Adverse Events With Transvenous Implantable Cardioverter-Defibrillators
A Prospective Multicenter Study

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Background—A newly developed classification system relates adverse events to the surgical procedure or the function of the implantable defibrillator.

Methods and Results—Adverse events were monitored during prospective clinical evaluation of the Medtronic model 7219 Jewel ICD and were classified according to the definitions of the ISO 14155 standard for device clinical trials into 3 groups: severe and mild device-related and severe non–device-related adverse events. In addition, events were related to the surgical procedure, treatment with the device, or cardiac function. Seven hundred seventy-eight patients were followed up for an average of 4.0 months after ICD implantation. In total, 356 adverse events were observed in 259 patients. At 1, 3, and 12 months after ICD implantation, 99%, 98%, and 97% of the patients, respectively, survived; 95%, 93%, and 92%, respectively, were free of surgical reintervention; and 79%, 68%, and 51%, respectively, were free of any adverse event. Twenty patients died: 6 deaths were related to the surgical procedure, 12 deaths were considered unrelated to ICD treatment, and 2 patients died of an unknown cause. Of 111 nonlethal severe adverse device effects, 47 required surgical intervention, 19 times for correction of a dislodged lead. Inappropriate delivery of therapy was observed 128 times in 111 patients, and the events were typically resolved by reprogramming or drug adjustment. Nine of these required rehospitalization.

Conclusions—Approximately 50% of patients experience an adverse event within the first year after ICD implantation. The observed adverse event rate depends on the definitions and the prospective monitoring. The incidence of inappropriate therapy emphasizes the need for improved detection algorithms and for quality-of-life evaluations, especially when considering ICD treatment in high-risk but arrhythmia-free patients. (Circulation. 1998;98:663-670.)

Key Words: events, adverse n tachyarrhythmias n defibrillation n implantable cardioverter defibrillator (ICD)

It has been suggested that indications for ICDs should be expanded to include prophylactic treatment of patients at high risk for ventricular arrhythmias; then it becomes important to assess the risk for side effects from this treatment more strictly, especially regarding the most common problem, ie, inappropriate therapy due to detection of supraventricular tachycardia, which sometimes can be proarrhythmic and even fatal.

The European Community and the International Standards Organization (ISO) have provided a standard for strict classification of adverse events observed during trials with implantable medical devices, defining an adverse event as any undesirable clinical occurrence and taking into account the severity as well as the relationship to the implanted device. It does not, however, give any information regarding the underlying technical or clinical cause and whether or not the event is related to the surgical implantation or to test procedures. In 1993, a policy statement on ICD patient outcome was published by the North American Society of Pacing and Electrophysiology. This document recommends classification of deaths into cardiac and noncardiac. Cardiac deaths are further classified into sudden and nonsudden. In addition, it requested that outcome reports should include all major ICD-related morbidity.

To better understand which adverse events are caused by defibrillator treatment in general and which are related to the surgical procedure, we expanded the current classification system and used it prospectively for all adverse events observed during a multicenter clinical trial of a new ICD system implanted in 778 patients.

The aim of this study was to report the incidence of adverse events during the initial months after abdominal or pectoral implantation of an ICD system with a transvenous lead system. Patients undergoing ICD replacements were excluded from this analysis.

Methods

Classification of Events
According to the European standards, an “adverse event” is “any undesirable clinical occurrence in a subject whether it is considered
An "adverse device effect" is defined as a device-related adverse event. Adverse events can be severe or mild; severe events cause hospitalization or undue prolongation of hospitalization because of potential disability or danger to life, necessitate intervention, or cause death. For this study, all other events have been labeled "mild," and "intervention" has been interpreted as either surgical intervention or reprogramming of the device with the specific purpose of avoiding an otherwise required hospitalization.

Adverse events have thus been classified as either severe adverse device effects or severe non-device-related events or mild adverse device effects. Mild, non-device-related events have not been considered in this study.

To give more specific information about the events, a subclassification was applied (see Figure 1) that considered the following.

