving an ICD. Women were less likely than men to receive ICDs both for primary and secondary prevention.

Recent data indicate that women are at greater risk for complications and benefit less from ICDs.[53] Women who receive ICDs tend to be older with more co-morbidities. They are more likely to die of non-arrhythmic causes than men. In-hospital complications for ICDs were substantially greater for women than men both in implants for primary and secondary prevention. This was true for all complications and major adverse events. This information has been substantiated in the INTRINSIC RV trial.[54]

Policing effect of ICD in the US population

In the US patients need to complete a National Cardiovascular Data Registry (NCDR) form to receive an ICD. The plan is to

TABLE 1: Indications for Implantable Cardioverter Defibrillator

Class I: ICD therapy is indicated in patients:
■ Who are survivors of cardiac arrest due to ventricular fibrillation or haemodynamically unstable sustained VT after evaluation to define the cause of the event and to exclude any completely reversible causes;
■ With structural heart disease and spontaneous sustained VT, whether haemodynamically stable or unstable;
■ With syncope of undetermined origin with clinically relevant, haemodynamically significant sustained VT or ventricular fibrillation induced at electrophysiological study;
■ With LVEF less than 35% due to prior myocardial infarction who are at least 40 days post-myocardial infarction and are in NYHA functional Class II or III;
■ With non-ischaemic dilated cardiomyopathy who have an LVEF less than or equal 35% and who are in NYHA functional Class II or III;
■ With LV dysfunction due to prior myocardial infarction and are at least 40 days post-myocardial infarction, have an LVEF less than 30%, and are in NYHA functional Class I; and
■ With non-sustained VT due to prior myocardial infarction, LVEF less than 40%, and inducible ventricular fibrillation or sustained VT at electrophysiological study.
Class IIa: ICD implantation is reasonable:
■ For patients with unexplained syncope, significant LV dysfunction, and non-ischaemic dilated cardiomyopathy;
■ For patients with sustained VT and normal or near-normal ventricular function;
■ For patients with hypertrophic cardiomyopathy who have 1 or more major risk factor for SCD;
■ For the prevention of SCD in patients with arrhythmogenic right ventricular dysplasia/cardiomyopathy who have 1 or more risk factor for SCD;.
■ To reduced SCD in patients with long-QT syndrome who are experiencing syncope and/or VT while receiving beta blockers;
■ For non-hospitalised patients awaiting transplantation;
■ For patients with Brugada syndrome who have had syncope;
■ For patients with Brugada syndrome who have documented VT that has not resulted in cardiac arrest;
■ For patients with catecholaminergic polymorphic VT who have syncope and/or documented sustained VT while receiving beta blockers; and
■ For patients with cardiac sarcoidosis, giant cell myocarditis, or Chagas disease.
Class IIb: ICD therapy may be considered:
■ In patients with non-ischaemic heart disease who have an LVEF of less than or equal to 35% and who are in NYHA functional Class I;
■ For patients with long-QT syndrome and risk factors for SCD;
■ In patients with syncope and advanced structural heart disease in whom thorough invasive and non-invasive investigations have failed to define a cause;
■ In patients with a familiar cardiomyopathy associated with sudden death; and
■ In patients with LV non-compaction.
Class III: ICD therapy is not indicated for:
■ Patients who do not have a reasonable expectation of survival with an acceptable functional status for at least 1 year, even if they meet ICD implantation criteria specified in the Class I, IIa, and IIb recommendations above;
■ Patients with incessant VT or ventricular fibrillation;
■ Patients with significant psychiatric illness that may be aggravated by device implantation or that may preclude systematic follow-up;
■ NYHA Class IV patients with drug-refractory congestive heart failure who are not candidates for cardiac transplantation or implantation of a CRT device that incorporates both pacing and defibrillation capabilities;
■ For syncope of undetermined cause in a patient without inducible ventricular tachyarrhythmia and without structural heart disease;
■ When ventricular fibrillation or VT is amenable to surgical or catheter ablation (e.g. atrial arrhythmias associated with Wolff-Parkinson-White syndrome; right ventricular or LV outflow tract; idiopathic VT; or fascicular VT in the absence of structural heart disease); and
■ Patients with ventricular tachyarrhythmias due to completely reversible disorder in the absence of structural heart disease (e.g. electrolyte imbalance, drugs, or trauma).

