Cardiovascular disease is a leading cause of global mortality, accounting for almost 30% (17.5 million) of all deaths in the year 2005. It is estimated that approximately 20% to 40% of all cardiovascular deaths are sudden cardiac deaths (SCDs), and the majority are caused by ventricular tachyarrhythmias. The following sections discuss “where we are” and “where we are heading” in device management of ventricular tachyarrhythmias (ventricular tachycardia [VT]/ventricular fibrillation [VF]).

Where are we?
Device management of spontaneous tachyarrhythmias dates to the early 1970s, when pacemakers were adapted to treat supraventricular tachycardias (SVTs). Compelled by the loss of a friend to SCD, Dr. Mirowski worked with engineers who eventually developed the first commercial implantable cardioverter-defibrillator (ICD) in the mid-1980s. First-generation ICDs were simple “shock-only devices” without pacing for bradycardia or antitachycardia pacing (ATP). Shocks were delivered via epicardial patches sewn onto the heart during thoracotomy. It was these simple devices that established the genesis of today’s ICD industry. Several significant technological improvements coupled with the clinical outcome data from trials allowed the ICD to become a frontline treatment for SCD survivors and patients with recurring VT/VF. First, the incorporation of a biphasic shock waveform significantly improved shock efficacy. This, in turn, paved the way for the use of transvenous leads. Finally, advances in ICD design allowed a significant reduction in device size, from approximately 110 to 35 cc. Also, having established a reliable safety net, ICDs now combine VF shock therapy with ATP to treat monomorphic VT, the predominant ventricular tachyarrhythmia. Finally, arrhythmia detection has advanced from being solely based on ventricular rate to incorporating sophisticated dual-chamber algorithms including electrogram morphology information to discriminate SVT from VT/VF. With these advances, annual ICD implantation rates in the United States increased from 9,000 in 1990 to 143,000 in 2005.

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Significant capabilities of modern ICDs include monitoring and diagnostic features for cardiac disease management. Tachyarrhythmia episode counters, heart rate patterns, and stored electrograms as well as self-diagnostic information such as battery status, capacitor charge time, and lead integrity greatly enhanced the clinicians’ ability to accurately determine the rhythm triggering device therapy as well as to identify potential problems with the ICD system. In addition to providing therapy for sustained ventricular tachyarrhythmias, newer devices are capable of providing information to assist in the management of comorbidities common in ICD recipients. Heart rate variability and atrial fibrillation rhythm and rate control parameters have provided some value in managing patients and predicting clinical outcomes. For example, in patients receiving cardiac resynchronization pacing therapy, heart rate variability has been shown to be lower in those with high risk for mortality and hospitalization, including a decrease in heart rate variability prior to hospitalization. With increasing use of sensors and memory capabilities, the number of diagnostic parameters will continue to grow. Strategies for communicating critically important information have also evolved with time. In the earliest generation of devices, information could be downloaded only during the follow-up visit. In the next generation, an auditory alarm could alert patients to device malfunctions. The patient, in turn, would communicate with the medical caregiver regarding these alerts. In the most recent devices, critically important information is transmitted automatically from a home-based unit to the physician or to a call center. Full interrogation of devices can be conducted by accessing a secure web site. The information is transmitted using short-distance telemetry from the implanted device to the base unit located at home and then via the Internet. Some devices can communicate information via a cellular phone, and this mobile technology allows communication of urgent information even when the patient is not at home. It will become increasingly important to demonstrate the value of these diagnostics to ensure that patient care is being optimized and that the caregiver is not burdened with irrelevant information.

In addition to providing therapy for ventricular tachyarrhythmias, ICDs now provide a host of features that specifically target management of a patient’s heart failure status.
Data from the DAVID (Dual Chamber and VVI Implantable Defibrillator) trial highlighted an unanticipated adverse cardiovascular outcome with unnecessary long-term right ventricular apical pacing. Thus, today’s devices include algorithms to minimize ventricular pacing in patients who historically would have been paced with conventional dual-chamber pacing. A biventricular pacing feature is now used in ICDs for many heart failure patients in the wake of trials that demonstrated improvement in New York Heart Association class, quality of life, and mortality in patients receiving cardiac resynchronization therapy. ICDs also have the capability of measuring thoracic impedance to monitor pulmonary edema. Preliminary data have shown its potential for predicting impending decompensation from fluid overload. Finally, the COMPASS-HF (Chronicle Offers Management to Patients with Advanced Signs and Symptoms of Heart Failure) trial showed that continuous monitoring of intracardiac pressure improved outcomes in patients with chronic heart failure. This feature currently is incorporated into an ICD undergoing clinical investigation. As with other device features, the ability to continuously track fluid volume via pressure sensors could offer an advantage over intermittent recording of patient status by acute right heart catheterization or by variables such as body weight or B-type natriuretic peptide. However, prospective comparison of continuous intracardiac pressures and optimized home care, including frequent transmissions of weights, has not been performed. Diagnostic information as well as algorithms for termination and prevention of atrial tachyarrhythmias have been included in certain ICDs. These features may provide outcome benefit in a subset of patients (e.g., patients with atrial fibrillation and congestive heart failure) but require evaluation in prospective trials.