1. The relationship of the event to the ICD therapy, eg, procedure-related or not, ICD-therapy–related or not.
   - A procedure-related event is defined as being directly or indirectly caused by the surgical implantation procedure.
   - An ICD-therapy–related event is an event related to the implanted ICD system, including leads and nonimplantable equipment used but excluding procedure-related events.

2. Temporal relation of the event to the surgical procedure, ie, within (perioperative) or after (nonperioperative) 30 days after implantation.

3. Mechanism of the event, ie, cardiac or noncardiac, for non-device-related events and arrhythmia-related or not.
   - Deaths were also classified as sudden or nonsudden. Sudden death was defined as a death occurring without preceding symptoms or within 1 hour after the onset of or sudden change in symptoms. An unexpected, insufficiently documented, and unwitnessed death was conservatively also classified as sudden.

Adverse Event Committee
Four experienced cardiologists and 2 representatives of the manufacturing company scrutinized and classified all events by consensus. The company representatives ensured access to all clinical data and supported technical interpretation of events but did not have any impact on the final event classification.

Patients
Seven hundred seventy-eight patients (demographics listed in Table 1) received implants between March 1993 and November 1994 in 63

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**Figure 1.** Classification tree. A total of 356 adverse events were observed in 259 of 778 patients during an average follow-up period of 4.0 months.
TABLE 1. Clinical Characteristics of 778 Patients Receiving a Model 7219 ICD

| Clinical Characteristics |  
|--------------------------|---|
| Age, y                   | 58.1±13  
| Percent female           | 18.4  
| Indication for ICD implantation, % |  
| SCD, cardiac arrest      | 43.4  
| VT                       | 39.2  
| SCD/cardiac arrest and VT | 12.3  
| Other                    | 4.9  
| LV ejection fraction, %  | 39.1±17  
| NYHA classification, %   |  
| I                        | 22.6  
| II                       | 53.3  
| III                      | 23.1  
| IV                       | 0.9  
| Underlying cardiac disease, %  |  
| CAD                      | 58.0  
| MI                       | 54.2  
| CMP                      | 29.8  

ICD indicates implantable cardioverter defibrillator; SCD, sudden cardiac death; LV, left ventricular; CAD, coronary artery disease; MI, myocardial infarction; and CMP, cardiomyopathy.

European centers, with either Medtronic model 7219 C (392 patients) or model 7219 D (386 patients) Pacer Cardioverter Defibrillator.

Devices

The ICDs provide defibrillation and cardioversion shocks from 0.4 to 34 J, antitachycardia pacing therapies (burst, ramp and ramp +), noninvasive electrophysiological test procedures, and 5 seconds of electrogram storage and have a size and weight that allow pectoral implantation (80 cm³ and 129 g for model 7219 C). All ICDs were implanted with a tripolar, right ventricular (RV) screw-in lead (model 6936, bipolar pace/sense, 5-cm defibrillation coil). For model 7219 C, this was the only lead connected because this device uses the generator can as the second defibrillation electrode. Model 7219 D requires an additional lead in the superior vena cava for which either model 6933 (5-cm electrode coil) or model 6937 (8 cm coil) was used. If defibrillation threshold was unacceptably high, model 7219 D was connected with a third, subcutaneous (model 6939, 58 patients) or epicardial (model 6721, 6 patients) lead. Model 7219 C, this was the only lead connected because this device uses the generator can as the second defibrillation electrode. Model 7219 D requires an additional lead in the superior vena cava for which either model 6933 (5-cm electrode coil) or model 6937 (8 cm coil) was used. If defibrillation threshold was unacceptably high, model 7219 D was connected with a third, subcutaneous (model 6939, 58 patients) or epicardial (model 6721, 6 patients) lead. Model 7219 C was implanted pectorally in the subcutaneous (9%) or submuscular (88%) position (3% unknown), whereas the 7219 D version was implanted abdominally or pectorally (40/60 ratio).

Implantation, Perioperative Testing, Follow-Up, and Reporting of Adverse Events

After the leads were positioned, the efficacy of pacing, sensing, and defibrillation was assessed.