(Adapted from Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Anti-arrhythmia Devices) developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. J Am Coll Cardiol. May 27 2008;51(21):e1-62.

continue the registry despite hundreds of thousands applicants having been registered. The form is complex and a deterrent for implanting an ICD. Nevertheless, several important pieces of information have resulted from the registry.[55] Electrophysiologists were found to be the most common implanting physicians. Electrophysiologists did a better job at implanting ICDs than non-electrophysiologists. Non-electrophysiology cardiologists and thoracic surgeons had substantially higher complication rates than the electrophysiologists. This was true for both single and dual chamber ICDs and cardiac resynchronisation therapy devices.

ICD advisories and risks in perspective

Over the past several years, there have been many reports of ICD problems and risks. These risks have been taken out of proportion to what they actually represent. For example, the Guidant Ventak Prizm AVT had an advisory date of June 2005 and the current risk of failure was 0.0095%.[56,57] Removing all these ICDs would increase the risk of mortality and adverse effects by many orders of magnitude. There have also been advisories developed by both St. Jude and Medtronic. Of greater concern is the Fidelis Medtronic lead. The failure rate in long-term follow-up is 5% and may be as great as 10%.[58] However, the risk of extraction of these leads may be at least this high. It is uncertain if placing a new lead will lower the risk due to the risk of infection and other complications. On the other hand, if this lead fails with disruption in the installation, patients can receive inappropriate shocks and die as a result. Remote monitoring may help decrease this risk.

Several registries have been developed, helping to better define the risks of maintaining leads and placing new leads and devices. The risk of complications from ICDs in general practice may far exceed that seen in controlled clinical trials. Therefore the actual benefit of an ICD in clinical practice may not be anywhere near what is seen in controlled clinical trials.

Types of ICDs: How to select

Three kinds of ICDs exist:

- Single-chamber ICDs;
- Dual-chamber ICDs; and
- Cardiac Resynchronisation Therapy ICDs.

It remains uncertain who should get a dual chamber ICD versus a single chamber ICD. Most of the controlled clinical data showing benefits have looked at single chamber ICDs and ICDs that reduce right ventricular pacing. New pacing algorithms can minimise the risk of right ventricular pacing in dual chamber ICDs. Dual chamber ICDs have potential benefits as they can pace the atria (and ventricles) as necessary and help identify the specific arrhythmia that led to the shock. While not all the data have shown that dual chamber devices can better discriminate the need for therapy, they can help post hoc determine what the arrhythmia was and what therapy maybe best in the future. There is no consensus about which type of an ICD (single or dual chamber) is the best to implant for most patients.[59,60] Based on NCDR data (only accessible by members), implanting physicians in the United States use dual chamber devices far more frequently than single chamber devices.

Resynchronisation therapy ICDs are for selected high risk patients with low LVEFs and wide QRS complexes, especially those with left bundle branch block. Cardiac resynchronisation devices can reduce the risk of SCD and substantially improve functional class in patients with significant congestive heart failure[61] with pacing alone even if no defibrillation back-up is present.[62]

Appropriate and inappropriate shocks

It is still unclear if ICD shocks, especially inappropriate shocks, can affect outcomes adversely. Data from the SCD-HeFT trial would suggest that receiving a shock versus no shock is associated with a hazard ratio of 11.27 ($p < 0.001$) for death. The hazard ratio of an appropriate versus no appropriate shocks is 5.68 ($p < 0.001$). The hazard ratio of inappropriate shocks versus no inappropriate shocks is 1.98 ($p = 0.002$).[63] The actual meaning of these remains uncertain since inappropriate shocks are often due to atrial fibrillation which in itself is associated with increased risk of death. Similar data were found in the MADIT II population.[64]

While there are those who state that any shock can affect outcomes adversely, this contention is nonsensical when an ICD shock is for a life-threatening arrhythmia: without it the patient would be dead. Furthermore, all data suggesting adverse effects of shocks is flawed by the fact that those patients who received a shock are clearly different than those who do not receive shocks: one group has an arrhythmia and the other group does not. Alternatively, perhaps fewer shocks are needed and anti-tachycardia pacing may

help reduce the need for shocks when a sustained ventricular tachyarrhythmia occurs.

