

ELECTROPHYSIOLOGY

Implantable cardioverter-defibrillators

Derek T Connelly
The Cardiothoracic Centre—Liverpool NHS Trust,
Liverpool, UK

Sudden cardiac death is a common problem, and increasing numbers of patients are surviving a first episode of a life threatening ventricular arrhythmia. In the absence of an acute myocardial infarction, patients who survive either ventricular fibrillation or sustained ventricular tachycardia have a high risk of further episodes, which may be fatal.¹ Until recently, class I and class III antiarrhythmic drugs have been the standard treatment for patients with malignant ventricular arrhythmias. Amiodarone² and sotalol³ have been shown to be superior to class I drugs, but despite using the best appropriate medical treatment, arrhythmia recurrence rates are still 40–50% at five years.

There is now growing evidence to support the wider use of implantable cardioverter-defibrillators (ICDs) as primary treatment in certain patients with serious ventricular arrhythmias. These devices were developed in the 1970s, with the first human implant in 1980.⁴ Original devices had a single therapy option of defibrillation only; the generator was implanted in the abdomen, and thoracotomy was required for electrode placement. With advances in technology the units have become smaller (current ICDs are little bigger than a pacemaker) and can be implanted pectorally. With improvements in sensing, the latest devices offer graded therapeutic responses to a sensed ventricular arrhythmia. Antitachycardia pacing, low energy synchronised cardioversion, and high energy defibrillation shocks can be given via a single transvenous lead.

Implant procedure

Implantation of an ICD is now technically very straightforward, and only a little more complicated than pacemaker implantation. As with pacemaker implantation, strict attention to asepsis is necessary, and prophylactic antibiotics are generally used. In the past, ICD implants were performed under general anaesthesia; however, many centres now implant these devices using a combination of local anaesthesia and intravenous sedation. Usually an incision 5–8 cm in length is made in the left infraclavicular region, and a pocket is fashioned for the generator either subcutaneously or deep to the pectoralis major muscle. A ventricular lead (for sensing, pacing, and defibrillation) is inserted via the cephalic or subclavian vein, and if appropriate an atrial lead is also inserted. Standard tests of pacing and sensing are performed, as for pacemaker implantation.

It is then important to induce ventricular fibrillation, in order to test that the device can detect the arrhythmia and defibrillate effectively with an adequate safety margin. Ventricular fibrillation is usually induced either by delivering a small shock (via the device) synchronous with the T wave, or less commonly by alternating current at 50 Hz or by rapid ventricular pacing. It is customary to test efficacy of defibrillation at an output energy at least 10 J less than the maximum stored energy of the device (that is—if the device can deliver a maximum of 30 J, defibrillation testing is performed at 20 J or less). If defibrillation is successful at this energy level on two consecutive occasions, the implant is completed; if not, an additional intravascular or subcutaneous lead may be required.

Programming and follow up

Before hospital discharge, the pacing and sensing functions of the device are tested, and chest radiographs (posteroanterior and lateral) are obtained (fig 1). The device is programmed to detect and treat episodes of ventricular tachycardia and fibrillation, the precise programmed values being governed by the patient's clinical history, maximum sinus rate, and rates of any documented ventricular (and supraventricular) arrhythmias. Separate “zones” can be programmed for detection of ventricular fibrillation (for example, rate > 200–220/min) and ventricular tachycardia, and some devices allow for two separate ventricular tachycardia detection zones. Additional discriminatory features, such as sudden onset, beat-to-beat variability, QRS width and/or morphology, and (if available) atrial rate can also be programmed in order to help discriminate between atrial and ventricular arrhythmias. Even if the patient only has a history of ventricular fibrillation, it is customary to program the device for detection and treatment of ventricular tachycardia, as many patients will present with new onset ventricular tachycardia after the implant. Ventricular fibrillation is usually treated with shocks at the maximum energy of the device (fig 2), but the ICD can be programmed to treat ventricular tachycardia by a variety of modalities of



Figure 1. Posteroanterior chest x ray showing positioning of ICD generator and lead.