Patients underwent a predischARGE test 3 to 7 days after implantation with induction of ventricular tachyarrhythmia (VT). After discharge, patients visited the outpatient clinic after 1 month and then every 3 months or in case of any adverse event.

Adverse events were reported to the sponsor on adverse-event forms designed for efficient reporting of the essential aspects of the event. In addition, all data forms and ICD interrogation printouts were screened for unnoticed adverse events by the clinical monitor.

Statistics

Data are given as mean±SD. To account for variable lengths of follow-up, the probability of remaining event free was analyzed by the Kaplan-Meier method. Student’s t test was used for comparison of continuous variables, and a χ² test was used for comparison of categorical variables. A generalized linear model analysis was performed to relate occurrence rates of adverse events with implant rates in individual centers.

Ethics

All patients received oral and written information and gave voluntary written consent to participate in the study. The study protocol was approved by the local ethics committee of every participating hospital.

Results

Patients and Follow-Up

The average duration of follow-up was 4.0 months, with an SD of 4.6 months and a range of 0 to 21 months.

In total, 356 adverse events were reported in 259 of 778 patients (Figure 1; Table 1). Figure 2 presents the rates of freedom from death, surgical reintervention, severe adverse effects, and any adverse events at 1, 3, 6, and 12 months after implantation as calculated with Kaplan-Meier analysis.

The percentage of adverse events reported per hospital as a function of the number of implantations performed varied widely, but when the centers with fewer than 5 implantations were excluded (n=29), an average ratio of 48.8% was observed during the average follow-up period of 4.0 months. No significant linear relationship was found between the number of adverse events per patient and the number of implantations in a center (P=0.59).

Deaths

Twenty patients died during the study period; 6 died perioperatively (1 pulmonary embolism, 2 sepsis, and 3 cardiac failure) (Table 2). All deaths except 2 were witnessed in the hospital. Two deaths were classified as “unknown and occurring suddenly” because they were unwitnessed, insufficient information was available, and they occurred outside the hospital.

The first patient was 71 years old, had sustained a myocardial infarction, and had left ventricular ejection fraction of 25% (NYHA functional class IV). During 6 months of follow-up, he had several episodes of monomorphic VT, which were successfully treated, mainly with ATP. On the day of death, 4 episodes occurred (3 were VF with a cycle length <240 ms, and 1 was a VT); all were successfully treated by the first therapy. The device was explanted, and analysis disclosed no malfunction. The timing of the 4 episodes stored in the ICD memory revealed no distinct relationship with the timing of death.

The second patient was 70 years old and had a history of cardiac arrest. His left ventricular ejection fraction was 10% (NYHA class III). The patient was inaduble, but during follow-up no spontaneous episodes were observed. At the 1-month follow-up, the device worked according to specifications. The patient died out of hospital, unwitnessed. He was found without respiration but with his pupils still reacting to light and with clinical signs of electromechanical dissociation. The ICD was neither interrogated nor explanted.
Six of the deaths were classified as ICD-procedure–related: sepsis (n = 3; 2 were perioperative, 1 patient died 42 days after implantation), nonperioperative hemodynamic compromise (n = 2), and perioperative thromboembolism (n = 1). Another 11 patients died of progressive heart failure (3 during the perioperative phase), and the deaths were classified as cardiac. One patient died of terminal cancer (nonperioperative, classified as noncardiac).

**TABLE 2. Causes of Death**

<table>
<thead>
<tr>
<th>Causes</th>
<th>Cardiac Arrest</th>
<th>Non-Sudden Cardiac</th>
<th>Non-Sudden Non-Cardiac</th>
</tr>
</thead>
<tbody>
<tr>
<td>Witnessed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In hospital</td>
<td>2</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>Out of hospital</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unwitnessed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In hospital</td>
<td>15</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Out of hospital</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arrhythmia related</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Not arrhythmia related</td>
<td>14</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Perioperative</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonperioperative</td>
<td>2</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>ICD on</td>
<td>2</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>ICD off</td>
<td>6</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Interrogation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Available</td>
<td>1</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Not available</td>
<td>1</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Autopsy performed</td>
<td>1</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Autopsy not performed</td>
<td>2</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

ICD indicates implantable cardioverter-defibrillator.

