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Sudden Death in Implantable Cardioverter-Defibrillator Recipients: Clinical Context, Arrhythmic Events and Device Responses

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Objectives. **We sought to investigate the nature of terminal events and potential contributory clinical and nonclinical (e.g., device-related) factors associated with sudden death (SD) in recipients of an implantable cardioverter-defibrillator (ICD).**

Background. **The ICD is very effective in terminating ventricular tachycardia (VT) or ventricular fibrillation (VF), but protection against SD is not absolute. Little is known about the nature and potential causes of SD in patients with ICDs.**

Methods. **We analyzed 25 cases of out-of-hospital SD among patients enrolled in the clinical investigation of the Cadence Tiered-Therapy Defibrillator System.**

Results. **All patients (24 men and 1 woman, mean age 62 ± 10 years) received epicardial lead systems. The majority (92%) had coronary artery disease and a previous myocardial infarction (MI), with a mean left ventricular ejection fraction 0.25 ± 0.07. At device implantation, the mean defibrillation threshold was 13 ± 5 J. Sudden death occurred 13 ± 11 months later. Twenty patients (80%) had received appropriate ICD therapies before death, and 18 (72%) were receiving ≥1 antiarrhythmic drugs at the time of death. Sudden death was tachyarrhythmia-associated in 16 patients (64%), non-tachyarrhythmia-associated in 7 (28%) and indeterminate in 2 (8%). In the 16 patients with tachyarrhythmia-associated SD, the overall first therapy success rate in tachycardia and fibrillation zones was 60% and 67%, respectively. However, despite protracted therapies (≥2 shocks) in 7 (66%) of 12 patients who received fibrillation therapies, the final tachyarrhythmic episode was ultimately terminated by the ICD in 15 (94%) of the 16 patients, whereas 1 patient died after multiple (initially successful) internal and external shocks for intractable VT/VF during exercise. In 10 patients (40%) one or more, primarily clinical, factors potentially contributory to SD were identified: heart failure (n = 8), angina (n = 2), hypokalemia (n = 1), adverse antiarrhythmic drug treatment (n = 1) and acute MI (n = 1). An additional 10 patients (40%) had experienced an increase in frequency of ICD shocks within 3 months of SD. Appropriate battery voltages and normal circuitry function were found in all devices interrogated and analyzed after death.**

Conclusions. **In this select group of patients receiving a third-generation ICD, SD was associated with VT or VF events in nearly two-thirds of patients, and death occurred despite ultimately successful, although often protracted, device therapies. These observations, along with evidence of recent worsening clinical status, suggest acute cardiac mechanical dysfunction as a frequent terminal factor. In recipients with ICDs, SD directly attributable to device failure seems to be rare.**

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The efficacy of implantable cardioverter-defibrillator (ICD) therapy for treatment of ventricular tachyarrhythmias has been well documented (1). However, the protection afforded by the ICD against sudden arrhythmic death is not absolute. Insight into the nature of terminal events associated with sudden death (SD) in ICD recipients has been limited by the relatively low incidence of this outcome as well as the inability, until recently, to document the arrhythmias occurring just before death. A few reports have described terminal events in patients with first-generation ICDs who died suddenly (2–5). In the largest of these studies (5), involving 51 cases of SD, nearly two-thirds occurred in association with known or presumed tachyarrhythmia, with one or more contributory factors, such as battery depletion or device deactivation, identified in more than half of the patients. The extent to which these observations in patients with first-generation ICD also apply to the occurrence of SD in patients with newer devices is not known.

The event storage capability of the more recent generation of ICDs, including intracardiac electrograms (6), offers the possibility of better characterization of terminal arrhythmias associated with SD (7). At the same time, various technologic features of the newer devices, such as biphasic shock (which provides for lower defibrillation energy [8]) and antibradycardia pacing, might have a positive impact on patient outcome, whereas enhanced programmability, with the potential for suboptimal device responses (9), might have adverse consequences.

The objectives of this study were twofold: first, to determine the arrhythmic events associated with SD in recipients of a

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Abbreviations and Acronyms

CHF = congestive heart failure
DFT = defibrillation threshold
EHR = extended high rate
EMD = electromechanical dissociation
ICD = implantable cardioverter-defibrillator
LVEF = left ventricular ejection fraction
MI = myocardial infarction
SD = sudden death
VF = ventricular fibrillation
VT = ventricular tachycardia

third-generation ICD and, second, to identify clinical and possible device-related factors that might have contributed to the patients' death, and whether or not such factors, if any, might be potentially preventable.