Correspondence to:
Dr Derek T Connelly,
The Cardiothoracic
Centre—Liverpool
NHS Trust, Thomas
Drive, Liverpool
L14 3PE, UK
connelly@liv.ac.uk

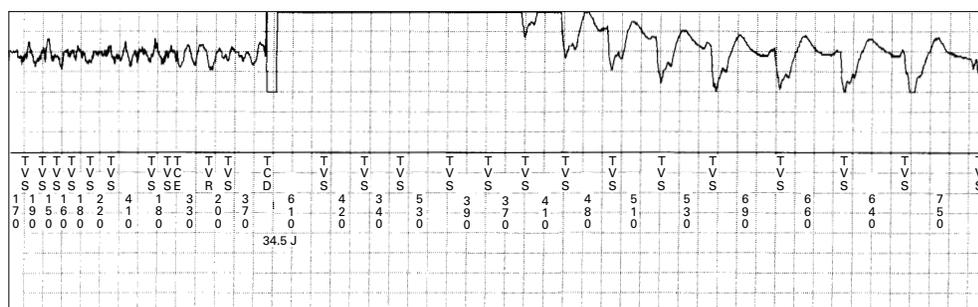


Figure 2. Stored intracardiac electrograms from an ICD which treated a spontaneous episode of ventricular fibrillation with a 34 J shock.

antitachycardia pacing (fig 3) or if necessary by low energy cardioversion shocks. Some centres routinely test the efficacy of antitachycardia pacing modalities at a post-implant electrophysiological study. However, many implanters now consider this unnecessary, since spontaneous episodes of ventricular tachycardia are often easier to terminate than tachycardias induced in the laboratory, and a standardised antitachycardia pacing algorithm appears to be effective in the majority of patients.

Most patients can be discharged home 24–48 hours after implantation. Patients are usually followed up 4–6 weeks post-implant, then at 3–6 monthly intervals. At each follow up visit, the device is interrogated, standard pacing and sensing tests are performed, and the device memory is interrogated. Details of any stored arrhythmic events are downloaded and printed, and correlated with the patient's symptoms. If necessary, appropriate programming changes (either in arrhythmia detection or treatment) can be made, or alterations in the patient's medication can be instigated.

Complications of ICDs

ICDs are much simpler to implant now than they were five years ago, and the complication rate is diminishing. Nevertheless, all the complications of cardiac pacing (for example, infection, erosion, conductor/insulation fracture, over- and undersensing) can occur with ICDs, and many of these complications may

require operative revision or even replacement of the system, which can be a major undertaking. Additional problems may occur, the most common being inappropriate shocks, usually for atrial fibrillation or (less commonly) sinus tachycardia. Such complications can usually be treated or circumvented either by additional antiarrhythmic medication or by further programming of the tachycardia detection parameters. Rarely, when rapid uncontrolled atrial fibrillation leads to inappropriate shocks (or when atrial fibrillation induces ventricular tachycardia) it may be necessary to perform radiofrequency ablation of atrioventricular conduction and pace the patient permanently (either via the ICD or using a separate permanent pacemaker).

Clinical trials of ICDs

ICDs are effective at treating ventricular arrhythmias but until recently there has not been clear evidence that they reduce mortality. Recently, the results of three large randomised controlled trials of ICD treatment have been published.^{3–7} Their results are summarised in table 1.

A meta-analysis of these three trials has been published recently.⁸ In the three studies, 934 patients were treated with an ICD and 932 with amiodarone. In over 2000 patient years of follow up in each group, there were 200 deaths in patients treated with an ICD and 255 deaths in patients treated with amiodarone. This

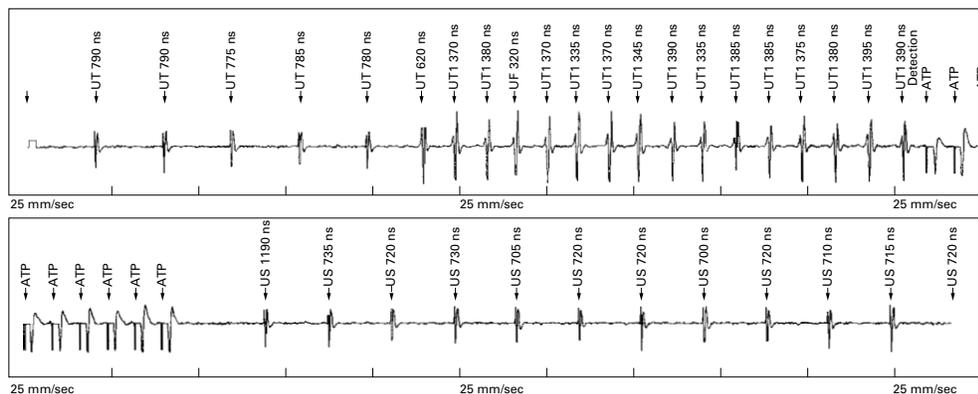


Figure 3. Stored intracardiac electrograms from an ICD showing spontaneous onset of ventricular tachycardia with a cycle length of 380 ms (rate 158/min) treated by a burst of antitachycardia pacing (ATP), which restored sinus rhythm.