**TABLE 3. Severe and Mild Adverse Events Due to the ICD System**

<table>
<thead>
<tr>
<th>Event</th>
<th>Severe</th>
<th>Mild</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased defibrillation requirements</td>
<td>8</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>Inappropriate VT/VF detection</td>
<td>9</td>
<td>119*</td>
<td>128*</td>
</tr>
<tr>
<td>Sensing problems</td>
<td>8</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Elevated pacing threshold/loss of capture</td>
<td>5</td>
<td>9*</td>
<td>14*</td>
</tr>
<tr>
<td>Failure to terminate VT/VF</td>
<td>6</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>Lead specific problems</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Hospitalization because of fear of shocks or appropriate shocks</td>
<td>5*</td>
<td>0</td>
<td>5*</td>
</tr>
<tr>
<td>Adjustment of medication/reprogramming</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>External equipment used</td>
<td>0</td>
<td>19</td>
<td>19*</td>
</tr>
<tr>
<td>Long capacitor charge time</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>ICD implant test protocol</td>
<td>1</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>45*</td>
<td>169*</td>
<td>214*</td>
</tr>
</tbody>
</table>

ICD indicates implantable cardioverter-defibrillator.

No deaths in this group; *including patients with multiple events.
additional surgical intervention, and 169 events in 143 patients were classified as mild.

**Severe Events**

Eight patients were hospitalized after observation of an increase in defibrillation energy requirements, but the implanted lead system was modified subsequently in only 4 of them.

T-wave oversensing, seen in 5 patients, and double sensing of the QRS complex resulting in inappropriate therapy were resolved by reprogramming the sensitivity during hospitalization. Decreased sensing efficacy was corrected in 2 patients by RV-lead repositioning. Undersensing with no detection of an ongoing true arrhythmia was never reported during the study.

In 9 patients, inappropriate detection of VT or VF with subsequent therapy delivery was reported; these events were classified as severe because it was necessary to hospitalize the patient or to reprogram the ICD on an urgent basis to avoid in-hospital monitoring of the patient. In 1 patient, AV-node ablation was performed to resolve the event.

Loss of capture/elevated pacing thresholds and failure to terminate an appropriately detected VT/VF episode with all 4 available therapies were reported in 5 and 6 patients, respectively. These events required either hospitalization or emergency reprogramming of the ICD; in 1 patient, the RV lead was repositioned to ensure pacing capture.

In 8 patients, hospitalization was reported to allow adjustment of medical regimen, to reprogram the ICD, or just to alleviate fear of shocks.

One patient was hospitalized after the induction of atrial fibrillation at the 3-month follow-up visit during performance of a VF-defibrillation test.

**Mild Events**

The event with the highest incidence rate was “inappropriate detection and subsequent therapy delivery” and was observed 119 times in 102 patients. Of 294 patients who received ICD therapy during the follow-up period, 116 patients had ≥1 inappropriate detections of supraventricular arrhythmias (pooled mild and severe events). In 49% of these patients, this problem was solved by reprogramming, and in 21%, by a change in medication. In 1%, other actions were taken, but in 29%, no specific action at all was taken.

The category of mild events also includes 19 events related to the external implant support equipment. An unacceptably long capacitor charge period was observed once before ICD implantation and atrial fibrillation was induced 5 times because of delivery of protocol-required test shocks.

**Procedure-Related Adverse Events**

Altogether, 102 adverse events related to the surgical procedure were observed in 95 patients; 6 resulted in death (Table 4). Kaplan-Meier analysis showed a 12-month surgery-free survival rate of 92.4% (Figure 2).

Centers with more than 50 patients enrolled in the study (n=4) had an average ratio of the number of “surgery-requiring events” to the number of patients of 0.067, and centers with 5 to 10 implantations (n=18) had a ratio of 0.066: no significant linear relation was found between these parameters (P=0.29).