Methods

Study group. Between July 1989 and April 1993, a total of 1,846 patients received, as part of a clinical investigation, the Cadence (V-100) Tiered-Therapy Defibrillator System (Ventritex, Sunnyvale, California) for treatment of life-threatening ventricular tachycardia (VT) and ventricular fibrillation (VF). After a mean follow-up of 13 ± 11 months (range 0 to 45) outcome data were available in 1,649 patients: 37 (2%) had an SD, 168 (10%) had a non-SD and the remaining 1,447 (88%) were alive. Of these 37 patients who died suddenly, 7 were excluded at the outset of our analysis: 3 because of physician nonparticipation in the study; 3 whose ICDs had been intentionally deactivated beforehand; and 1 who died suddenly before hospital discharge, after receiving defibrillation leads only. Five (17%) of the remaining 30 patients died in the hospital, during the first week after the operation; they were all monitored and observed to receive multiple ICD shocks for VT or VF, with eventual asystole/electromechanical dissociation (EMD). Each of the five patients had been hemodynamically stable up to the onset of VT/VF, but two had evidence of acute myocardial infarction (MI) on postmortem examination. As postoperative deaths in ICD recipients have been attributed to arrhythmia "exacerbation" after implantation of epicardial-lead ICDs (10,11), and may not be representative of SD events in an outpatient setting, we restricted the study group to the remaining 25 patients who had an out-of-hospital SD with active ICDs.

Device system and implantation. The Cadence ICD is a multiprogrammable device capable of backup bradycardia pacing and "noncommitted" antitachycardia pacing, cardioversion and defibrillation with biphasic shocks (12). Detailed information on the detected tachyarrhythmic events, including each delivered therapy and its duration and outcome, is available for each of the most recent 11 episodes. The device stores intracardiac electrograms corresponding to the most recent (≤3) tachyarrhythmic events, along with the time and date of the events. The device's extended high rate (EHR) detection feature incorporates a "timer" that allows antitachycardia therapies to be attempted for only a programmable length of time (10 to 120 s); if the timer expires, the device proceeds to the more aggressive fibrillation zone therapies (12).

Written informed consent for implantation of this device (investigational at the time) was obtained from all patients after approval by the Institutional Review Boards of each of the participating centers (see Appendix). All 25 patients received epicardial lead systems consisting of two defibrillating patches and epicardial (n = 14) or endocardial (n = 11) rate-sensing leads. Four patients had concomitant myocardial revascularization.

Patient follow-up and data collection. A complete evaluation of device function, including VT and VF therapy, was performed before and 6 weeks after hospital discharge, and per the discretion of the individual electrophysiologist depending on clinical circumstances (e.g., addition or change in antiarrhythmic drug therapy). Thereafter, patients were seen at a minimum of once every 3 months, or sooner in cases of device discharges. At each visit, the device was interrogated and all diagnostic-therapy data, including intracardiac electrograms, stored since the previous visit were recorded. Retrieved data obtained from postmortem device evaluation were analyzed with emphasis on the number of detected and treated tachyarrhythmic episodes and the outcome of each therapy. These and any other pertinent data were reviewed after being submitted to Ventritex from each of the participating centers.

Death classification. *Sudden death* was defined as death occurring within 1 h of symptoms or during sleep or unwitnessed in a previously medically stable patient (13), and was further classified on the basis of the presence or absence of tachyarrhythmias at the time of death: 1) Tachyarrhythmia-associated: In witnessed patients, documented ICD shocks or VT/VF during resuscitation, plus new tachyarrhythmic events (from ICD data log) at the time of death; or, in unwitnessed patients, evidence of delivered ICD therapy on the day of death. Stored intracardiac electrograms of specific tachyarrhythmias were classified according to published criteria (6). Tachyarrhythmia cycle length was determined on the basis of an average of 10 beats immediately preceding a delivered or aborted therapy. 2) Non-tachyarrhythmia-associated: Death in the absence of stored, new tachyarrhythmic events in unwitnessed patients, or documented asystole or EMD not immediately preceded by antitachyarrhythmic ICD therapy in witnessed, monitored patients. 3) Indeterminate: Insufficient information regarding either postmortem device data or witnessed shocks or documented tachyarrhythmia at the time of death.

