PRIMARY PREVENTION OF SUDDEN DEATH USING ICD THERAPY: INCREMENTAL STEPS*

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Ever since its development by Dr. Michel Mirowski in the 1970s and its use in clinical practice in 1980, the implantable cardioverter-defibrillator (ICD) has improved survival in patients presenting with sustained ventricular tachycardia and ventricular fibrillation. Three recent randomized studies—Antiarrhythmic Drugs versus Implantable Defibrillator (AVID) (1), Canadian Implantable Defibrillator Study (CIDS) (2) and Cardiac Arrest Study Hamburg (CASH) (3)—have demonstrated that the ICD is superior to the best antiarrhythmic therapy in the prevention of death in patients who have already experienced an episode of sustained tachycardia arrhythmia. Although sub-analysis of AVID and CIDS data has suggested that antiarrhythmic drug therapy may be as good as ICD therapy in patients with relatively well-preserved ventricular function, this result remains to be confirmed prospectively (4), and ICD therapy remains the most efficacious therapy in the secondary prevention of sudden death (SD). However, because only a small percentage of patients who suffer a cardiac arrest in the U.S. each year survive to benefit from ICD therapy as secondary prevention, the use of the ICD for the primary prevention of SD has received increasing attention.

Prior studies. Four prospective studies have been completed in which the use of the ICD in the primary prevention of SD was evaluated. The final results of three of these studies have been published in manuscript form. In the CABG (Coronary Artery Bypass Graft) patch study (5), epicardial ICDs were not found to be a useful adjunct to bypass surgery. However, given the selected nature of the patient population and the changes in ICD technology, these results do not have a major impact on clinical practice today. The Multicenter Automatic Defibrillator Implantation Trial (6) and Multicenter Unsustained Tachycardia Trial (7) studies evaluated use of the ICD in the primary prevention of SD in patients with ischemic heart disease, left ventricular dysfunction and inducible sustained ventricular tachycardia. In both these studies, a dramatic survival benefit of the ICD was noted, and the Food and Drug Administration has approved the ICD for this indication.

The AMIOVIRT study, which has been reported only in preliminary form, was a partially randomized, partially uncontrolled observational study of patients with non-ischemic cardiomyopathy at risk for SD (8). In this study, amiodarone and the ICD were equally effective or ineffective at preventing death (no control group was used), but the small size of the study limited its power to detect moderate beneficial effects of the ICD.

The pathophysiology and incidence of SD in patients with ischemic and non-ischemic cardiomyopathy may differ somewhat. Because therapy for coronary artery disease is widely variable among different trials and has changed drastically over the past decade, differences in survival depending on the type of underlying heart disease are somewhat difficult to evaluate with certainty. Most heart failure trials have not been adequately powered to detect differences in survival between patients with different kinds of ischemic and non-ischemic cardiomyopathy. Studies using intra-operative mapping suggest that, whereas ventricular tachycardia in patients with coronary disease is often reentrant, the initiation of tachyarrhythmias in patients with non-ischemic cardiomyopathy is almost invariably focal.

These studies suggest that the mechanism of SD and predictors of survival may differ in patients with coronary artery disease and those with non-ischemic cardiomyopathy, suggesting that clinical data on each type of structural heart disease are needed.

New findings. Thus, the results of the study by Grimm et al. (10) have potential importance. These investigators compared the incidence of appropriate shocks in 49 patients, in whom the ICD was implanted prophylactically, with 26 patients who presented with syncope and with 26 others who presented with sustained ventricular tachycardia or ventricular fibrillation. The incidence of appropriate shocks was similar in each of the groups, but using multivariate analysis, the presence of sustained ventricular tachycardia/ventricular fibrillation was a predictor of appropriate ICD shocks. Nonetheless, 37% of the patients who received the ICD for the primary prevention of SD (left ventricular ejection fraction <0.30 and non-ischemic cardiomyopathy) had appropriate ICD shocks.

Study limitations. Some limitations to the study should be noted. One difficulty in evaluating either retrospective or prospective studies on primary prevention of SD in heart failure is the changing survival due to advances in medical therapy. Improvements in the therapy of heart failure, such as angiotensin-converting enzyme (ACE) inhibitors and beta-blockers, have dramatically increased survival in patients with both ischemic and non-ischemic cardiomyopathy. Of particular relevance to the results of this study, a dramatic survival improvement in patients with heart failure treated with beta-blockers was noted in the late 1990s and

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was surprisingly large in several trials (30% to 35%) (11,12). Although the frequency of use of ACE inhibitors was admirable in the present study, only one-third of patients were treated with beta-blockers. Had a substantially higher percentage of patients been treated with beta-blockers, the results might have demonstrated a lower incidence of appropriate ICD shocks. The use of ICD shocks as a surrogate for improvements in clinical outcome even in devices with electrogram recall also has some limitations. Even with electrogram recall, some ICD shocks, especially those from single-chamber devices, may be misclassified. In addition, even if the ventricular tachy-arrhythmia is appropriately detected, some arrhythmias that occurred spontaneously may terminate before causing adverse clinical outcome.

The results in 26 patients in whom ICDs were implanted for syncope in nonischemic cardiomyopathy are also interesting but somewhat difficult to interpret. A substantial percentage of patients presenting with syncope had appropriate ICD discharges. However, the incidence was not different from the incidence in patients in whom the ICDs were implanted for the primary prevention of SD. The ejection fraction in patients with syncope was somewhat higher than in those in whom the ICD was implanted for primary prevention, but the number of patients with syncope in whom the ejection fraction was not <0.3 was not reported and is not likely to be large enough for any independent conclusions to be drawn. Thus, whether syncope alone should represent an incremental indication for ICD therapy is not clear from the present study.

Despite these limitations, the present report represents a large series of patients with non-ischemic cardiomyopathy who underwent ICD implantation for the primary prevention of SD. Although background medical therapy and the retrospective nature of this study mitigate against drawing sweeping conclusions, the results do suggest that further research on ICD therapy for the primary prevention of SD in patients with non-ischemic cardiomyopathy is needed. Two currently ongoing trials that have completed or nearly completed enrollment—the SCD-Heft Trial and the DEFINITE Trials (13)—should help define whether the ICD should have a role in the primary prevention of SD in patients with non-ischemic cardiomyopathy, as it currently does in patients with ischemic heart disease.

It should also be noted that prophylactic implantation of an ICD is not the only or even perhaps the most cost-effective therapy that should be directed at the primary prevention of SD. Therapy to prevent structural heart disease, an improved understanding of which neurohumoral factors contribute to the risk of SD in heart failure, improvements in CPR, bi-ventricular pacing, and more widespread use of the automatic external defibrillator are all likely to have a role—along with the ICD—in preventing SD.

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REFERENCES