**TABLE 4. Adverse Events Related to the Surgical Procedure**

<table>
<thead>
<tr>
<th>Event</th>
<th>Deaths</th>
<th>Severe</th>
<th>Mild</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumothorax/hemothorax</td>
<td>0</td>
<td>6</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>RV perforation/tamponade</td>
<td>0</td>
<td>5</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Wound/pocket problems (infections excluded)</td>
<td>0</td>
<td>13</td>
<td>14</td>
<td>27</td>
</tr>
<tr>
<td>Lead or ICD dislodgment/migration</td>
<td>0</td>
<td>21*</td>
<td>2</td>
<td>23*</td>
</tr>
<tr>
<td>Hemodynamic compromise</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Fever/sepsis/infection</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Pain/reduced mobility</td>
<td>0</td>
<td>5</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>Thrombosis/embolism</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Lead connection</td>
<td>0</td>
<td>6*</td>
<td>0</td>
<td>6*</td>
</tr>
<tr>
<td>Procedure-induced arrhythmia</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>66*</td>
<td>30*</td>
<td>102*</td>
</tr>
</tbody>
</table>

*Including patients with multiple events.

Twenty-seven wound problems (seroma, hematoma; infections excluded) were the most common procedure-related adverse events.

The second most common adverse event was lead/ICD-can dislodgment, which was observed in 23 instances; 1 patient experienced dislodgment twice. The electrode most often dislodged was the RV lead (n=16), observed primarily with abdominal ICD implants; the pectorally implanted ICD was repositioned in 2 patients.

Infection occurred in 6 patients, of whom 3 died of this condition. General antibiotic prophylaxis was prescribed in 87% of participating centers, whereas 4% of the centers prescribed it only to high-risk patients. All patients who died of an infection, however, had received antibiotic prophylaxis. Four thromboembolic events were observed during follow-up. Aspirin treatment was prescribed in 3 of these patients, and none received coumarin or warfarin. Twenty-five percent of all patients received aspirin, and 10% received warfarin/coumarin after implantation, during at least the first month of follow-up.

**Severe Adverse Events Not Related to ICD Treatment**

Altogether, 40 adverse events not related to ICD treatment were registered (Table 5). The majority, 31, were cardiac in origin. Fourteen events caused the patient’s death, nearly exclusively because of congestive heart failure (n=11). Twenty nonlethal events were registered: 14 were due to incessant VT/VF, 5 to acute myocardial infarction or unstable angina, and 1 to the occurrence of an unspecified type of supraventricular arrhythmia. Six non–device-related events were also found not to be cardiac in origin.

**Non–Device-Related Adverse Events of Unknown Cause**

One patient experienced dyspnea requiring hospitalization (Table 5). The event remained unexplained despite extensive...
TABLE 5. Non–Device-Related Severe Adverse Events

<table>
<thead>
<tr>
<th>Category</th>
<th>Deaths</th>
<th>Severe</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
<td>11</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>Hospitalization for atrial arrhythmias</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Incessant VT/VF</td>
<td>0</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>AMI/unstable angina</td>
<td>0</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Thyrotoxicosis</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Cancer</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Stroke</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Gastrointestinal problem</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Unknown cause</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
<td>26</td>
<td>40</td>
</tr>
</tbody>
</table>

AMI indicates acute myocardial infarction.

Discussion

Adverse events, prospectively monitored in patients treated with third-generation ICDs, were described and classified for the first time according to the new European Community and ISO standards for clinical trials on implantable medical devices. Despite technology enhancements, adverse events were observed in 259 of the 778 patients: merely inappropriate detection, and procedure-related events. Efforts should be undertaken to minimize these, especially if ICD therapy should be advocated for prophylactic use in high-risk patients.