Statistical analysis. Numeric values are expressed as the mean value ± SD or percentage. Comparisons were made using the Student *t* test, with p values <0.05 considered significant.

Table 1. Summary of Clinical, Implantation, Follow-Up and Postmortem Device Data on the 25 Study Patients

Pt. No	Age/ Gender	OHD	EF	NYHA Functional Class	Clinical Presentation	Implant Data		No. of Premortem VF Tests*	History of Appropriate† ICD Rx	Change in premortem (≤3 mos) Clinical Status	AA Drug at Time of Death
						DFT (J/V)	R Wave (mV)				
1	79/M	CAD	0.3	II	VT	8/350	7	2	Yes	CHF, ↑ shocks	PA, AM
2	61/M	IDCM	—	II	VT	8/350	5	1	Yes	↑ Shocks	Toc, Enc
3	51/M	CAD	0.3	II	Syncope	11/400	6	2	Yes	↑ Shocks	Am
4	61/M	CAD	0.2	II	VT	10/550	16	2	Yes	↑ Shocks	Ethm
5	67/M	CAD	—	II	VT	16/490	13	2	No	CHF	None
6	52/M	CAD	0.3	II	VF	16/470	13	3	Yes	No	Am
7	41/M	CAD	0.3	III	VT	8/550	20	1	No	—	None
8	74/M	CAD	0.3	II	VF	17/600	19	2	No	No	None
9	53/M	CAD	0.2	II	VT	11/350	7	2	Yes	↑ Shocks	Mx
10	45/M	CAD	0.2	II	VF	10/450	6	2	No	CHF, angina	None
11	75/F	CAD	0.4	I	VT	7/300	14	2	Yes	No	None
12	68/M	CAD	0.1	III	VT	20/550	5	2	Yes	CHF	Am
13	60/M	CAD	0.2	II	VF	12/300	10	2	Yes	CHF, ↑ shocks	Q, Mx
14	67/M	CAD	0.3	II	Syncope	11/400	13	2	Yes	CHF	Mx
15	74/M	IDCM	0.3	I	VT	20/550	20	1	Yes	No	PA
16	66/M	CAD	0.3	II	VT	—/300	13	2	Yes	↑ Shocks	Q
17	59/M	CAD	0.2	II	VT	16/580	16	2	Yes	Angina	Toc, Pf
18	70/M	CAD	—	II	VT	24/600	10	1	Yes	No	Q, Mx
19	60/M	CAD	0.37	I	VT	11/390	21	2	Yes	CHF	Sot
20	51/M	CAD	0.23	II	VT	—/650	11	2	Yes	CHF, ↑ shocks	PA, Mx
21	67/M	CAD	0.20	III	Syncope	13/450	10	1	No	No	Am
22	66/M	CAD	0.18	II	VT	15/470	22	2	Yes	No	—
23	69/M	CAD	0.31	II	VT	10/453	6	0	Yes	↑ Shocks	—
24	56/M	CAD	0.30	II	VF	—/750	11	2	Yes	↑ Shocks	Sot
25	48/M	CAD	—	II	VT	—/200	12	1	No	No	Pf

Results

Baseline clinical and implantation data. Baseline characteristics of the 25 study patients are summarized in Table 1. There were 24 men and 1 woman with a mean age of 62 ± 10 years (range 41 to 79), and 92% had coronary artery disease with a previous acute MI and a mean left ventricular ejection fraction (LVEF) of 0.25 ± 0.07 (range 0.12 to 0.40); five patients had previous coronary artery bypass graft surgery. Seventeen patients presented with sustained VT, five with VF and three with syncope and inducible sustained VT. A mean of 2.6 ± 1.4 (range 0 to 5) antiarrhythmic drugs were tried before ICD therapy. At device implantation, the mean defibrillation threshold (DFT) was 460 ± 126 V (13 ± 5 J), and the R wave amplitude was 12 ± 5 mV (range 5 to 22).

