The Utilization of the Implantable Defibrillator — a European Enigma

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Introduction

In the 20 years since Michel Mirowski and co-workers implanted an ICD into their first patient[1], the implantable cardioverter defibrillator (ICD) has become recognized as the therapy of first choice for managing patients at high risk of sudden cardiac death from ventricular tachyarrhythmias. Multiple clinical series and recently completed prospective, randomized trials have shown that ICDs are irrefutably superior to antiarrhythmic drugs in reducing sudden death, and improving overall survival[2–6]. Furthermore, major technological advances have made the implant and follow-up of ICDs nearly as simple and straightforward as with pacemakers. Figure 1 shows the rapid increase in numbers of patients receiving ICDs, as well as some of the major technological milestones and important studies, which have contributed to this growth.

But, when one looks deeper into the impressive increase in ICD use, it becomes evident that it is largely U.S.A. driven (Fig. 2). It is this polarized

Figure 1  Growth in numbers of patients receiving ICDs, from 1980 to the present, in parallel with major milestones in ICD technology and significant ICD and antiarrhythmic drug studies. (Reprinted, with permission, from Nisam S. Can implantable defibrillators reduce non-arrhythmic mortality? J Intr Cardiac Electrophysiol 1998; 2: 371–5.)

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adoption of ICD therapy — reflecting vastly different implant rates in Europe and in the U.S.A. — which is the focus of our paper. We will show below that epidemiological factors cannot account for this approximate five fold difference in ICD implantation rates. This point is underscored by the fact that the rates of adoption of related cardiovascular device interventions — as will also be shown hereafter — do not show such huge variations, as is seen with the ICD. So, it would appear that the disparity in the use of this remarkable therapy is truly a ‘European enigma’, a phenomenon unique in medicine, which warrants at the very least a critical look at possible causes, and speculation on what the future may bring.

Epidemiology

Figure 3 depicts the rates for cardiovascular deaths in 1995 in the major European countries, and in the U.S.A. There are some notable differences, varying from lows of 2·5 and 3·1 cardiovascular deaths per 1000 population in France and Spain to highs of 4·0 in the U.K. and 4·3 in Germany, respectively. What is interesting is that the mean rates for cardiovascular deaths were exactly the same: 3·6 in Europe and in the U.S.A.!

Device interventions

Approximately four patients out of five suffering from ventricular tachyarrhythmias, and therefore potential candidates for ICDs, have coronary artery disease as their underlying cause. Thus, ICD use should be correlated with interventions such as PTCA*, pacemaker implantation, and heart valve surgery. A pacemaker, although not used primarily for disease related to underlying coronary disease, is a very similar therapeutic device with which ICD utilization can be compared. Figure 4 compares the mean rates for each of these interventions in Europe and in the U.S.A. during 1999. The utilization rate for PTCA, pacemakers and heart valves (per million population) are seen to be approximately 50% of those for the U.S.A., but for ICDs, Europe’s rate is only one-fifth that in the U.S.A. A poignant example comes from comparing pacemaker and ICD use in the two continents. Pacemaker use in Europe lags the U.S.A. rate by a little over 40%, whereas usage

*We have taken data for PTCA use, rather than coronary stenting, simply because the former is a ‘mature’ therapy with fairly stable usage rates, whereas rates of stent use are still undergoing great yearly and regional fluctuations.
of ICDs — so similar in implant technique and technology — is 80% lower in Europe vis-à-vis the U.S.A.

**Discussion**

It is not unusual for new therapies, in particular those requiring ‘high-tech’ equipment and expertise, to take some time to become fully implemented in different geographies. However, in the field of ICD therapy, most of the new technologies reached Europe earlier than the U.S.A. due simply to constraints from the Food and Drug Administration. An important example is the use of endocardial defibrillator leads, used almost exclusively in European countries from about 1991, whereas full FDA commercial approval only came in 1994. In more recent years, the lag time between U.S.A. and European availability of newer ICD technologies and models has been shortened to only a few months.

Thought leaders in Europe have long been aware of — and have actively used — ICDs from nearly the...
beginning (the first European implants were undertaken by Coumel and co-workers in 1982, followed by Breithardt, Klein and others in 1984). There is no evident difference favouring the U.S.A. in terms of publications and clinical trials on new ICD models or features. In fact, the two earliest randomized, prospective trials of the use of an ICD vs antiarrhythmic drug therapy for secondary prevention of (sudden) mortality began in Germany and Holland\(^7,8\).

