Abstract

Since the first clinical use of implantable defibrillator in human, the technology and the function of implantable cardioverter-defibrillator (ICD) have been much improved and now, ICD can be implanted within the chest wall. ICD is the most reliable therapy to prevent sudden cardiac death (SCD) in patients with documented VT/VF and the efficacy is most clear in patients with depressed heart function. It is now extended as a tool of the primary prevention of SCD in high risk patients after myocardial infarction. However, such beneficial effect is not applicable to DCM though patients might have depressed heart function. ICD is not free from procedure- or device-related problems which need to be resolved. From unknown causes, VT/VF might recur in an incessant form and an emergency admission is needed. Therefore, even during ICD therapy, patients often require antiarrhythmic drugs or catheter ablation.

Key words: implantable cardioverter-defibrillator, sudden cardiac death, ventricular tachycardia, ventricular fibrillation

Introduction

In the USA, 300,000 people are reported to die suddenly each year (1) but the number in Japan has not yet been fully elucidated. From some epidemiologic studies (2, 3), the victims of sudden cardiac death (SCD) are estimated to be about 30 thousands annually. For SCD due to tachyarrhythmias; ventricular tachycardia (VT) or ventricular fibrillation (VF), DC shock is the only reliable therapy to terminate VT/VF and ICD is established as the most reliable therapeutic tool since its first human use in 1980 by Mirowski et al (4). ICD is now indicated for documented VT/VF, or aborted SCD for secondary prevention (5–8). Furthermore, recent trials have shown the efficacy of ICD in preventing SCD in high risk patients after myocardial infarction (9–11).

The underlying heart diseases of VT/VF differ somewhat between Japan and Western countries. Only one-third of the patients with VT/VF have prior myocardial infarction in Japan (Fig. 1), but myocardial infarction is the most common cause of VT/VF in the USA. Thus, the background of VT/VF is different in Japan which might affect the indication of ICD therapy and the efficacy or the diurnal pattern of shock deliveries of ICD (12).

Historical Aspects

Mirowski et al was the first who developed and used automatic defibrillators in 1980 (4). One patient had previous myocardial infarction and developed refractory angina pectoris and VF. VF was not related to myocardial ischemia and was refractory to many antiarrhythmic drugs. The other two patients had hypertrophic cardiomyopathy and developed VF. One had been treated with septal myotomy and a pacemaker. At electrophysiologic study, induced hypotensive VT or VF could be terminated by the automatic defibrillator and thereafter, 3 patients underwent implantation (1).

At that time, many electrophysiologists and cardiac surgeons were seeking other therapeutic interventions such as catheter ablation, mapping-guided cardiac surgery as well as antiarrhythmic drug therapy. Meanwhile, the technology and the function of the defibrillator have been improved dramatically. Now ICD poses the following functions.

1) Defibrillation. After sensing spontaneous VF, the device starts to charge and delivers electrical currents at 15-34J.
2) Anti-bradycardia pacing. When electrical shock is delivered within the ventricular cavity, standstill is often induced which needs back-up pacing.
3) Anti-tachycardia pacing. Most sustained monomorphic VT is due to reentry (13) and rapid pacing can terminate VT effectively but only in some selected patients (14, 15). Rapid pacing is given at progressively shorter cycle lengths starting at a predetermined cycle length. The number of stimuli can be set by a programmer. Some VT may
degenerate into VF by rapid pacing and needs defibrillation.

4) Cardioversion. VT can be converted to sinus rhythm by electrical shock at low energy: <10J. This is another function in terminating VT.

5) Memory storage and programmability. All devices have a function to store memory and therapeutic events are recorded with intracavitary electrograms. The data can be retrieved and used to prove inappropriate shock deliveries of ICD (16). The settings of functions of ICD can be altered as desired.

With these functions, the device is now called an implantable cardioverter-defibrillator (ICD). The most striking feature of development of ICD is the down-sizing to 50 ml or less and it can be now implanted in the chest wall. The leads can be inserted into the subclavian vein and ICD can be implanted without thoracotomy. Most current ICDs deliver currents of the biphasic wave form with superior defibrillation efficacy in comparison with monophasic wave forms (17).