Follow-up events. Sudden death occurred 13 ± 11 months (range 0.2 to 45) after device implantation. All but one patient (no. 23), who had spontaneous, appropriate device therapies in the first week after implantation had ≥1 postimplantation assessment of device function showing appropriate detection and termination of induced VF and, when applicable, VT. Twenty-one patients (84%) had a history of ≥1 appropriate device therapy for either VT or VF, or both. Eighteen patients (72%) were receiving ≥1 antiarrhythmic drug at the time of death, including amiodarone alone or combined with another agent in five patients.

Characterization of terminal events. Death was witnessed in 18 (72%) of the 25 patients. In 13 of the 18 witnessed patients with available relevant data, 8 (62%) had no premonitory symptoms before collapse, and the remaining 5 (38%) complained of chest pain or respiratory distress within minutes of, or immediately preceding, collapse. Eight (44%) of the 18 witnessed patients were reported to have received ICD shocks at the time of collapse; 4 (22%) were observed specifically not to have received shocks; and in the remaining 6 (34%), information on shock delivery was available. In 20 patients for whom EMS was summoned soon after collapse, the following rhythms were reported (Table 1): VF in 5, VT in 3 and paced/EMD in the remaining 12. All 20 patients received advanced resuscitative measures with an unsuccessful outcome. Six of the seven unwitnessed patients had been seen in stable condition within 1 to 24 h before death.

Postmortem device analysis. Device interrogation was completed after death in 22 (88%) of 25 patients: 15 (68%) had new tachyarrhythmic events stored at the time (witnessed patients) or on the day of death (unwitnessed patients), and the remaining 7 (32%) had no new stored tachyarrhythmic events. Retrieved electrograms corresponding to the most recent ≤3 stored tachyarrhythmic events showed VT or VF in 14 patients and "make-break" potentials resulting from cut rate-sensing leads during autopsy in one patient (no. 25). The

Table 1. Continued

	Terminal Events				Postmortem ICD Analysis (mos)			
Follow-up (mos)	Location at Onset	Witnessed	Reported Shocks	First Documented Rhythm‡	New Stored Tachyarrhythmic Events§	Battery (V)	Shock Impedance‖	Detected Malfunction¶
18	OOH	Yes	Yes	VF	Yes	5.9	47	No
0.3	OOH	Yes	Yes	VT	Yes	>6.0	34	No
17	OOH	Yes	Yes	VF	Yes	5.8	47	No
7	OOH	Yes	Yes	Paced	Yes	>6.0	—	—
15	OOH	Yes	Yes	Paced	Yes	>6.0	—	No
32	OOH	Yes	Yes	VF	Yes	5.1	53	No
3	OOH	Yes	Yes	VF	—	—	—	—
6	OOH	Yes	Yes	VF	—	—	—	—
14	OOH	Yes	—	VT	Yes	>6.0	60	No
26	OOH	Yes	—	VT	Yes	>6.0	—	No
19	OOH	Yes	—	Paced	Yes	>6.0	40	No
45	OOH	Yes	—	Paced	Yes	5.3	—	No
36	OOH	Yes	—	Paced	Yes	5.6	—	No
5	OOH	No	—	Paced	Yes	>6.0	43	No
0.03	OOH	No	—	Paced	Yes	>6.0	28	No
23	OOH	No	—	—	Yes	>6.0	—	No
25	OOH	Yes	No	Paced	No	>6.0	—	No
2	OOH	Yes	No	Paced	No	>6.0	—	No
39	OOH	Yes	No	Paced	No	5.3	—	No
3	OOH	No	—	Paced	No	>6.0	—	No
0.2	OOH	No	—	—	No	>6.0	—	No
23	OOH	No	—	—	No	6.0	—	No
3	OOH	No	—	—	No	>6.0	—	No
16	OOH	Yes	—	—	—	—	—	—
0.5	OOH	Yes	No	Paced	Yes	>6.0	—	No