The Prepare Parameters Evaluation Trial (PREPARE) has demonstrated that strategic programming of tachycardia detection and therapy parameters can reduce ICD shocks. This uniform programming approach is better than the individually guided programmed setting to detect tachyarrhythmias.[65]

A new study, the Multicentre Automatic Defibrillator Implantation Trial-Reduced Inappropriate Therapy (MADIT-RIT) trial is underway. This study is comparing three programming schema (standard rate, high rate and prolonged detection) to see which will reduce unneeded shocks without incurring excess risk. Fifteen hundred patients are planned for this study and the study is now enrolling. The outcome is the time to first inappropriate therapy. Other endpoints include total mortality.

ARE THERE TOO MANY ICD IMPLANTS?

The question about the need for ICD implantation raises several important medical and philosophical issues. Many patients who receive ICDs ultimately will be at risk for death from other causes and not benefit from an ICD. This is clear from the SCD-HeFT data.[7] Patients with long QT syndrome and Brugada syndrome may have risk of SCD as low as 0.5 % per year, yet implants continue for those patients.[66,67] Further, there are no randomised studies in many populations for whom devices are routinely placed.

ICDs can also complicate some end-of-life decisions. There is no consensus about when to turn off a device. The actual promise of ICDs and what should be expected in the long-term should be discussed upfront with patients. Furthermore, there is a so-called "Dick Cheney effect". Dick Cheney, the former US vice president, received an ICD as he was considered at risk for SCD even though he did not meet the strict criteria. Like Dick Cheney, many patients fit into the "grey zone" where they have mild impairment of ventricular function but do not reach LVEF ≤35%.

As the public considers the need for ICDs and evaluates the utility for ICDs, it becomes even more questionable at what level the ICD would be appropriate. For example, Consumer Reports, an American publication that evaluates various consumer products for the public need and benefit, have considered the ICD to be one of "10 overused medical tests and treatments". In an article about "how US healthcare bill got to record-breaking $2 trillion", they state "… how consumers can navigate a healthcare system that rewards costly and often unnecessary tests and procedures and de-emphasises preventive care". On ICDs they state that "one third might not need them, research shows".[68] This shows how the public considers a therapy. In fact, if one in 14 used the ICD as a life saving device, it would likely be worth implanting these devices.

This public media view has also been highlighted in the New York Times which stated that "nine of 10 people who get ICDs received no medical benefit".[69] This is probably correct but it is a jilted view of a valid medical therapy. In fact, they stated that "ICDs have saved the lives of 10% of the greater than 600 000 people in this country who received them". This means a large number of people have benefited from ICDs. They also stated "people must weigh the risks of infection and malfunction after they have an electronic device anchored inside their hearts and its wires threaded through their arteries". Clearly, the general population does not understand exactly what an ICD is, what it does and who it benefits. It highlights the idea that the general population and even the federal government probably should not be put in a position of judging how to use medical therapies and devices.

ARE THERE TOO FEW ICDs IMPLANTED?

Data from the United States shows that only about 35% of those who meet ICD criteria actually get the device. A study from the Netherlands also highlights this issue. In terms of primary prevention, only 7% of those patients with LVEF ≤30% actually received an ICD.[70] Patients at risk for SCD who did not meet this criterion did not receive an ICD. With respect to those patients who had spontaneous poorly tolerated VT, only 10% received ICDs. In fact, of the 135 patients with ICD indication, only 19 received an ICD. Of those 1 751 patients who did not have an ICD indication, none of them received an ICD.

Several opinions have been published including a recent state-of-the-art paper by Tung et al. stating that "potential hazards of ICD therapy will enable physicians to have a more mutually informed and balanced dialogue with their patients".[71] This has been com-

mented on by Epstein stating that the risks of ICD therapy are potentially over-emphasised in lieu of the substantial benefits.[72]

SCD remains a major killer. Most victims are not even identified before death. For many individuals at risk, we have no data to know whether or not they should have an ICD implant. Furthermore, many individuals, if not most, are at borderline risk for SCD.