**ICD Guidelines**

One area in which the U.S.A. has been far more pro-active with regard to ICDs is in terms of regularly updating the official guidelines (see Table 1)\(^9\). Here it is important to emphasize that such guidelines, by definition, emanate from general clinical consensus, not vice-versa. Of course, a natural consequence of clinicians reaching such agreements is the increased application of these guidelines by other physicians and institutions. Perhaps just as importantly, these guidelines serve to provide clinicians with much stronger arguments to deal with their respective health reimbursement authorities. Applying this process to the ICD situation, our American colleagues acknowledge the importance of the guidelines (including FDA approval) in their dealings with the Health Care Financing Agency (HCFA) and third party private insurance organizations such as Blue Cross or Blue Shield. With each new set of guidelines as listed in the table, physicians in the U.S.A. were able to offer ICD therapy to larger or new groups of at-risk patients. The most recent revision of these guidelines, published by the AHA/ACC and endorsed by NASPE, was published in April 1999\(^10\). In contrast, the most recent official European guidelines were written 1991\(^11\) and have not been revised until now. In the absence of updated guidelines incorporating the considerable body of new science, physicians in Europe have had to negotiate on their own with their hospital administrations and/or health authorities, an obviously much weaker bargaining position than their U.S.A. colleagues who could avail themselves of published medical society support.

### Table 1 Evolution in guidelines for ICD implantation

<table>
<thead>
<tr>
<th>Year</th>
<th>Indications for ICD implantation</th>
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<tbody>
<tr>
<td>1980</td>
<td>Resuscitated from at least two episodes of cardiac arrest, neither associated with acute MI, and one of which had to occur despite AARx(^3)</td>
</tr>
<tr>
<td>1982</td>
<td>One or more episodes of VF or haemodynamically unstable VT, not associated with acute MI (or other transient reversible causes), but with evidence — from EP testing or Holter monitoring — of incomplete protection by AARx</td>
</tr>
<tr>
<td>1986</td>
<td>Same, except relaxation of the requirement for initial EP inducibility and non-suppressibility following AARx</td>
</tr>
</tbody>
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| 1991 | A. Class I Indications (General consensus that ICD indicated):  
1. \(\geq 1\) episodes of spontaneous sustained VT/VF in patients in whom EP testing and/or Holter monitoring could not be used to accurately predict efficacy of other therapies  
2. Recurrent spontaneous sustained VT/VF, despite EP — or Holter monitoring — guided AARx  
3. Spontaneous sustained VT/VF in case of a patient’s non-compliance with — or intolerance of — AARx  
4. Patients with spontaneous sustained VT/VF, who remain persistently inducible at EP study, while on ‘best’ AARx or following VT surgery or catheter ablation  
B. Class II Indication (ICD an acceptable option, but no consensus):  
1. Cardiac arrest due to VT or VF, not due to a transient or reversible cause  
2. Spontaneous sustained VT  
3. Syncope of undetermined origin with clinically relevant, haemodynamically significant sustained VT or VF induced at EP study when drug therapy is ineffective, not tolerated, or not preferred  
4. Non-sustained VT with coronary disease, prior MI, LV dysfunction, and inducible VF or sustained VT at EP study, that is not suppressible by a Class I AARx |
| 1998 | A. Class I Indications\(^10\) (General consensus that ICD indicated):  
1. Cardiac arrest due to VT or VF, not due to a transient or reversible cause  
2. Spontaneous sustained VT  
3. Syncope of undetermined origin with clinically relevant, haemodynamically significant sustained VT or VF induced at EP study when drug therapy is ineffective, not tolerated, or not preferred  
4. Non-sustained VT with coronary disease, prior MI, LV dysfunction, and inducible VF or sustained VT at EP study, that is not suppressible by a Class I AARx  
B. Class IIb Indications (ICD an acceptable option, but no consensus):  
1. Cardiac arrest presumed due to VF when EP testing is precluded by other medical conditions  
2. Severe symptoms attributable to sustained VT/VF while awaiting cardiac transplantation  
3. Familial or inherited conditions carrying a high risk for life-threatening VT/VF, such as long QT syndrome or hypertrophic cardiomyopathy  
4. Non-sustained VT with coronary artery disease, prior MI, and LV dysfunction, and inducible sustained VT/VF at EP study  
5. Recurrent syncope of unknown aetiology in the presence of ventricular dysfunction and inducible VT/VF at EP study, when other causes of syncope have been excluded |

MI=myocardial infarction; AARx=antiarrhythmic drug therapy; EP=electrophysiological; VT/VF=ventricular tachycardia/ventricular fibrillation; LV=left ventricular.
Financial considerations — ICD ‘cost-effectiveness’

Finances are often suggested as an important reason for the difference in ICD use between the two continents. But the acceptance by third party reimbursement agencies and insurance carriers in the U.S.A. was not achieved without effort, as there were (and still are) many barriers which had to be overcome. Some of our American colleagues, in dealing in the recent past with ‘managed care’ organizations and Medicare, have had to ‘...argue on a patient by patient basis about patients we felt were deserving of an ICD.’ (personal communication. Dr David Cannom, L.A. Calif) They have also given examples of how federal agencies have ‘...operated on physician attitudes in order to curtail spending on ...ICDs.’ (personal communication. Dr Rich Fogoros, Pittsburgh, PA). However, pressure from physicians, sometimes combined with persistent demands from the patients and their families — and without doubt, the fear in the U.S.A. of legal consequences (patient family law suits) — have certainly all contributed to the health insurance companies accepting the need to reimburse ICD therapy. Whether cost-effectiveness studies (see below) played a role in facilitating reimbursement in the U.S.A. is not clear, but there is a general acknowledgement that ICD therapy is as, if not more cost-effective, than numerous other readily reimbursed interventions.