The European Community and ISO5,6 defined an adverse event as any undesirable clinical occurrence, whether device-related or not. Prospective monitoring in 778 patients resulted in ≈0.1 event per patient per follow-up month during the initial months after ICD implantation. Actuarial analysis showed that adverse event occurrence rate is highest during the initial 1 to 3 months after ICD implantation. Clearly, the definitions used influence the total number of reportable events. With the new classification system, more details of the implantable device under evaluation are monitored, giving better insight into the clinical and technological aspects.

Patient Deaths

In a recent study by Epstein et al,8 a classification system for deaths similar to our system was developed to more specifically characterize deaths in ICD trials. This system was used in a clinical trial comprising 1250 ICD patients: altogether, 79 deaths were observed.

Sudden cardiac death, occurring within 1 hour and after a sudden change of symptoms, was observed in 22 patients. Procedure-related deaths occurred in 7 instances. As in the present study, none were considered to be related to the ICD treatment.

Pratt et al9 reported 109 deaths among 834 implant recipients during an average follow-up period of 20±13 months. Sixty-eight were cardiac, and 17 were classified as sudden. Classification depended on the information available in autopsies. Without autopsy reports (29/109=27%), the rate of sudden death would have increased from 2.0% to 2.9%. In the present study, 4 of the 20 deaths were documented by an autopsy report. Obviously, the availability of these autopsy reports did not influence the classification of the deaths.

Therefore, the data from the present study and those from Epstein et al8 and Pratt et al9 seem to agree that most deaths were cardiac and not related to device treatment. Despite the availability of approximately equal rates of autopsy reports, there was a lower incidence of sudden death but a higher incidence of procedure-related deaths in the present study. This discrepancy cannot be clarified completely from the available data.

Trappe et al12 reported that 13 of 335 patients, with an average of 22 months of follow-up, developed an infection after ICD implantation; 7 patients died.

Even though in this study, the majority of the patients received antibiotic prophylaxis, 3 patients died of infection. By definition, all these events were classified as “ICD-procedure–related” events, although no direct link to the surgical implantation procedure itself was demonstrated. The occurrence of these 3 fatal events, as well as another 2 severe and 1 mild event, emphasizes that postoperative infections causing sepsis or endocarditis are not uncommon and carry an ominous prognosis in a defibrillator population; every effort should be undertaken to provide adequate preventive measures. Mounsey et al13 showed a significant beneficial effect in patients receiving antibiotic prophylaxis before pacemaker implantation.

Procedure-Related Adverse Events

Despite single defibrillation leads and smaller devices, the incidence of wound problems and lead dislocations is still too high. The anticipated higher incidence of wound-related problems in pectoral ICD implantations was not observed in this study, but improvements of surgical technique could further reduce the incidence.

The observed incidence of lead dislodgments (10%) is lower than observed in other studies,14,15 possibly related to a shorter follow-up period and/or fewer patients receiving implantation of subcutaneous patches. As reported by Hoffmann et al,11 the dislodgments were found to be related primarily to abdominal rather than pectoral implants, and in the former case primarily to RV-lead dislodgments.

Device-Related Events

Inappropriate Therapy

The high incidence of inappropriate therapy is in line with other reports emphasizing that inappropriate detection/therapy is the most common adverse event observed among ICD patients.23 With “shock-only” devices, the incidence of these events during long-term follow-up has ranged between 16% and 21%.16,17 Former et al18 reported inappropriately detected episodes in 10 of 102 patients with implants during an average follow-up period of 9.4 months. In the present study, 116 of the 778 patients with implants or of the 294 patients with a therapy delivered experienced inappropriate episode detection followed by a therapy, despite a short follow-up...
time. This higher incidence rate might be related to the possibility of retrospectively classifying the episodes on the basis of the stored intracardiac electrograms. Most events were mild and were resolved by reprogramming or by changing the drug regimen.

Inappropriate therapy, apart from being painful, can also be proarhythmic. Pinski and Fahy reported ≈36 patients with ICD-induced arrhythmias, of which 2 caused the patient’s death (range, 0.4% to 8%). The risk for proarhythmia seems to be most common in situations with fast supraventricular rhythms with a concomitant increase in sympathetic discharge, rate-related decrease in ventricular refractoriness, or myocardial ischemia.