ICDs IN SOUTH AFRICA

ICD implant rates in South Africa are not as high as they are in several other countries including the United States. Government reimbursement appears to be low. Those with private insurance may have a much greater chance of receiving an ICD. The potential benefit of ICDs in reducing the risk of SCD and lowering total mortality is not necessarily the same in South Africa as it is in the United States. Underlying cardiac diseases may be different between countries and risks of SCD even for the same condition may vary by country. In South Africa, there is a greater incidence of valvular heart disease and idiopathic cardiomyopathy than in the United States. There are also more deaths from non-cardiovascular causes including communicable disease so that SCD in the South African population may pale in comparison to other causes of death and disease.

CONCLUSION

ICDs represent a step forward in the treatment of patients with cardiovascular disease when there is a risk for SCD. ICDs can improve total mortality in those patients who have high risk of SCD due to VT or VF. There are continuing challenges that must be considered including identifying when ICDs provide real benefit in the light of risk and cost.

REFERENCES

1. Robertson RM. Sudden death from cardiac arrest-improving the odds. N Engl J Med. 2000;343(17):1259-1260.
2. Stein C. Out-of-hospital cardiac arrest cases in Johannesburg, South Africa: a first glimpse of short-term outcomes from a paramedic clinical learning database. Emerg Med J. 2009;26(9):670-674.
3. Gang UJ, Jons C, Jorgensen RM, et al. Heart rhythm at the time of death documented by an implantable loop recorder. Europace. 2010;12(2):254-260.
4. Passman R, Kadish A. Shouldn't everyone have an implantable cardioverter-defibrillator? Circulation. 2009;120(22):2166-2167.
5. Myerburg RJ, Reddy V, Castellanos A. Indications for implantable cardioverter-defibrillators based on evidence and judgement. J Am Coll Cardiol. 2009;54(9):747-763.
6. Packer DL, Prutkin JM, Hellkamp AS, et al. Impact of implantable cardioverter-defibrillator, amiodarone, and placebo on the mode of death in stable patients with heart failure: Analysis from the Sudden Cardiac Death in Heart Failure Trial. Circulation. 2009;120(22):2170-2176.
7. Olshansky B, Wood F, Hellkamp AS, et al. Where patients with mild to moderate heart failure die: Results from the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT). Am Heart J. 2007;153(6):1089-1094.
8. Al-Khatib SM, Shaw LK, O'Connor C, et al. Incidence and predictors of sudden cardiac death in patients with diastolic heart failure. J Cardiovasc Electrophysiol. 2007;18(12):1231-1235.
9. Moss AJ, Fadl Y, Zareba W, et al. Survival benefit with an implanted defibrillator in relation to mortality risk in chronic coronary heart disease. Am J Cardiol. 2001;88(5):516-520.
10. Farrell TG, Bashir Y, Cripps T, et al. Risk stratification for arrhythmic events in post-infarction patients based on heart rate variability, ambulatory electrocardiographic variables and the signal-averaged electrocardiogram. J Am Coll Cardiol. 1991;18(3):687-697.
11. Costantini O, Hohnloser SH, Kirk MM, et al. The ABCD (Alternans Before Cardioverter Defibrillator) Trial: strategies using T-wave alternans to improve efficiency of sudden cardiac death prevention. J Am Coll Cardiol. 2009;53(6):471-479.
12. Gold MR, Ip JH, Costantini O, et al. Role of microvolt T-wave alternans in assessment of arrhythmia vulnerability among patients with heart failure and systolic dysfunction: Primary results from the T-wave Alternans Sudden Cardiac Death in Heart Failure Trial Sub-study. Circulation. 2008;118(20):2022-2028.
13. Chow T, Kereiakes DJ, Onufer J, et al. Does microvolt T-wave alternans testing predict ventricular tachyarrhythmias in patients with ischaemic cardiomyopathy and prophylactic defibrillators? The MASTER (Microvolt T-wave Alternans Testing for Risk Stratification of Post-Myocardial Infarction Patients) trial. J Am Coll Cardiol. 2008;52(20):1607-1615.
14. Buxton AE, Lee KL, Fisher JD, et al. A randomised study of the prevention of sudden death in patients with coronary artery disease. Multicentre Unsustained Tachycardia Trial Investigators. N Engl J Med. 1999;341(25):1882-1890.
15. Thomas KE, Josephson ME. The role of electrophysiology study in risk stratification of sudden cardiac death. Prog Cardiovasc Dis. 2008;51(2):97-105.
16. Burke AP, Tracy RP, Kolodgie F, et al. Elevated C-reactive protein values and atherosclerosis in sudden coronary death: Association with different pathologies. Circulation. 2002;105(17):2019-2023.