In 1985, ICD was approved by FDA in the USA and the clinical trial of ICD was started in 1990 in Japan and its use was approved in 1996. By the end of 2000, the number of patients implanted with ICD reached 80,000 in the world.

Secondary Prevention of SCD

In the early stages of ICD therapy, all defibrillator implantees were required to have survived 2 or more out-of-hospital cardiac arrests but toward the end of 1980, many cardiologists accepted ICD as the definitive therapy of fatal ventricular tachyarrhythmias (18, 19). The effectiveness of ICD was initially evaluated only by observing the ability to terminate VT/VF by ICD. Using the ICD shocks as a substitute for out-of-hospital SCD, better long-term results were obtained in comparison with hypothetical survivorship (20, 21).

However, if every ICD shock represents episode of VT/VF is associated with some concerns as follows

ICD may deliver a shock but it might be unnoticed by the patient. Furthermore, it is likely that each ICD shock does not represent fatal VT or VF since some VT can be well tolerated. Sometimes, ICD delivers shocks inappropriately for tachyarrhythmias other than VT/VF (Fig. 2). It includes supraventricular tachyarrhythmias such as atrial fibrillation, atrial flutter, or sinus tachycardia, oversensings of intra- or extracardiac electrical noise (22). Inappropriate ICD shocks have been avoided by the analysis of the electrograms stored within the device (16) or by dual chamber ICD (23).

A reduction of SCD in patients with ICD therapy was confirmed in comparisons with control patients without ICD (24, 25). Thereafter, as the single most definite indicator evaluating the efficacy of ICD therapy, subsequent studies showed an improved rate of freedom from all-cause mortality. At that time, though ICD worked effectively, it was assumed that ICD in patients with cardiac dysfunction is a temporizing measure and patients will die soon from heart failure: ICD switches the mode of death from SCD to heart failure but a series of randomized ICD trials were performed in the early 1990s to determine whether or not ICD prolongs life (26–29).

For secondary prevention, randomized clinical trials comparing ICD with antiarrhythmic drug therapy were performed in the USA (6), Canada (7) and Europe (8). Patients were resuscitated after near fatal VF or sustained VT. In AVID trial (6), ICD was compared with amiodarone (90%) or sotalol (10%). In CASH trial (7), amiodarone, metoprolol, and propafenone were compared with ICD therapy in VF survivors. During the follow-up for 2–3 years, ICD was found to be superior to antiarrhythmic drugs for increasing survival (30).

Of note, patients with EF<0.26 were the most improved with ICD and in patients with a relatively well-reserved ejection fraction (EF>0.35), there was no benefit of ICD compared with amiodarone therapy (31). Similar results were observed in another study (7): when patients were stratified into 4 risk groups on the basis of reduced ejection fraction, advance age, and New York Heart Association Functional

Figure 1. The underlying heart diseases of VT or VF. VT or VF associated with old myocardial infarction occupies 30% of the total (n=315). OMI: old myocardial infarction, CM: hypertrophic or dilated cardiomyopathy, ARVC: arrhythmogenic right ventricular cardiomyopathy, Sarc: Cardiac sarcoidosis, LV An: left ventricular aneurysm unassociated with coronary artery disease, Post op: postoperative cases for congenital heart diseases; tetralogy of Fallot or double outlet of right ventricle, I-LVVT: idiopathic VT of left ventricular origin, R-RVVT: idiopathic VT of right ventricular origin.
Figure 2. Inappropriate shock delivery of ICD. A: The first arrow means the end of detection of tachycardia and the start of charging. Then a shock for cardioversion (CV) was given but failed to terminate tachycardia. Sinus tachycardia was detected as VT. Using dual chamber ICD, supraventricular tachyarrhythmias could be discriminated from VT or VF. B: Sensing of T-wave (shown by arrow in the upper column) led to a delivery of shock at 30J (DC). This problem is difficult to resolve because the increased sensing threshold may result in a sensing failure. EGM: intracavitary electrogram. Sensed electrograms were shown by markers. Interval means the interval between successive electrograms.
class, a 50% relative risk reduction was found in the highest risk group but not in the other lower risk groups. From these clinical trials, it can be said that patients with moderate to severe left ventricular dysfunction will achieve the greatest benefit from ICD therapy.