Examining the issue of cost-effectiveness, a cleverly-conceived European study by Valenti et al.[12] (Fig. 5) actually showed that — due to significant reductions in re-hospitalization following ICD implantation — the costs for an ICD are essentially ‘amortized’ within about a year and a half, leading Levy to write an editorial entitled, ‘Is the ICD cost-effective?’[13]. Looking at this question critically, there are numerous medical interventions carried out routinely in Europe with less favourable cost-effectiveness than ICD therapy: kidney dialysis in the elderly, surgery for single vessel coronary artery disease, liver transplantation, etc. The table below from Steinhaus et al.[14] indicates the range of cost-effectiveness (in terms of ‘life-years-saved’) of commonly practiced interventions in the U.S.A. The costs of these interventions would be fairly similar in Europe, and show the ICD at or below the cost-effectiveness of these other therapies.

The Dutch cost-effectiveness study,[15] showed significant cost impact related to the high mortality and high rate of cross-overs to ICDs of patients randomized to conventional therapy. The difference in mortality (35% for conventional therapy, vs 14% for ICD therapy) led to the final conclusions: S94 per day alive for conventional therapy patients, compared to S63 for the ICD ‘...a net S11,300 (saved costs) per patient per life-year-saved.’ The MADIT cost-effectiveness study, in which the ICD-randomized patients benefited by 0.86 years increased longevity compared to the drug-treated group (mostly amiodarone), resulted in the overall cost-effectiveness ratio of S12 500 per life-year saved (for transvenous implantations, with devices lasting ≥4 years).[16] For their respective studies, Wever et al. and Mushlin et al. emphasized that quality-of-life evaluations enhanced the quality life year cost-effectiveness ratios favouring ICD treatment. We pointed out several years ago that the cost-effectiveness of the ICD was intimately

Figure 5 The number of hospitalizations and days of re-hospitalization in the year prior to, and in the year following, ICD implantation. (Reproduced, with permission, modified from Ref.[12].) =pre-ICD; =post-ICD.

Table 2 ICD cost effectiveness: comparison to other common therapies (Reprinted, with permission, from Ref.[14])

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cost (S)</th>
</tr>
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<tbody>
<tr>
<td>Treatment of hypertension</td>
<td>23 200</td>
</tr>
<tr>
<td>Heart transplantation</td>
<td>26 900</td>
</tr>
<tr>
<td>Estrogen replacement</td>
<td>32 900</td>
</tr>
<tr>
<td>Neonatal intensive care</td>
<td>55 000–38 800</td>
</tr>
<tr>
<td>Renal dialysis</td>
<td>58 000</td>
</tr>
<tr>
<td>Coronary artery bypass</td>
<td>7200–44 200</td>
</tr>
<tr>
<td>ICD*</td>
<td>7500</td>
</tr>
</tbody>
</table>

*Transvenous/pectoral/ increased longevity.

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related to the risk group of patients being treated, with patients having high arrhythmic risk naturally showing much more favourable cost-effectiveness than cohorts at relatively low risk\textsuperscript{[17]. This same point has been illustrated in the Markhov model study by Owens et al.\textsuperscript{[18]}, showing that for risk groups where ICD reduces mortality by 40% or more, its cost-effectiveness is under $30k per life year saved (as in MADIT); in contrast, the cost-effectiveness ratio for a lower risk group, where the ICD advantage is only 20% exceeds $60k*.

Sensitivity analysis, assuming ICD generator life-time ≥ 4 years and peri-op mortality ≤ 1%.

...
that the 1998 U.S.A. guidelines will undergo further revision. For instance, based on the persuasive results from MUSTT, it is probable that the 4th Class 1A indication shown in Table 1 (the so-called ‘MADIT indication’) will be relaxed, deleting the requirement to show non-responsiveness in the electrophysiology laboratory to a class 1A drug, such as procainamide.

As indicated above, ‘guidelines’ are certainly not the entire explanation for the observed disparity in ICD use between the two continents. Nevertheless, these new and forthcoming guidelines, taken by practicing cardiologists as a firm endorsement of the important studies mentioned above, will certainly have some impact in improving the current trends. Beyond this, we also anticipate that MUSTT will have a much stronger and more immediate impact than the previous studies, on European physicians’ attitudes.

Final remarks

The evidence favouring ICD therapy, coming from the accumulated clinical experience and underscored by the multiple randomized, prospective trials has and is moving European leaders to officially acknowledge the role of the ICD, either as primary therapy, or a serious option in patients at risk of sudden death. This fact, coupled with the continuing technological improvements in the devices, making their implantation and follow-up ever more similar to pacemakers, will undoubtedly lead current ICD implanters to increase their numbers and new institutions to begin with the therapy. Cost-saving measures — both at the implanting centres (e.g. minimal pre- and post-implant tests) and hospitalization — as well as price concessions from the manufacturers, as the numbers of devices increases, should further support the growth of ICD therapy in Europe.

References