17. Albert CM, Manson JE, Cook NR, et al. Moderate alcohol consumption and the risk of sudden cardiac death among US male physicians. Circulation. 1999;100(9):944-950.
18. Albert CM, McGovern BA, Newell JB, et al. Sex differences in cardiac arrest survivors. Circulation. 1996;93(6):1170-1176.
19. Chan J, Knutsen SF, Blix GG, et al. Water, other fluids, and fatal coronary heart disease: The Adventist Health Study. Am J Epidemiol. 2002;155(9):827-833.
20. Friedmann E, Thomas SA. Pet ownership, social support, and one-year survival after acute myocardial infarction in the Cardiac Arrhythmia Suppression Trial (CAST). Am J Cardiol. 1995;76(17):1213-1217.
21. Zicha S, Tsuji Y, Shiroshita-Takeshita A, et al. Beta-blockers as anti-arrhythmic agents. Handb Exp Pharmacol. 2006(171):235-266.
22. Jessup M, Abraham WT, Casey DE, et al. 2009 focused update: ACCF/AHA Guidelines for the Diagnosis and Management of Heart Failure in Adults: A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines developed in collaboration with the International Society for Heart and Lung Transplantation. Circulation. 2009;119(14):1977-2016.
23. Goraya TY, Jacobsen SJ, Kottke TE, et al. Coronary heart disease death and sudden cardiac death: A 20-year population-based study. Am J Epidemiol. 2003;157(9):763-770.
24. Corrado D, Basso C, Pavei A, et al. Trends in sudden cardiovascular death in young competitive athletes after implementation of a pre-participation screening programme. JAMA. 2006;296(13):1593-1601.
25. Investigators CAST. Preliminary report: Effect of encainide and flecainide on mortality in a randomised trial of arrhythmia suppression after myocardial infarction. N Engl J Med. 1989;321(6):406-412.
26. Echt DS, Liebson PR, Mitchell LB, et al. Mortality and morbidity in patients receiving encainide, flecainide, or placebo. The Cardiac Arrhythmia Suppression Trial. N Engl J Med. 1991;324(12):781-788.
27. Julian DG, Prescott RJ, Jackson FS, et al. Controlled trial of sotalol for one year after myocardial infarction. Lancet. 1982;1(8282):1142-1147.
28. Waldo AL, Camm AJ, deRuyter H, et al. Effect of d-sotalol on mortality in patients with left ventricular dysfunction after recent and remote myocardial infarction. The SWORD Investigators. Survival With Oral d-Sotalol. Lancet. 1996;348(9019):7-12.
29. Camm AJ, Pratt CM, Schwartz PJ, et al. Mortality in patients after a recent myocardial infarction: A randomised, placebo-controlled trial of azimilide using heart rate variability for risk stratification. Circulation. 2004;109(8):990-996.
30. Burkart F, Pfisterer M, Kiowski W, et al. Effect of anti-arrhythmic therapy on mortality in survivors of myocardial infarction with asymptomatic complex ventricular arrhythmias: Basel Anti-arrhythmic Study of Infarct Survival (BASIS). J Am Coll Cardiol. 1990;16(7):1711-1718.
31. Cairns JA, Connolly SJ, Roberts R, et al. Randomised trial of outcome after myocardial infarction in patients with frequent or repetitive ventricular premature depolarisations: CAMIAT. Canadian Amiodarone Myocardial Infarction Arrhythmia Trial Investigators. Lancet. 1997;349(9053):675-682.
32. Julian DG, Camm AJ, Frangin G, et al. Randomised trial of effect of amiodarone on mortality in patients with left-ventricular dysfunction after recent myocardial infarction: EMIAT. European Myocardial Infarct Amiodarone Trial Investigators. Lancet. 1997;349(9053):667-674.
33. Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Anti-arrhythmia Devices) developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. J Am Coll Cardiol. 2008;51(21):e1-62.
34. Zipes DP, Camm AJ, Borggrefe M, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: A report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death). J Am Coll Cardiol. 2006;48(5):e247-346.
35. Investigators. AVID. A comparison of anti-arrhythmic drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. The Anti-arrhythmics versus Implantable Defibrillators (AVID) Investigators. N Engl J Med. 1997;337(22):1576-1583.
36. Sheldon R, Connolly S, Krahn A, et al. Identification of patients most likely to benefit from implantable cardioverter defibrillator therapy: The Canadian Implantable Defibrillator Study. Circulation. 2000;101(14):1660-1664.
37. Sanders GD, Hlatky MA, Owens DK. Cost-effectiveness of implantable cardioverter defibrillators. N Engl J Med. 2005;353(14):1471-1480.
38. Bardy GH, Lee KL, Mark DB, et al. Amiodarone or an implantable cardioverter defibrillator for congestive heart failure. N Engl J Med. 2005;352(3):225-237.
39. Kadish A, Dyer A, Daubert JP, et al. Prophylactic defibrillator implantation in patients with non-ischaemic dilated cardiomyopathy. N Engl J Med. 2004;350(21):2151-2158.
40. Moss AJ, Hall WJ, Cannom DS, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicentre Automatic Defibrillator Implantation Trial Investigators. N Engl J Med. 1996;335(26):1933-1940.
41. Moss AJ, Zareba W, Hall WJ, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med. 2002;346(12):877-883.
42. Hohnloser SH, Kuck KH, Dorian P, et al. Prophylactic use of an implantable cardioverter defibrillator after acute myocardial infarction. N Engl J Med. 2004;351(24):2481-2488.
43. Bigger JT, Jr. Prophylactic use of implanted cardiac defibrillators in patients at high risk for ventricular arrhythmias after coronary-artery bypass graft surgery. Coronary Artery Bypass Graft (CABG) Patch Trial Investigators. N Engl J Med. 1997;337(22):1569-1575.
44. Kuck KH, Cappato R, Siebels J, et al. Randomised comparison of anti-arrhythmic drug therapy with implantable defibrillators in patients resuscitated from cardiac arrest: The Cardiac Arrest Study Hamburg (CASH). Circulation. 2000;102(7):748-754.