However, some patients with VT/VF (10–20%) might have no demonstrable heart disease and their cardiac function is entirely normal. This includes idiopathic VF and congenital long QT syndrome. Among idiopathic VF, Brugada syndrome is well established as characterized by peculiar ECG findings in the precordial leads: a right bundle branch block-like pattern with ST elevation (32). The other is congenital LQT syndrome and these patients show normal cardiac function (33). Both may develop polymorphic VT or VF and when fatal ventricular arrhythmias are documented, ICD therapy is indicated.

The current indications of ICD in patients with VT/VF are shown in Table 1 (34). The guidelines of AHA/ACC are essentially the same as those in Japan (34, 35). As to hemodynamically stable VT with remote myocardial infarction, there is a controversy in the risk evaluation but patients with spontaneous sustained VT are usually indicated for ICD (36, 37). Indications for specific cardiac disorders are also shown in Table 2.

### Primary Prevention of SCD

In high risk patients after myocardial infarction with low EF and frequent ventricular premature complexes or non-sustained VT, CAST (38) showed a limitation of antiarrhythmic drug therapy for the prevention of sudden cardiac death. Among antiarrhythmic drugs, amiodarone showed a benefit in patients at high risk of SCD, especially for patients with cardiac dysfunction with or without frequent asymptomatic ventricular arrhythmias (39–44).

A randomized trial comparing the efficacy of ICD therapy with amiodarone was undertaken in MADIT (9). Patients had previous myocardial infarction and depressed cardiac function: EF. 0.35 with non-sustained VT. At electrophysiological study, sustained VT was induced in all patients. Procainamide failed to prevent VT induction and they were treated by ICD or by conventional antiarrhythmic drugs selected on the basis of electrophysiological study or empirically using amiodarone (9). At 2 years, there was a 54% reduction of mortality in the ICD group compared to antiarrhythmic drug therapy. Moss presented the results of the subanalysis of MADIT which clearly showed that the survival benefit of ICD therapy was greater than conventional therapy only in those with an ejection fraction of less than 0.26 (45). The benefit of ICD therapy in patients with depressed left ventricular function was further confirmed by the MADIT II trial where the entry criterion was EF. 0.30

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### Table 1. Indications of ICD Therapy as the Secondary Prevention of SCD

<table>
<thead>
<tr>
<th>Class</th>
<th>Indications</th>
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<tbody>
<tr>
<td>Class I</td>
<td>1. Documented VF&lt;br&gt;2. Spontaneous sustained VT with structural heart diseases associated with,&lt;br&gt;(1) Syncope during VT&lt;br&gt;(2) LV ejection fraction &lt;40% and BP fall &lt;80 mmHg, or neurological symptoms or chest pain.&lt;br&gt;(3) Stable VT when drug therapy is ineffective, not tolerated, or not preferred.</td>
</tr>
<tr>
<td>Class IIA</td>
<td>1. Sustained VT associated with structural heart diseases but not inducible after catheter ablation&lt;br&gt;2. Sustained VT associated with structural heart diseases, LV ejection fraction &lt;40%, and no effective drug.</td>
</tr>
<tr>
<td>Class IIb</td>
<td>None</td>
</tr>
<tr>
<td>Class III</td>
<td>1. VT or VF due to acute or reversible causes&lt;br&gt;2. Frequent episodes of VT or VF&lt;br&gt;3. Curable VT or VF by catheter ablation (idiopathic VT or VF in WPW syndrome)&lt;br&gt;4. Limited life expectancy (&lt;6 months)&lt;br&gt;5. Conditions where no agreement/cooperation of patient can be obtained like psychiatric illness&lt;br&gt;6. NYHA Class IV drug-refractory congestive heart failure but not candidate for cardiac transplantation.</td>
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</table>

Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective.

