Commentary

Debate: Do all patients with heart failure require automatic implantable defibrillators for the prevention of sudden death?

Sidney Goldstein

Henry Ford Hospital, Detroit, Michigan, and Case-Western Reserve University, Cleveland, Ohio, USA

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Abstract

Recent clinical trials indicate that approximately two-thirds of patients in New York Heart Association (NYHA) class II and III, who comprise almost 90% of patients with heart failure, die suddenly. Patients in NYHA class IV usually die of progressive heart failure. Implantation of implantable cardioverters defibrillators (ICDs) in this population would represent a huge logistic problem and economic expense. Clinical trials have recently demonstrated that β-blocker therapy with carvedilol, bisoprolol, and toprol XL decrease the sudden death rate by almost 50%, in addition to impacting significantly on death due to worsening heart failure. This medical approach is beneficial to all patients, and should be our major therapy. However, it is reasonable to attempt to identify that subpopulations of heart failure patients who could benefit from an ICD.

Keywords: β-blockers, heart failure, sudden death

Sudden death has been recognized as an important public health problem for over four centuries. In the 18th century, Pope Clement XI became concerned with the increase in occurrence of sudden death in Rome, and charged his papal physician Geofredo Lancisi to investigate its cause to no avail. Through the centuries the instantaneous nature of death has provided both a scientific and spiritual challenge to investigators to understand its mechanism. Despite the interest and intense investigation, neither Lancisi nor subsequent investigators have advanced our understanding of either the physiologic triggers of the event, or the nature of the event itself. There have been numerous electrocardiographic recordings of the event, but they have provided little insight into its mechanism. Cardiac arrest is largely expressed as ventricular fibrillation, but in approximately 20% of patients the event is due to asystole.

With the development of emergency medical care systems, relatively large populations of resuscitated cardiac arrest became available for both retrospective and prospective study. These studies indicate that cardiac arrest usually occurs in individuals who are known to have cardiovascular disease and who have left ventricular dysfunction [1]. Although sudden death can occur as the first expression of coronary heart disease, and usually as an acute myocardial infarction, even in these individuals prior

ACE = angiotensin-converting enzyme; ICD = implantable cardioverter–defibrillator; NYHA = New York Heart Association.

evidence of left ventricular damage or dysfunction is present. In addition, many individuals with nonischemic left ventricular dysfunction also experience sudden cardiac arrest. Investigators have used animal models and single-cell preparations in an attempt to understand the mechanism of ventricular fibrillation in order to prevent its occurrence. All of these attempts have been frustrated by the instantaneous and transient nature of the physiologic phenomena that precipitate cardiac arrest.

For a large part of the past half century, a great deal of research was focused on the suppression of ambient ventricular beats as a surrogate marker of the efficacy of antiarrhythmic drugs. The number of pharmacologic blind alleys that were entered are too numerous to recount, but it is clear that no agent directed at the suppression of ventricular premature beats has been found to be either safe or effective. The most recent investigations with amiodarone carried out in Europe [2] and Canada [3] failed to demonstrate any convincing evidence for its use for the prevention of sudden death, although the concomitant use of β-blockers with amiodarone appeared to offer some advantage.

With unusual prescience and technologic skill, Mirowski realized that antiarrhythmic therapy was a blind alley and began the development of the automatic internal defibrillator almost 40 years ago, and reported its first successful use in humans in 1980 [4]. That device is refined to such a degree that it is now easily implantable; it is small in size, but still large in cost. Its proven efficacy has spawned a large industry of both physicians and biotech companies that are directed at the expanded clinical use of the device.

Although the American Heart Association and the American College of Cardiology have reported implantation guidelines [5], common clinical practice has led to a significant deviation from those guidelines. The ease of implantation and the fear of recurrent sudden death have encouraged both the patient and physician to 'creep-up' on the guidelines. There is little argument that implantation of the ICD in patients with recurrent ventricular fibrillation or symptomatic ventricular tachyarrhythmias in the absence of acute myocardial infarction or ischemia is beneficial [6]. Even in this regard, however, the definition has been vague and has provided a window through which any syncopal episode, with little more than the presence of complex ventricular ectopy, has become fair game for the implantation of the ICD in patients with left ventricular dysfunction. Many of the patients who receive an ICD would have been better been treated with revascularization or β-blocker therapy. It is essential to understand this practice reality as we embark on the following discussion.