*Includes prehospital discharge tests; patient no. 23 had no testing but received several spontaneous, appropriate therapies before death. †Therapy for ventricular tachyarrhythmias, before the terminal event, documented by either telemetry/Holter monitor or stored intracardiac electrograms. ‡Obtained by the emergency medical service or from hospital telemetry; all patients in paced rhythm were in electromechanical dissociation. §From time or day of death; date and time of final ≤3 tachyarrhythmia episodes obtained from retrieved, stored intracardiac electrograms. ‖Provided only if the last high voltage therapy occurred in the last (most recent) tachyarrhythmia episode listed in the Therapy Sequencing data log. ¶Based on analysis performed at Ventritex on returned devices. AA = antiarrhythmic; Am = amiodarone; CAD = coronary artery disease; CHF = congestive heart failure; DFT = defibrillation threshold; EF = ejection fraction; Enc = encainide; Ethm = ethmozine; ICD = implantable cardioverter-defibrillator; IDCM = idiopathic dilated cardiomyopathy; J = joule; Mx = mexiletine; NYHA = New York Heart Association; OHD = organic heart disease; OOH = out of hospital; PA = procainamide; Pf = propafenone; Q = quinidine; Rx = therapy; Sot = sotalol; Toc = tocainide; VF = ventricular fibrillation; VT = ventricular tachycardia; V = volts.

cycle lengths of stored VT and VF events were 260 to 370 ms and ≤250 ms, respectively. In each of the 14 patients these final ≤3 VT or VF events were stored within seconds to minutes apart, consistent with closely timed recurrent VT/VF. Appropriate battery voltages (>5.1 V) were noted in all 22 patients whose devices were interrogated after death, and shock impedance was in the normal range (28 to 60 ohms) in the 8 patients with available data (Table 1). Analysis performed at Ventritex on the 21 returned generators showed no evidence of circuitry malfunction.

Tachyarrhythmia-versus nontachyarrhythmia-associated SD. Based on documentation of VT/VF during attempted resuscitation, witnessed ICD shocks (presumptive VT/VF) or stored ICD data, or a combination, SD was considered tachyarrhythmia-associated in 16 patients, nontachyarrhythmia-associated in 7 and indeterminate in 2 (Fig. 1). Of the two indeterminate cases (both witnessed), information on ICD shocks, EMS documented rhythm or device interrogation was not available in one patient (no. 24); the other patient (no. 25) most likely represented a nontachyarrhythmia-associated death because the patient had received no shocks at the time of collapse.

As shown in Table 2, relying on various criteria, the proportion of known or presumed tachyarrhythmic events in witnessed patients ranged from 67% (based on reported ICD shocks) to 79% (based on stored electrograms showing VT or VF). Three (43%) of the seven unwitnessed patients were presumed to have tachyarrhythmia based on evidence of new tachyarrhythmic events stored on the day of death.

Comparison of clinical characteristics of patients with tachyarrhythmia- versus nontachyarrhythmia-associated SD. Although the number of patients in either of these categories is small, the two groups were similar with respect to mean age, prevalence of coronary artery disease, baseline LVEF, New York Heart Association functional class, preterminal new or worsening congestive heart failure (CHF), use of antiarrhyth-

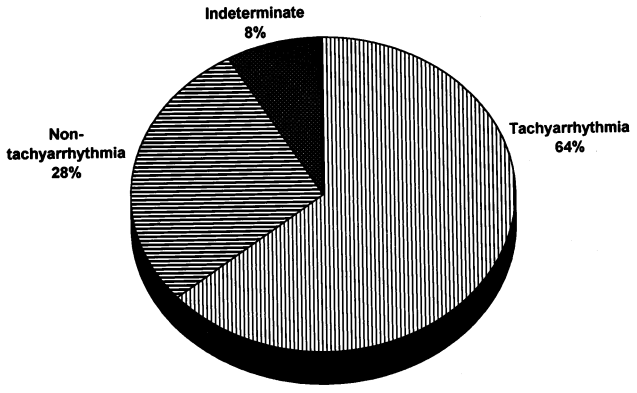

Figure 1. Pie chart illustrating the proportions of types of arrhythmic events associated with SD in ICD recipients who died out of the hospital.

mic drugs at the time of death and prevalence of symptoms just before witnessed collapse; and a similar proportion of patients (75%) in each group had used their devices against tachyarrhythmias before the terminal event. Moreover, both groups had similarly programmed bradycardia pacing rate (≥40 beats/min), including one patient (no. 19) who had a separate VVI pacemaker with a programmed lower rate of 70 beats/min; and a similar proportion of witnessed patients in each group had no premonitory symptoms before collapse.

Results of antitachyarrhythmia therapy in cases of tachyarrhythmia-associated SD. Table 3 summarizes tachyarrhythmia detections and ICD therapies in patients with tachyarrhythmia-associated SD, excluding those patients (nos. 7 and 8) who did not have postmortem ICD interrogation.