REFERENCES

45. Connolly SJ, Gent M, Roberts RS, et al. Canadian implantable defibrillator study (CIDS): A randomised trial of the implantable cardioverter defibrillator against amiodarone. Circulation. 2000;101(11):1297-1302.
46. Olshansky B, Poole JE, Johnson G, et al. Syncope predicts the outcome of cardiomyopathy patients: Analysis of the SCD-HeFT study. J Am Coll Cardiol. 2008;51(13):1277-1282.
47. Levy WC, Lee KL, Hellkamp AS, et al. Maximising survival benefit with primary prevention implantable cardioverter-defibrillator therapy in a heart failure population. Circulation. 2009;120(10):835-842.
48. Bunch TJ, Day JD, Olshansky B, et al. Newly detected atrial fibrillation in patients with an implantable cardioverter defibrillator is a strong risk marker of increased mortality. Heart Rhythm. 2009;6(1):2-8.
49. Stevenson WG, Ridker PM. Should survivors of myocardial infarction with low ejection fraction be routinely referred to arrhythmia specialists? JAMA. 1996; 276(6):481-485.
50. Phurrough SE, Salive ME, Baldwin JF, et al. (2004). Proposed Decision Memo for Implantable Defibrillators (CAG-00157R2). [online] Retrieved May 28, 2010 from http://www.cms.gov/mcd/viewdraftdecisionmemo.asp?from2=viewdraft decisionmemo.asp&id=139&.
51. Hernandez AF, Fonarow GC, Liang L, et al. Sex and racial differences in the use of implantable cardioverter defibrillators among patients hospitalised with heart failure. JAMA. 2007;298(13):1525-1532.
52. Curtis LH, Al-Khatib SM, Shea AM, et al. Sex differences in the use of implantable cardioverter defibrillators for primary and secondary prevention of sudden cardiac death. JAMA. 2007;298(13):1517-1524.
53. Peterson PN, Daugherty SL, Wang Y, et al. Gender differences in procedure-related adverse events in patients receiving implantable cardioverter defibrillator therapy. Circulation. 2009;119(8):1078-1084.
54. Russo AM, Day JD, Stolen K, et al. Implantable cardioverter defibrillators: Do women fare worse than men? Gender comparison in the INTRINSIC RV trial. J Cardiovasc Electrophysiol. 2009;20(9):973-978.
55. Curtis JP, Luebbert JJ, Wang Y, et al. Association of physician certification and outcomes among patients receiving an implantable cardioverter defibrillator. JAMA. 2009;301(16):1661-1670.
56. Guidant initiates worldwide physician communications regarding important safety information and corrective action about implantable cardiac defibrillators. [online] Retrieved May 28, 2010 from http://bostonscientific.mediaroom.com/index.php?s =64&item=177.
57. Gould PA, Krahn AD. Complications associated with implantable cardioverter defibrillator replacement in response to device advisories. JAMA. 2006;295(16): 1907-1911.
58. Samsel T. (2009). Sprint fidelis model 6949 lead performance. [online] Retrieved May 28, 2010 from http://www.medtronic.com/product-advisories/physician/sprint-fidelis/PHYSLETTER-2009-03-13.htm.