Indications

The indications for ICD placement have undergone a major evolution. Early ICDs were narrowly indicated for SCD survivors or patients resistant to antiarrhythmic drug therapy. In 1997, the AVID (Antiarrhythmics Versus Implantable Defibrillators) trial established the superiority of ICDs over antiarrhythmic drugs for secondary prevention of SCD in patients with coronary artery disease and low ejection fraction. Not long after, multiple studies, including MADIT (Multicenter Automatic Defibrillator Implantation Trial), MADIT-II, and MUSTT (Multicenter Unsustained Tachycardia Trial), established the value of ICDs for the primary prevention of SCD. Most recently, SCD-HeFT (Sudden Cardiac Death–Heart Failure Trial) demonstrated the superiority of ICDs over amiodarone for ischemic and nonischemic patients with congestive heart failure and low ejection fraction. As a result of these series of trials, the number of patients in the United States who potentially could benefit from ICD has grown nearly 4.5-fold, from 270,000 to 1.3 million. In spite of these advances, patients with ICDs still die, a proportion of which are sudden deaths. Clearly, the ability of ICDs to prevent SCD is not infallible. In some patients, defibrillation may not be possible, or the thresholds may be extremely high under extreme settings of metabolic imbalance, ischemia, and/or acute myocardial infarction. Electromechanical dissociation is a common cause of sudden death in ICD recipients and accounted for 45% of such deaths in one study.

Challenges to increase acceptance of ICDs

Today, fewer than 20% of patients in countries with developed economies who have indications for an ICD receive the device. There are several key challenges for increasing the acceptance of ICD therapy. The first challenge is to further determine the subgroup of patients who can most benefit from this technology and therefore improve the overall cost-effectiveness. Cost-effectiveness varies significantly depending on the patient receiving the device. Most trials to date have focused on the highest-risk subgroups because they yield event rates sufficiently high to design trials with reasonably small numbers of patients. These subgroups constitute only approximately 30% of all patients at risk for SCD. The lifetime cost-effectiveness of ICD therapy in this subgroup can vary from $40,000 to $80,000 per life-year saved, a value that is within the range of other medical therapies accepted in developed economies. However, improvements in device longevity, cost of implant, risk stratification, and long-term overall cost of device therapy can further improve cost-effectiveness. Better understanding of the patient’s needs allows physicians to use devices of varying prices today. The latest devices with the most desirable features tend to have higher prices because of the cost of research and development in a rapidly evolving technology.

The second challenge is to improve the technology, facilitating implant and follow-up from the physician’s perspective and lowering morbidity from the patient’s perspective. Patients want ICDs that are smaller, result in fewer shocks, have less pain associated with defibrillation, require minimal follow-up, and last a long time so that the devices do not require replacement. The third challenge is to increase the awareness of this therapy among physicians and patients. The fourth issue and the one that has received much attention lately is ensuring product reliability and open communication with physicians and patients. If patients are to maintain trust in these lifesaving products, it is critically important that all companies have processes incorporated into the design and development to maintain the highest quality. All major manufacturers have reported pacemaker/defibrillator advisories associated with a risk of device malfunction. The manner in which this information is communicated to the customers is critically important. The Heart Rhythm Society recently made recommendations on communication to physicians and patients regarding device malfunction and corrective actions. Many of these recommendations have been standard practice at some companies. We need to address all of these challenges if im-
plantable defibrillators are to make a significant impact in reducing the incidence of SCD worldwide.

**Where are we heading?**

One of the key technological challenges today is to reduce the number of inappropriate shocks delivered by ICDs, most of which result because of supraventricular tachyarrhythmias. Detection algorithms discriminate ventricular from supraventricular tachyarrhythmias by using timing as well as morphology of electrical cardiac signals. Although these algorithms will continue to improve, an alternative strategy would be to deliver therapy based on hemodynamic status. For example, measurement of intraventricular blood pressure using sensors could determine the urgency of terminating the tachyarrhythmia, irrespective of whether it is ventricular or supraventricular in origin. Acute animal experiments with a pressure sensor on a right ventricular defibrillation lead have shown promising preliminary results but require further testing. To date, right ventricular pressure sensor leads have undergone successful chronic clinical testing for heart failure management but not on a defibrillation lead. Another key issue has been the discomfort associated with shocks. Even if defibrillation thresholds are reduced 15% to 20% by optimizing electrodes and waveforms, they are unlikely to impact the shock discomfort. Fortunately, improvements in ATP have significantly reduced the need for shocks.