Programmed ICD configuration at time of death. In 9 (64%) of 14 patients the devices were programmed in a tiered, two-zone mode. In 8 (57%) of the 14 patients the programmed voltage for the first defibrillation shock exceeded the implant DFT by 100 to 280 V (i.e., >10 J), but in 6 patients this voltage margin ranged only from −50 to 50 V. In cases where the device was programmed in a two-zone configuration, the EHR detection time was set between 10 and 90 s, and the detection interval was typically programmed equal to the tachycardia zone detection interval. However, in one patient (no. 11) the EHR detection interval was unconventionally set equal to the fibrillation zone detection interval (≤330 ms) and, in addition, only a single therapy was specified for the tachycardia zone (i.e., the second through fourth tachycardia zone therapies were programmed "OFF" without a high-rate "timer" limit).

Table 2. Evidence of Terminal Tachyarrhythmic Events in the 25 Patients Who Had Out-of-Hospital Sudden Death

	Witnessed (n = 18)	Unwitnessed (n = 7)	Patients With Postmortem ICD Data (n = 21)*
Reported shocks	8/12 (67%)†	NA	8 (38%)
Documented VT or VF	8/17 (47%)‡	0	8 (38%)
Shocks or VT/VF	10 (56%)	NA	10 (48%)
Stored tachyarrhythmic EGMs from day of death§	11/14 (79%)	3 (43%)	14 (67%)

*Excludes three patients (nos. 7, 8 and 24) lacking postmortem interrogation and one patient (no. 25) whose stored intracardiac electrograms were filled with postmortem "make-break" potentials from cut rate-sensing leads. †Information regarding shock delivery (presence or absence) was available in only 12 of the 18 witnessed patients. ‡Obtained from 17 patients monitored by emergency medical service. §Denominator values refer to number of patients in a given category with available implantable cardioverter-defibrillator data. Data expressed as number (%) of patints. EGMs = electrograms; NA = not applicable; other abbreviations as in Table 1.

Tachyarrhythmia detections and therapy data. Between the time of last ICD interrogation and death (42 ± 29 days [range 5 to 90]), an average of 18 (range 1 to 108) and 11 (range 0 to 80) VT and VF detections, respectively, were recorded, for which an average of 23 (range 0 to 94) shocks were delivered and 3.7 (range 0 to 11) were aborted (for presumed nonsustained tachyarrhythmic episodes). Three patients (nos. 5, 12 and 14) received ≤2 shocks and one patient (no. 13) received only antitachycardia pacing for seven episodes of tachyarrhythmias.

Success rate of first therapies. Although most tachyarrhythmia therapies were *ultimately* successful (see later discussion), the first and, in some cases, subsequent therapies did not terminate the tachyarrhythmias. Specifically, of 11 patients who received shocks for tachyarrhythmias in the fibrillation zone, the first therapy was *unsuccessful* on ≥1 occasion in 7 (64%), yielding an overall first-therapy success rate of only 67% based on the total number of VF episodes (i.e., 62 successes in 92 episodes). Among the seven patients who received at least two consecutive fibrillation zone shocks on one or more occasion, four (nos. 2, 6, 9 and 11) (Table 3) required all six shocks (the maximal number delivered by the device for any given tachyarrhythmia episode). For tachyarrhythmias in the tachycardia zone, in 6 (75%) of 8 patients initial antitachycardia pacing therapy failed on ≥1 occasion, representing an overall success rate of 60% (i.e., 30 of 50 episodes).

Outcome of final therapy. Despite delivery of consecutive ≥2 fibrillation zone therapies in seven patients, all VT/VF episodes were *ultimately* terminated by the device in 11 (85%) of 13 patients; one patient (no. 10) had only nonsustained (aborted) events. One patient (no. 4) with an ethmozine-induced rise in DFT died during a treadmill test after multiple, initially effective, ICD and, after device inactivation, external shocks for intractable VT/VF. In an additional witnessed patient (no. 5) who received two appropriate ICD shocks (Fig. 2, A and B), the final intracardiac electrogram (Fig. 2C) registered ≈38 min after the patient's collapse, showed inappropriate redetection of "sinus rhythm" in the presence of ongoing polymorphic VT. The two patients (nos. 7 and 8) without postmortem ICD data were both witnessed at the time of collapse and reported by emergency medical staff and emergency room personnel to have received successful ICD shocks for recurrent VF, but eventually developed EMD.