Table 1 Trials of ICDs in patients with ventricular tachycardia/ventricular fibrillation

	Number in trial	Control treatment	Mean follow up	ICD mortality	Control mortality	p Value
AVID ⁵	1016	Amiodarone or sotalol	18 months	25% at 3 years	36% at 3 years	< 0.02
CIDS ⁶	659	Amiodarone	36 months	8.3% per year	10.2% per year	0.142
CASH ⁷	288	Amiodarone or metoprolol	57 months	36%	44%	0.081

equates to a 28% reduction in mortality in the ICD group (95% confidence intervals (CI) 60% to 87%, $p = 0.0006$). Importantly, the meta-analysis showed that patients who presented with ventricular tachycardia had as much to gain from a defibrillator as those whose index arrhythmia was ventricular fibrillation, and patients in all functional classes appeared to benefit. There did not appear to be any benefit from epicardial ICDs (mainly implanted before 1991). Patients with left ventricular ejection fraction of 35% or below had more to gain (34% reduction in mortality compared to amiodarone) than those with preserved ventricular function (no significant difference in mortality compared to amiodarone).

Several studies have also assessed the efficacy of defibrillator treatment for “primary prevention” in patients at high risk for sudden death who have not yet had a clinical event. The MADIT study⁹ studied 196 high risk survivors of myocardial infarction with impaired left ventricular function and non-sustained ventricular tachycardia on ECG monitoring. Patients recruited to this trial had to have an inducible sustained ventricular arrhythmia at electrophysiological study which could not be suppressed by an antiarrhythmic drug. These patients were randomly allocated to treatment with an ICD or an antiarrhythmic drug (amiodarone in 80% of the cases). The trial was terminated in 1996 after demonstrating a 54% reduction in mortality with defibrillator therapy compared to antiarrhythmic drug treatment.

More recently, the MUSTT study¹⁰ recruited patients who had prior myocardial infarction, impaired left ventricular function, spontaneous episodes of non-sustained ventricular tachycardia, and inducible sustained ventricular tachycardia at electrophysiological study. Patients were randomly allocated to a “control” group, who received no specific antiarrhythmic treatment (353 patients), and an electrophysiologically guided treatment group, who received antiarrhythmic drugs if the tachycardia could be suppressed by drugs (158 patients), or an ICD if drugs were ineffective at electrophysiological study (161 patients). The five year mortality in this study was 48% in those not treated with antiarrhythmic medication; patients on antiarrhythmic drugs fared marginally worse, but those treated with an implantable defibrillator had a five year mortality rate of 24% ($p < 0.001$). These results from the MUSTT study support the data from the MADIT study, and show that patients with prior myocardial infarction, impaired left ventricular function, and non-sustained ventricular tachycardia can be stratified by electrophysiological study. Patients

with inducible sustained ventricular arrhythmias are highly likely to benefit from prophylactic ICD implantation, even though they have not yet had a major spontaneous arrhythmic event.

The CABG Patch trial¹¹ was a trial of prophylactic ICD treatment in patients undergoing surgical revascularisation. Patients recruited to the CABG Patch trial had ejection fractions of less than 36% and an abnormal signal averaged ECG, but there was no necessity for either spontaneous or inducible ventricular arrhythmias. In this study of 900 patients, there was no benefit for prophylactic ICD implantation.

There are several other ongoing trials which are comparing the efficacy of ICD therapy with either no specific antiarrhythmic treatment or drugs such as amiodarone in high risk patients with heart failure or with poor left ventricular function postmyocardial infarction (see box on next page).

Cost effectiveness of ICDs

There is no doubt that the ICD is an expensive piece of medical technology, the total cost of the hardware for an implant approaching £20 000 (nearly US\$30 000). Although the cost has not come down in recent years, the battery life has been extended considerably: devices implanted 10 years ago had a battery life of only two years, whereas modern devices are expected to last seven to nine years.