Ideally, the risk of experiencing a supraventricular tachycardia should be assessed before implantation of an ICD. However, Schmitt et al demonstrated that this arrhythmia was present before implantation in only 35% of patients receiving inappropriate therapy due to atrial fibrillation, and Page et al showed that most episodes of paroxysmal atrial fibrillation tend to be asymptomatic.

Weber et al reported an 18% incidence of inappropriate therapy in 462 patients followed up for an average of 24 months. Preoperatively documented atrial fibrillation, a maximum heart rate during exercise close to the detection interval, and a low detection rate were found to be independent risk factors for inappropriate therapy.

Various algorithms have been developed to avoid false detection, and these seem to distinguish supraventricular from ventricular arrhythmias relatively well, although they do have certain limitations. For example, the “sudden-onset” criterion will not detect an exercise-induced sinus tachycardia converting into a slow ventricular tachycardia (VT), and it cannot distinguish a suddenly started, fast-conducting regular atrial flutter from a VT. The “rate stability criterion” will have difficulty in rejecting atrial fibrillation with a fast and rather regular ventricular response and may delay detection of VTs with irregular intervals. These limitations and the lack of controlled studies evaluating the specificity, sensitivity, and safety of these algorithms have probably contributed to their infrequent use.

Another important reason for inappropriate detection is that antiarrhythmic treatment in ICD patients tends to cause an overlap in rate between VTs and the sinus rate. In a study by Paul et al, only 11% of patients without antiarrhythmic medication had sinus rates exceeding the rate of VT, whereas this proportion increased to 35% in patients with a single antiarrhythmic drug and to 63% of patients on combination therapy.

This emphasizes the need for improved detection algorithms in the next generation of ICDs, especially if indications should be widened to include prophylactic treatment in high-risk patients and efforts are undertaken to evaluate changes in quality of life in ICD patients.

Sensing Problems
T-wave oversensing and double sensing of QRS complexes may lead to inappropriate arrhythmia detection. The observation of 6 such events emphasizes the need for regular, careful evaluation of oversensing during normal sinus rhythm and during pacing.

In line with the report of Callans et al, most sensing problems were overcome by reprogramming.

Limitations of the Study
This report relies on adequate data reporting by the individual investigators. The adverse event rate per patient differed substantially between centers. There was no relation, however, between this ratio and the number of implantations at each center. The study protocol did not require defibrillation threshold testing at follow-up, nor were chest radiographs mandatory at each follow-up visit, which, together with the absence of other potential tests, may have led to underestimation of actual adverse events.

Mild, non–device-related adverse events were not collected in a systematic way and therefore have not been included in this report.

Another limitation of this study is that the protocol registered data only on medical and technical events. Thus, it was not possible to assess the incidence of psychosocial problems related to ICD therapy, which are well known to occur in this patient group and which should be considered especially in comparisons of ICD therapy with other therapies.

As with any classification system, some shortcomings and clinical irrelevancies are present.

1. The hospitalization of a patient, making the adverse event by definition “severe,” does not always reflect the severity of the clinical impact; for instance, several patients were hospitalized once and 1 patient several times for 1 or 2 days to alleviate fear of shocks that he had not, as yet, experienced.

2. Adverse events that could have but had not yet resulted in severe outcomes such as an RV perforation, a failure of the last therapy to treat a VT or a VF episode, or a lead dislodgment were classified as “mild” because they were left untreated or were resolved by simple reprogramming or adjustment of the antiarrhythmic medication but did not cause hospitalization or a prolongation of the hospital stay. Because of the eventual “severe” outcome these events could result in, their classification as severe can be argued.

Conclusions
The total number of events reported in a given study clearly depends on the definitions used. The definitions of the European guidelines (EN 540) and of the International Organization of Standardization (ISO 14155) provide guidance for monitoring and classification of adverse events. Subclassification of events is advisable to evaluate the safety and efficacy aspects of the new device and to emphasize clinically relevant aspects of the events.

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