59. Wilkoff BL, Cook JR, Epstein AE, et al. Dual-chamber pacing or ventricular backup pacing in patients with an implantable defibrillator: The Dual Chamber and VVI Implantable Defibrillator (DAVID) Trial. JAMA. 2002;288(24):3115-3123.
60. Olshansky B, Day JD, Moore S, et al. Is dual-chamber programming inferior to single-chamber programming in an implantable cardioverter defibrillator? Results of the INTRINSIC RV (Inhibition of Unnecessary RV Pacing With AVSH in ICDs) study. Circulation. 2007;115(1):9-16.
61. Bristow MR, Saxon LA, Boehmer J, et al. Cardiac-resynchronisation therapy with or without an implantable defibrillator in advanced chronic heart failure. N Engl J Med. 2004;350(21):2140-2150.
62. Cleland JG, Daubert JC, Erdmann E, et al. The effect of cardiac resynchronisation on morbidity and mortality in heart failure. N Engl J Med. 2005;352(15): 1539-1549.
63. Poole JE, Johnson GW, Hellkamp AS, et al. Prognostic importance of defibrillator shocks in patients with heart failure. N Engl J Med. 2008;359(10):1009-1017.
64. Daubert JP, Zareba W, Cannom DS, et al. Inappropriate implantable cardioverter defibrillator shocks in MADIT II: frequency, mechanisms, predictors, and survival impact. J Am Coll Cardiol. 2008;51(14):1357-1365.
65. Wilkoff BL, Williamson BD, Stern RS, et al. Strategic programming of detection and therapy parameters in implantable cardioverter defibrillators reduces shocks in primary prevention patients: Results from the PREPARE (Primary Prevention Parameters Evaluation) study. J Am Coll Cardiol. 2008;52(7):541-550.
66. Moss AJ, Schwartz PJ, Crampton RS, et al. The long QT syndrome. Prospective longitudinal study of 328 families. Circulation. 1991;84(3):1136-1144.
67. Antzelevitch C, Brugada P, Borggrefe M, et al. Brugada syndrome: Report of the second consensus conference endorsed by the Heart Rhythm Society and the European Heart Rhythm Association. Circulation. 2005;111(5):659-670.
68. 10 overused tests and treatments. [online] Retrieved May 28, 2010 from http://www.consumerreports.org/health/doctors-hospitals/medical-ripoffs/10-overused-tests-and-treatments/medical-ripoffs-ten-over_1.htm.
69. Feder BJ. (2008). Defibrillators are lifesaver, but risks give pause. [online] Retrieved May 28, 2010 from http://209.235.212.198/content/press_releases/nyt_defibs_are_lifesavers.pdf.
70. Borleffs CJ, Wilde AA, Cramer MJ, et al. Clinical implementation of guidelines for cardioverter defibrillator implantation: Lost in translation? Neth Heart J. 2007; 15(4):129-132.
71. Tung R, Zimetbaum P, Josephson ME. A critical appraisal of implantable cardioverter defibrillator therapy for the prevention of sudden cardiac death. J Am Coll Cardiol. 2008;52(14):1111-1121.
72. Epstein AE. Benefits of the implantable cardioverter defibrillator. J Am Coll Cardiol. 2008;52(14):1122-1127.