Recently, patients with heart failure have become a potential target population for implantation of an ICD. It is estimated that there are almost 5 million individuals with heart failure in the USA. Initially, the device was considered as a bridge to transplantation, because the mortality rate, often sudden death, in patients waiting for a donor heart was high. It soon became clear, however, that most of the patients who were dying on the transplant waiting list were dying of rhythm disturbances as a complication of worsening heart failure [7]. In these patients, use of an ICD had little benefit. As electrophysiologists became aware of the natural history of heart failure, they realized that sudden death was actually a greater problem in patients with NYHA class II and III than in those with advanced heart failure. Recent clinical trials have emphasized that sudden death represents almost two-thirds of the mortality in mild-to-moderate heart failure [8]. Heart failure therapy for most of the past decade has been based primarily on angiotensin-converting enzyme (ACE) inhibitors, which had little effect on arrhythmic death.

The striking decrease in sudden death in the recent β-blocker trials [8–10] has provided, for the first time, a pharmacologic approach to sudden death. These observations could have been assumed from studies in post-myocardial infarction patients with congestive heart failure [11], in whom propanolol was shown to have a profound effect on sudden death. The recent trials have demonstrated an decrease in total mortality in addition to a decrease in sudden death by 40–50%, without any adverse effects and excellent tolerance. Therapy with β-blockers has provided an entirely new approach to both the treatment of heart failure and the prevention of sudden death. The reduction in sudden death mortality was observed across a broad spectrum of subgroups studied in the Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure (MERIT-HF) [8], the largest β-blocker mortality trial, regardless of ejection fraction or heart failure etiology. Not only do these drugs decrease the incidence of sudden death, but they also have an important effect on total cardiovascular mortality and death due to worsening heart failure [8]. Treatment with carvedilol, bisoprolol and metoprolol in the three major randomized clinical trials [8–10] decreased the total mortality by approximately 35% and sudden death by 45%. More recently, patients in NYHA class III–IV who were treated with spironolactone experienced a 29% decrease in incidence of sudden death, in addition to a 31% decrease in cardiovascular deaths [12]. It is possible that a combination of these drugs could make an even larger impact on sudden death prevention.

The annual cardiovascular mortality rate in patients with heart failure treated with ACE inhibitors and β-blockers is now approximately 7% in NYHA class II and III patients. Although sudden death remains an important problem, to which a device could appropriately be applied, this solution would pertain to less than 5% of the heart failure patients treated with β-blockers. It can be estimated that,

if the ICD was implanted in 100 patients treated with ACE inhibitors and β-blockers, sudden death could be prevented in five individuals over the next year. This is presuming that the AID would prevent all of the deaths due to ventricular fibrillation or asystole and that none of the sudden deaths were due to acute progression of the primary disease. Because many of these individuals have ischemic heart disease, it can be presumed that some will experience further loss of ventricular function as a result of myocardial infarction. Asystole is also assumed to be successfully treated by the ICD, because most of the devices have pacing capability.

The estimated benefit that could be achieved by ICD is rather small and would be obtained at a considerable cost. This cost is significant in the face of the almost 5 million individuals in the USA with heart failure. Little has been said about the risk or side effects of the device when left in place for years or the discomfort of inappropriate discharge. It is clear, however, that ICD implantation and its safety have improved during the past few years.

The device that Mirowski [4] developed over 40 years ago has moved far beyond his vision at that time. The appropriate role for the ICD is still being explored. A number of major trials [13,14] are now underway to examine the benefit of these devices in heart failure patients. Although these trials fall short in their design, because they do not mandate β-blocker therapy, they will expand our understanding of the usefulness of ICD in heart failure. Perhaps a more appropriate research direction would be to try to identify those persons within the large population of heart failure patients who would benefit the most from implantation of an ICD. Unfortunately, the easiest answer to the question of who should have the device implanted is to implant it into everyone. This appears to be the most expedient if not efficient approach to the problem, and the one that appears to hold sway in today's clinical practice. I would submit that the benefit of the ICD must be judged in terms of both the socioeconomic and medical costs. In the interval period, it is clear that the addition of β-blocker therapy to the treatment of the broad spectrum of patients with heart failure has provided important protection from sudden death and death due to progressive heart failure. It is my view that the ICD will add little additional benefit to the treatment of patients with mild-to-moderate heart failure.

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Author's affiliations: Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, Michigan, and Case-Western Reserve University, Cleveland, Ohio, USA

Correspondence: Dr Sidney Goldstein, Henry Ford Hospital, Detroit, MI 48202, USA. Tel: +1 313 916 2727; fax: +1 313 916 8205; e-mail: sgoldst1@hfhs.org