Class II: Conditions for which there is conflicting evidence and/or divergence of opinion about the usefulness/efficacy.

IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.

IIb: Usefulness/efficacy is less well established by evidence/opinion.

Class III: Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/effective and in some cases may be harmful.

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From Japanese Joint Guidelines of Nonpharmacological Therapy of Cardiac Arrhythmias (34).
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Table 2. ICD Indications in Specific Disorders

<table>
<thead>
<tr>
<th>Brugada Syndrome</th>
<th>Class I</th>
<th>Class IIa</th>
<th>Class IIb</th>
<th>Class III</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>1. Cardiac arrest/aborted SCD</td>
<td>1. Brugada ECG pattern without VF/syncope but with SCD in family member and VF or polymorphic VT induced at electrophysiological study</td>
<td>1. Brugada ECG pattern without VF/syncope but with SCD in family member and VF or polymorphic VT not induced at electrophysiological study</td>
<td>1. Brugada ECG pattern without VF, syncope and SCD in family member and VF or polymorphic VT not induced at electrophysiological study</td>
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<td></td>
<td>2. Documentation of VF or polymorphic VT with spontaneous termination</td>
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<td></td>
<td>3. Syncope of undetermined origin with Brugada ECG pattern and VF or polymorphic VT induced at electrophysiological study</td>
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</table>

Long QT syndrome

<table>
<thead>
<tr>
<th>Class I</th>
<th>Class IIa</th>
<th>Class IIb</th>
<th>Class III</th>
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<tbody>
<tr>
<td>1. Aborted SCD or documented VF.</td>
<td>1. No syncope but with non-sustained VT associated with coronary artery disease or DCM, LV dysfunction (EF &lt;40%), and inducible VF or sustained VT at electrophysiological study that is not suppressed by antiarrhythmic drug.</td>
<td>1. No syncope but with non-sustained VT associated with coronary artery disease or DCM, LV dysfunction (EF &lt;40%), and inducible VF or sustained VT at electrophysiological study, drugs are not tested.</td>
<td>1. No syncope but with non-sustained VT associated with coronary artery disease or DCM, LV dysfunction (EF &lt;40%), and inducible VF or sustained VT at electrophysiological study,药物 are not tested.</td>
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<table>
<thead>
<tr>
<th>Class IIa</th>
<th>Class IIb</th>
<th>Class III</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Recurrent syncope with documented Torsade de Pointes or SCD in family and refractory to β-blocker</td>
<td>1. Non-sustained VT with no structural heart disease.</td>
<td>1. Non-sustained VT with no structural heart disease but preserved LV function (EF &gt;40%).</td>
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<td>2. Non-sustained VT with structural heart disease but preserved LV function (EF &gt;40%).</td>
<td>3. Non-sustained VT with structural heart diseases and LV dysfunction (EF &lt;40%) but VT or VF is not inducible at electrophysiological study.</td>
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From Japanese Joint Guidelines of Nonpharmacological Therapy of Cardiac Arrhythmias (34).