Several studies in the early 1990s attempted to estimate the cost of implantable defibrillators per life year saved. These studies were conducted before the publication of the major trials documenting the efficacy of the ICD in reducing mortality, and therefore involved estimates of the likely improvement in mortality and the likely lifetime costs of treatment by antiarrhythmic drugs or by ICD. More recently, data based on true costs and actual longevity have begun to emerge from the randomised trials. The cost analysis of the MADIT study¹² showed that the average survival for the group treated with a defibrillator over four years was 3.66 years, compared with 2.80 years for conventionally treated patients. The accumulated net costs in the ICD and conventional groups were \$97 560 and \$75 980 respectively. This equates to a cost of \$27 000 (£18 500) per life year saved for the ICD group. If all the ICDs were modern transvenous systems, the costs would be lower at \$23 000 (£16 000) per life year saved. This figure is not excessive, and is comparable with the cost effectiveness of several other accepted medical procedures.

Ongoing trials of ICD versus medical treatment

- SCD-HeFT
 - New York Heart Association functional class II/III, left ventricular ejection fraction < 35%
 - randomised to ICD, amiodarone, or control
 - primary end point is total mortality
 - secondary end points: quality of life, cost effectiveness, incidence of ventricular tachycardia/ventricular fibrillation
- MADIT-2
 - patients > 1 month post-myocardial infarction, left ventricular ejection fraction < 30%
 - randomised to ICD or control
 - post-randomisation: non-invasive markers, electrophysiological study
 - primary end point is total mortality
 - secondary end points: quality of life, cost effectiveness
- DINAMIT
 - patients 6–40 days post-myocardial infarction, left ventricular ejection fraction < 35%
 - decreased heart rate variability or mean 24 hour heart rate > 80/min
 - randomised to ICD or control
 - primary end point is total mortality

Similar cost effectiveness analyses have been performed on the data from the AVID and CIDS¹³ studies, and the estimated costs per life year saved in those analysis were considerably higher. The AVID trial was stopped prematurely after a mean follow up period of only 18 months (compared to 27 months in the MADIT study). Any studies such as these which are terminated early will tend to overestimate the costs in the group treated with defibrillators (which are paid for at implantation) compared with those treated with drugs (the costs of which continue to accumulate throughout the follow up period). Further data on cost effectiveness is likely to be produced from the meta-analysis of the AVID, CASH, and CIDS studies.

Quality of life in patients with ICDs

An ICD is not a cure. Patients are still considered to be at risk of an arrhythmia, which might cause syncope or cardiac arrest, if only for a few seconds before treatment is delivered. Inevitably many patients face significant lifestyle restrictions, and a minority of patients have severe psychological problems. Although the implant procedure is similar to pacemaker implantation, follow up of patients with ICDs tends to be more complex. Many

of the patients have coronary artery disease and poor left ventricular function, and are likely to require ongoing medical treatment for heart failure, ischaemia, and hyperlipidaemia.

Although some patients may develop an adverse psychological reaction to ICD implantation, it is important to be aware that these patients often improve with the passage of time as they become accustomed to having the device and adapt to their physical limitations. There is no doubt, however, that many patients tolerate defibrillation shocks very poorly, particularly if they experience multiple shocks (appropriate or inappropriate). For this reason, antiarrhythmic drugs may have a role in reducing the incidence of both ventricular and supraventricular arrhythmias in patients with ICDs. In one recent study,¹⁴ 302 patients were randomised to treatment with sotalol (160–320 mg/day) or placebo. Sotalol treatment reduced the mean (SD) frequency of shocks (both appropriate and inappropriate) compared to placebo (1.43 (3.53) shocks per year in the sotalol group *v* 3.89 (10.65) shocks per year on placebo).

The issue of fitness to drive in patients with ICDs is a contentious one. Up until five years ago, patients with ICDs in the UK faced a lifetime ban from driving. Since then the regulations in the UK have been gradually relaxed. Currently, ICD recipients may be allowed to drive provided that the device has been implanted for at least six months and has not delivered shock therapy or symptomatic antitachycardia pacing therapy for six months (except during formal clinical testing), and if previous discharges have not been accompanied by incapacity. Patients must stop driving for one month if the device (lead or generator) is revised, or if any change is made in antiarrhythmic treatment. Patients who have an ICD implanted for “primary prevention” need only refrain from driving for one month, unless they subsequently receive shocks from the device. Licences are subject to annual review. Patients with ICDs are permanently disqualified from driving lorries and buses. These recommendations are similar to the current North American¹⁵ and European guidelines on driving for patients with arrhythmias.