Potential contributing factors to SD. During the 3 months before death, 10 (40%) of the 25 patients had one or more

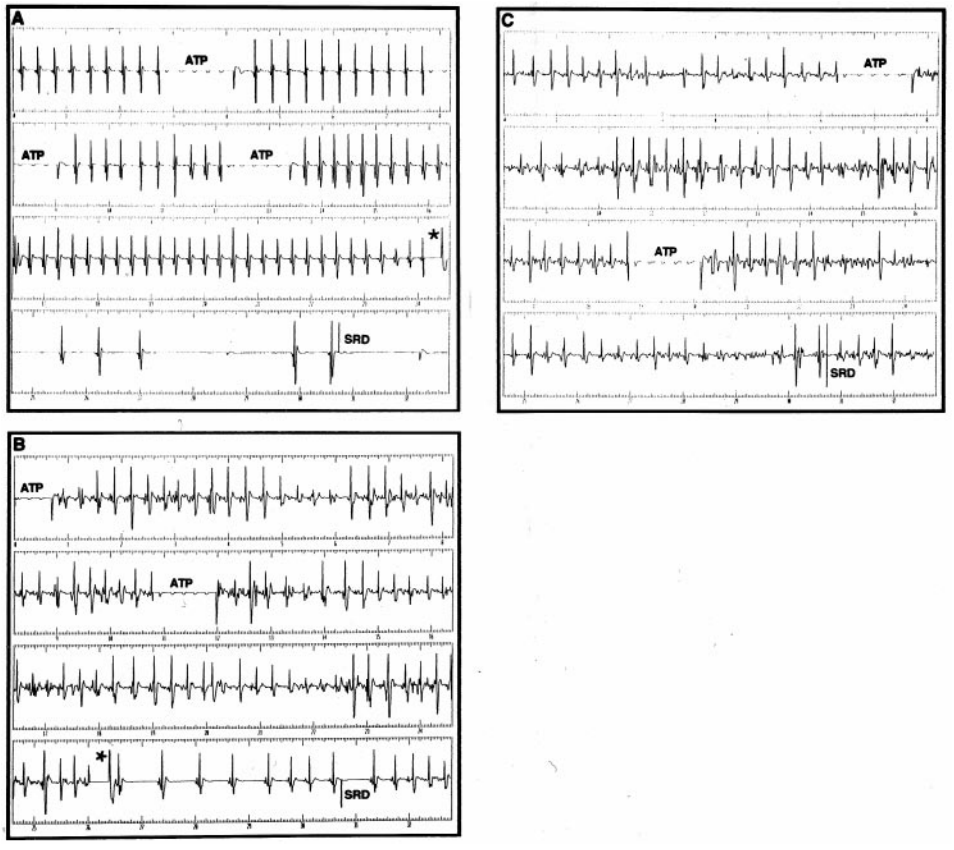

Figure 2. Final three stored tachyarrhythmic events (over a 38-min period) in patient no. 5, showing **(A)** sustained monomorphic VT terminated by a 550-V shock (*) after failed successive antitachycardia pacing therapies (ATP), occurring at 17:06 h with patient abruptly collapsing and, despite bystander cardiopulmonary resuscitation, found 6 min later by the emergency medical staff to be pulseless; **(B)** polymorphic VT successfully treated with a single shock after failed ATP, occurring at 17:43 h after unsuccessful advanced resuscitative efforts by the emergency medical staff and subsequently the emergency room staff; and **(C)** 1 min later, ongoing polymorphic VT, after ineffective ATP, inappropriately redetected as sinus rhythm (SRD). Note the progressive decrease and variability in the amplitude of the electrograms preceding SRD.

notable change in clinical status (Table 1): new or worsening CHF (n = 8) and angina (n = 2) and adverse antiarrhythmic drug effect (n = 1); and an additional 10 patients (40%) had an increase in the frequency (>3 episodes) of ICD shocks. At the time of death, hypokalemia (serum potassium of 2.0 mEq/liter) was identified in one patient (no. 12) and one patient (no. 5) had evidence of acute MI on postmortem examination.