Table 3. Indications of ICD for Primary Prevention of SCD

<table>
<thead>
<tr>
<th>Class I</th>
<th>Class IIa</th>
<th>Class IIb</th>
<th>Class III</th>
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<tbody>
<tr>
<td>Syncope of undetermined origin and nonsustained VT associated with coronary artery disease or dilated cardiomyopathy (DCM), LV dysfunction (EF &lt;40%), and inducible VF or sustained VT at electrophysiological study that is not suppressed by antiarrhythmic drug.</td>
<td>1. No syncope but with non-sustained VT associated with coronary artery disease or DCM, LV dysfunction (EF &lt;40%), and inducible VF or sustained VT at electrophysiological study that is not suppressed by antiarrhythmic drug.</td>
<td>1. No syncope but with non-sustained VT associated with coronary artery disease or DCM, LV dysfunction (EF &lt;40%), and inducible VF or sustained VT at electrophysiological study, drugs are not tested.</td>
<td>1. No syncope but with non-sustained VT associated with coronary artery disease or DCM, LV dysfunction (EF &lt;40%), and inducible VF or sustained VT at electrophysiological study,药物 are not tested.</td>
</tr>
<tr>
<td>1. No syncope but with non-sustained VT associated with coronary artery disease or DCM, LV dysfunction (EF &lt;40%), and inducible VF or sustained VT at electrophysiological study, drugs are not tested.</td>
<td>1. Non-sustained VT with no structural heart disease.</td>
<td>2. Non-sustained VT with structural heart disease but preserved LV function (EF &gt;40%).</td>
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<tr>
<td>2. Non-sustained VT with structural heart disease but preserved LV function (EF &gt;40%).</td>
<td>3. Non-sustained VT with structural heart diseases and LV dysfunction (EF &lt;40%) but VT or VF is not inducible at electrophysiological study.</td>
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From Japanese Joint Guideline of Nonpharmacological Therapy of Cardiac Arrhythmias (34).

After myocardial infarction. Only patients with EF. 0.26 showed a reduction of mortality rate while patients with EF 0.26–0.35 showed no benefit of ICD therapy. However, this is not applicable to patients with dilated cardiomyopathy (DCM). In two recent trials, patients with EF. 0.30 in CAT (46) or EF. 0.35 in AMIOVIRT (47) were randomly assigned to ICD therapy or amiodarone. The two trials were terminated prematurely because of a lower mortality at 1 year than expected. The number of patients was relatively small, 104 and 103 in CAT and AMIOVIRT, respectively and the mortality was not different between the ICD therapy and the amiodarone therapy group (46, 47). Therefore, though the sickest patients seem to benefit most by ICD therapy, it is strongly affected by the etiology of the cardiac diseases.

The current indications of ICD for the primary prevention of SCD are shown in Table 3 (34). The indications (primary and secondary prevention) of ICD in specific disorders are shown in Table 2. The prognosis of patients with Brugada syndrome is controversial especially in asymptomatic patients (48–50). Their prognosis seems good in Japan (51).
Problems and Complications

For patients at high risk of SCD, ICD therapy is the first line of therapy for secondary or primary prevention in patients at high risk of SCD. However, ICD patients may have several problems to be resolved. One is the inappropriate delivery of ICD shocks which causes pain or fright and worsens the quality of life of patients. Placement of the lead in the atrium can reduce inappropriate shock deliveries for supraventricular tachyarrhythmias (23), but shocks due to double counting of the ventricular electrograms or T-wave sensing is are still an unresolved problem (22). Rarely, sensing failure of VF is suspected which needs to be urgently resolved.

When anti-tachycardia pacing is attempted for the termination of VT, VT might degenerate into VF. This is a limitation of this tiered mode of therapy and defibrillation is essential as a back-up. Drugs might affect the termination of VT by rapid pacing and it is desirable to check the efficacy of antitachycardia pacing before and after drug therapy (14, 15).

From unknown causes, VT or VF may recur in an incessant form and ICD patients fall into a dreadful state from repeated shocks of ICD delivery (Fig. 3). In such patients, emergency hospitalization is mandatory and antiarrhythmic drugs, or sedation by general anesthesia have to be attempted. Emergency catheter ablation for monomorphic VT might be needed.

ICD therapy may be associated with procedure-related complications. These include mechanical injury of vessels and heart structure, thrombosis at the puncture site or along the lead system, and infection of the pocket of the generator or the lead system. The high cost is another problem.

Conclusions

ICD has been established as the most reliable therapy to prevent SCD in patients with VT/VF. It has also benefited patients with depressed heart function after myocardial infarction as the primary prevention of SCD. However, ICD is not free from procedure- or device-related problems which need to be resolved. Even during ICD therapy, patients often require additional therapeutic options such as antiarrhythmic drugs or catheter ablation.

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