ICD indications

In the UK, the National Institute for Clinical Excellence (NICE) has recently published guidance on the use of ICDs.¹⁶ The institute has stated that ICDs should be routinely considered for both primary and secondary prevention of life threatening arrhythmias. Their guidance is summarised in table 2. These indications are similar to those published by the American College of Cardiology and the American Heart Association,¹⁷ and by the North American Society of Pacing and Electrophysiology.¹⁸

Table 2 Indications for ICD implantation¹⁶⁻¹⁸**“Secondary prevention”**

For patients who present, in the absence of a treatable cause, with:

- Cardiac arrest caused by either VT or VF
- Spontaneous sustained VT causing syncope or significant haemodynamic compromise
- Sustained VT without syncope/cardiac arrest, and who have an associated reduction in ejection fraction (< 35%) but are no worse than NYHA functional class III heart failure

“Primary prevention”

For patients with:

- A history of previous myocardial infarction and *all* of the following:
 - non-sustained VT on Holter monitoring
 - inducible VT on electrophysiological testing
 - left ventricular dysfunction with an ejection fraction < 35% and no worse than NYHA functional class III heart failure
- A familial cardiac condition with a high risk of sudden death, including:
 - long QT syndrome
 - hypertrophic cardiomyopathy
 - Brugada syndrome
 - arrhythmogenic right ventricular dysplasia
 - following repair of tetralogy of Fallot

Patient groups in whom an ICD is usually *not* indicated

- Syncope of undetermined aetiology, VT/VF not inducible
- Incessant VT
- VT amenable to surgical or catheter ablation
- VT/VF due to transient or reversible cause
- Significant psychiatric illness that might be aggravated by device implant or may preclude systematic follow up
- Terminal illness with life expectancy < 6 months
- Patients with impaired left ventricular function undergoing coronary artery bypass graft surgery, without spontaneous or inducible VT
- Patients with NYHA functional class IV heart failure who are not candidates for heart transplantation

NYHA, New York Heart Association; VF, ventricular fibrillation; VT, ventricular tachycardia.

The NICE guidance in the UK also recommends that protocols for ICD implantation be developed, to include:

- early referral of appropriate patients;
- rapid decision making and implantation;
- conscious sedation rather than general anaesthesia;
- rehabilitation, including psychological preparation for living with an ICD;
- early discharge;
- efficient and comprehensive follow up;
- screening of high risk survivors of myocardial infarction.

Conclusions

The ICD implant rate in the UK is approximately 17 devices per million population per year. Although the rate has doubled over the past three years, the implant rate in the UK is still little more than half that for western Europe, and less than 10% of the rate in the USA. It is now clear from several randomised controlled trials that, in selected high risk patients, ICDs are more effective than anti-arrhythmic drugs in prolonging life. When faced with a patient who has had sustained ventricular tachycardia or successful resuscitation from ventricular fibrillation, physicians should now consider an ICD as first line treatment.¹⁶⁻¹⁸ Furthermore, when we are faced with post-myocardial infarction patients who have significant impairment of left ventricular function, it is now our duty to perform ambulatory ECG monitoring in order to detect those

Trial acronyms

AVID Antiarrhythmics Versus Implantable Defibrillators
CASH Cardiac Arrest Study Hamburg
CASCADE Cardiac Arrest in Seattle: Conventional versus Amiodarone Drug Evaluation
CIDS Canadian Implantable Defibrillator Study
DINAMIT Defibrillator In Acute Myocardial Infarction Trial
MADIT Multicenter Automatic Defibrillator Implantation Trial
MUSTT Multicenter Unsustained Tachycardia Trial
SCD-HeFT Sudden Cardiac Death in Heart Failure Trial

patients with asymptomatic non-sustained ventricular tachycardia. Such patients should be referred for electrophysiological study, as about 30% of them will have inducible sustained ventricular arrhythmias and will be likely to benefit from prophylactic ICD implantation.

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