There is also a need to make the devices easier to program and to reduce the time and cost of follow-up. The amount of data stored in the devices is increasing rapidly, resulting in an even greater need to communicate relevant information in a timely and efficient manner to the caregiver and the patient. Remote programming of devices should be possible in the future. The two driving forces of patient empowerment and the need to minimize the time required by physicians to follow their patients could have a significant impact on the technology. The size of these devices will continue to decrease as the energy density of batteries and capacitors increases. In the future, it may be possible to prevent a certain proportion of ventricular tachyarrhythmias. Although the event that precipitates a tachyarrhythmia is not well understood, acute ischemia, autonomic or physical stress, or electrolyte disturbances likely play an important role. In ambulatory recording of spontaneous VT/VF, acute ST elevation preceding VT/VF is sometimes observed. Could precursors of these events be detected with implanted sensors and an antithrombotic or anti-ischemic agent delivered through an integrated drug pump for such episodes? Will this be an effective strategy for preventing VT/VF? The technology for delivering agents through implantable pumps exists today. However, they must be miniaturized further to provide devices that can prevent ventricular tachyarrhythmias. Sensitive and specific sensors for detection of ST segment also are needed. These are research challenges that require investigation. Even if we cannot prevent the first VT/VF event, preventing a cluster of VT/VF events by pacing algorithms may be possible.

Lead technology will continue to improve with smaller leads that are less likely to develop fibrosis. Defibrillators without intracardiac leads that use subcutaneous electrodes for detection and defibrillation are presently being developed. These devices eliminate the morbidity associated with intracardiac leads. They require a subcutaneous electrode and have higher defibrillation energy requirements. In addition, they cannot deliver ATP or long-term anti-bradycardia pacing because the high energy levels required for pacing would be quite painful to the patient. Such devices are projected to undergo clinical testing soon.

**Figure 1** Implantable defibrillators: key developments.

➢ Shock-only defibrillator with epicardial leads
➢ Transvenous leads
➢ Biphasic shocks
➢ “Device can” as active electrode
➢ Size reduction
➢ Dual-chamber detection
➢ Atrial therapies
➢ Improved ventricular antitachycardia pacing
➢ Extensive diagnostics and monitoring
➢ Minimizing ventricular pacing
➢ Biventricular pacing for heart failure
➢ Remote monitoring
➢ Sensors for pulmonary edema
➢ Intracardiac pressure monitoring for heart failure

Future? 

➢ Hemodynamic sensors for reducing false-positive shocks
➢ Artificial intelligence systems and autoprogramming
➢ Prevention of ventricular tachycardia/ventricular fibrillation
➢ Implantable cardioverter-defibrillator without intracardiac leads
➢ Monitoring and management of comorbidities (e.g., ischemia, angina, hypertension, diabetes)
Over the last decade, ICDs have evolved from being primarily a defibrillator to being a cardiovascular disease management device for the treatment and monitoring of comorbidities such as atrial fibrillation and heart failure. This process of evolution is likely to continue, especially with monitoring and therapy for heart failure. Many of these patients also suffer from hypertension, diabetes, and angina. Monitoring and management of these comorbidities with appropriate sensors could become the next key development in the evolution of such devices (Figure 1).

Future Indications

One challenge confronting us today is the risk stratification of patients to ensure that only those patients who would benefit most from a device receive one, thus improving cost-effectiveness. The patients most vulnerable to VT/VF are those with an arrhythmogenic substrate and triggers. Risk stratifiers such as ejection fraction, interventricular conduction delay, T-wave alternans, signal-averaged late potentials, heart rate variability, and heart rate turbulence reflect the status of the substrate. More recently, clinical studies of T-wave alternans have shown significant promise.

The trigger can be an acute ischemic episode and/or runs of premature ventricular complexes, nonsustained VT, or sinus tachycardia possibly caused by autonomic disturbances. Genetic and protein markers possibly can be used to identify high-risk patients. The specificity of these risk stratifiers in predicting those patients most likely to develop VT/VF will be evaluated as large trials are conducted. One of the key limitations of many risk stratifiers is the static nature of the measurements. Measurements are made at one time during rest or exercise. In the future, it will be possible to make some of these measurements dynamically over longer periods using an implanted device. For example, having such algorithms in a pacemaker or implanting a small monitoring device could allow monitoring of these parameters in the ambulatory setting in order to risk stratify patients. In such a case, heart rate variability, T-wave alternans, etc., can be measured over long periods under various autonomic stressors. These strategies will allow for widespread use of this technology with a better ability to match this technology to those patients most likely to benefit. This should help reduce further the incidence of SCD. However, at present, evidence-based medicine dictates that patients who meet currently accepted indications according to established guidelines should receive this potentially lifesaving therapy.

References


