Commentary

# Debate: Do all patients with heart failure require implantable defibrillators to prevent sudden death?

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Received: 9 October 2000
Accepted: 9 October 2000
Published: 11 October 2000

*Curr Control Trials Cardiovasc Med* 2000, **1**:92–94


(Print ISSN 1468-6708; Online 1468-6694)

## Introduction

This issue of *Current Controlled Trials in Cardiovascular Medicine* contains two diametrically opposite views of whether all patients with heart failure require an implanted cardioverter-defibrillator (ICD) to prevent sudden death. Hsia *et al* [1] propose targeting the general population with mild to moderate heart failure with 'empirical' ICD therapy. Goldstein [2] on the other hand argues that this would represent a huge logistic and economic expense and that it would therefore be necessary to firstly identify the heart failure subpopulation that could benefit from this.

Before analysing the essence of this debate, let me first point out areas of agreement. Both sets of authors agree that angiotensin-converting-enzyme inhibitors (ACEIs) have a major impact on the prognosis of heart failure. It is the achievement of randomised clinical trials (RCTs) athat there is agreement on this point. Until the results of the CONSENSUS trial [3] were published, there was disagreement on the role of ACEIs, particularly in severe heart failure, because of their potential to reduce renal function. In fact, the steering committee of CONSENSUS was stunned when it was told by the data monitoring committee to stop the trial because of the large mortality reduction conferred by enalapril. They thought that the trial had to be stopped because of an excess mortality in the enalapril group. Both sets of authors also agree on the beneficial effect of beta-blockers. Again this is the achievement of research. Until recently, prescribing a beta-blocker for heart failure was considered malpractice and a reason for firing the junior doctor who did so.

## The essence of the debate

Let us now consider what I believe is the essence of the debate between Goldstein [2] and Hsia *et al* [1]. The crucial point seems to be that these authors disagree on the amount of research that is required before one can recommend targeting a large group of loosely defined patients with a specific therapy, drug or otherwise. Implantation of a defibrillator is a particular type of antiarrhythmic therapy. As far as anti-arrhythmic therapy is concerned, progress through research has been less straightforward than for ACEIs and beta-blockers. Twenty years ago it would be hard to come home from a major cardiology meeting without having been exposed to the dogma about sudden death prevention that prevailed at the time. This dogma was based on two correct clinical observations: first, ventricular arrhythmia is a risk factor for sudden death in patients with heart disease; second, there are drugs that suppress arrhythmias. From this, it was concluded that patients with heart disease should be targeted with procedures to detect arrhythmias, followed by drug treatment if arrhythmias were observed. The proponents of the dogma had little evidence from RCTs to prove their point, and the evidence available at the time did not support it. In fact, the whole thinking was based on a misconception that has proved difficult to jettison throughout the history of medicine, namely that removing the risk factor must logically also remove the risk. Nonetheless, the industry jumped on to this bandwagon by providing the ambulatory ECG equipment and the drugs required, and by promoting their widespread application. It took a rethinking of the whole concept [4] and the CAST study [5,6] to prove that

ACEI = angiotensin converting enzyme inhibitor; ICD = implanted cardioverter-defibrillator; RCT = randomised clinical trial; VF = ventricular fibrillation.

the *practice* of arrhythmia detection and suppression with the drugs used at the time was in fact a pipe dream that was killing rather than saving patients. 'Practice' was put in italics to stress that the issue here is not just the efficacy of a single drug, but of a particular type of clinical practice as a whole.

Admittedly, the *practice* of implanting an automatic defibrillator is different from the *practice* that was tested by CAST. The ICD has undoubtedly a much sounder pathophysiologic basis than the administration of drugs such as encainide and flecainide, among others. As pointed out by both Goldstein [2] and Hsia *et al* [1], ICD therapy is also supported by evidence from RCTs. Nonetheless, the lesson learnt from the history of antiarrhythmic treatment must not be forgotten. Interestingly, the largest ICD trial performed thus far did not show improved survival. This trial compared the *policies* of ICD versus no ICD in patients with left-ventricular dysfunction and ECG abnormalities who were undergoing coronary artery bypass surgery [7]. Neither Goldstein nor Hsia *et al* mention this. The trials quoted by Hsia *et al* to support their view [1] are relatively small and used mostly amiodarone as control. This raises the complex issue of how effective the latter is in improving survival. Furthermore, cynics would argue that we would probably not have heard that much about these trials had the results been negative. ACEIs and beta-blockers are probably the best-researched drugs used in clinical practice today. With these compounds, large RCTs have been done in a broad spectrum of patients. In total, thousands of patients have been studied. Other than the influence of the economics of the industries involved, it is difficult to see why the widespread use of ICDs should be recommended on the basis of evidence that is much more limited than the evidence that supports the use of ACEIs and beta-blockers. This is particularly so because the currently available evidence supporting ICDs leaves a number of questions unanswered. Some of these were are also raised by Goldstein [2] and by Hsia *et al* [1]. Do ICDs confer an additional reduction of total mortality on low-risk heart failure patients who are optimally treated medically? No treatment is risk-free. While this applies also to drugs, the risks associated with ICD implantation may not be worth taking in low-risk patients. (Sheldon *et al* [8] provide evidence for this from the Canadian Implantable Defibrillator Study [9].) Should ICDs be limited to patients who do not tolerate a beta-blocker, or do they also confer additional benefit to patients who are already using a beta-blocker? In patients with very sick hearts, does cardioversion for VF – or pacing for asystole – restore autonomous pump function for any length of time? Does the aetiology of heart failure have any bearing on the usefulness of ICDs? Hsia *et al* [1] point to the possibility of combining an automatic defibrillator and biventricular pacing functions in one device. But how effective is biventricular pacing in heart failure in the first place? Finally, there is the question of cost-effectiveness. Procedures such as implantation of an automatic cardioverter-defibrillator are expensive. We forget too easily that the use of brand-name drugs for years on end is expensive too. It follows that the cost-effectiveness of ICDs must be carefully considered for specific subgroups of patients. Hsia *et al* make no attempt to address the cost-effectiveness issue.

## Conclusion

In conclusion, it seems too early to follow Hsia *et al* as far as the widespread empirical application of ICDs in heart failure is concerned. Goldstein does not stand alone in this regard [10]. Larger trials than those carried out thus far are needed before current recommendations for ICD use [11] can be relaxed. As in trials of bypass surgery, two policies should be compared: 'ICD now' versus the policy of using ICD only after resuscitable cardiac arrest. The primary end point should be total mortality and in the analysis 'crossover' should be ignored. All patients should receive optimal drug therapy. Appropriate subgroup analyses and multiattribute risk stratification such as those used by Sheldon *et al* [8] should be prespecified in the protocol, and detailed pharmaco-economic data should be collected. We shall have to wait and see whether the trials underway quoted by Goldstein [2] and by Hsia *et al* [1] have eventually followed this pattern when the results are published.

Debates such as the one between Goldstein and Hsia *et al* in this issue of *Current Controlled Trials in Cardiovascular Medicine* serve the important purpose of defining directions for research. In the mean time clinical practice should follow established recommendations until these have been adapted by evidence-based *communis opinio*. Here the following applies: don't vote for the opposition before it has come to power…

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