Battery depletion or generator component failures were not identified in any of the 22 devices that were analyzed after death. Postshock tachyarrhythmia detection failure (patient no. 5) and inappropriate device programming (patient no. 11) theoretically might have played a role, because both can result in a delay or complete withholding of needed antitachyarrhythmia therapy. However, these potential device-related factors could not be definitively implicated in the causation of SD in any of the cases in our series (Fig. 2).

Discussion

In this multicenter experience with a third-generation ICD, out-of-hospital SD was associated with VT or VF in nearly two-thirds of cases. Death occurred despite successful, albeit often protracted, device therapy. In over one-third of cases we identified one or more clinical factors that might have contributed to SD, but none directly attributable to device failure.

Tachyarrhythmic versus nontachyarrhythmic SD. The finding in the present third-generation ICD experience that some two-thirds of SDs were associated with tachyarrhythmia is consistent with observations from earlier devices in which at least one-half of the cases of SDs occurred in association with VT or VF events (2–4,7).

The proportion of out-of-hospital SDs deemed nontachyarrhythmic (28%) in the present series is quite similar to that reported in patients without ICDs (14–16) and in patients with first-generation (nonpacing) ICDs (5), even though the incorporation of antibradycardia pacing in current devices might be expected to prevent, or at least reduce (17), the occurrence of bradyarrhythmic SD reported to occur in patients with nonpacing devices (18,19). This suggests that the mechanism(s) involved in bradyarrhythmic SD is far more complex than in cases of bradyarrhythmias due to conduction system disease, which, in general, are readily amenable to pacing therapy.

Sudden death and device-related factors. In contrast to earlier reports of SD in patients with first-generation ICDs (3–5), device-related factors, such as battery-depleted or deactivated ICDs and malfunctioning generators or defibrillation leads, did *not* appear to play a role in the present third-generation experience. However, relevant findings in two of our study patients bear mention: potentially deleterious, inappropriate device programming and device malsensing. In one patient (no. 11) unusual device programming (described earlier) might have resulted in prolonged, untreated recurrent VT that eventually led to VF, which, although ultimately terminated after multiple shocks (Table 3), may have caused irrevocable hemodynamic insult and death. The second patient (no. 5) had evidence on the final stored intracardiac electro-

Table 3. Summary of Device Responses and Outcome for Stored Tachyarrhythmic Events Obtained From Postmortem Device Analysis*

	Final Programmed ICD Variables						Tachyarrhythmic Therapy Events		
			Tiered Therapies†					No. of Shocks	
Pt. No.	Tachy Zone	Detection Intervals CL (ms)	First	Second	Final	Difference (V) Between First Fib Shock and DFT	No. of Detections	Aborted	Delivered‡
1	Tach	430	ATP	100	750		22		
	Fib	270	300	500	750	−50	11	4	15
2	Tach	480	ATP	200	750		4		
	Fib	330	500	650	750	150	6	0	13
3	Tach	360	ATP	300	750		1		
	Fib	270	600	650	750	200	80	5	82
4	Tach	375	300	500	750		11		
	Fib	280	650	750	750	100	3	5	26
5	Tach	350	ATP	550	750		3		
	Fib	270	550	650	750	50	0	0	2
6	Fib	360	750	750	750	280	9	10	16
9	Tach	415	ATP	300	750		2		
	Fib	300	400	650	750	50	4	0	12
10	Fib	330	500	650	750	50	3	4	0
11	Tach	460	ATP	OFF	OFF		105		
	Fib	330	500	650	750	200	3	2	8
12	Fib	360	650	750	750	0	1	4	2
13	Tach	430	ATP	100	550		7	0	0
	Fib	300	300	100	750	0	0	—	—
14	Fib	350	650	700	750	250	1	0	1
15	Fib	330	750	750	750	200	4	7	5
16	Tach	400	ATP	150	600		3		
	Fib	300	400	550	750	100	23	11	94

gram of inappropriate redetection of sinus rhythm in the setting of ongoing polymorphic VT (Fig. 2C); however, this event occurred ≈38 min after conversion of VT (without restoration of pulse) by the ICD (Fig. 2A). Previously, failure to redetect VF has been reported only in connection with laboratory-induced arrhythmias (20–23).

Reduced effectiveness of antitachyarrhythmia therapy. Although the ICD ultimately terminated most of the tachyarrhythmic episodes, the observed 64% first-shock (biphasic waveform) success rate for the final (≤11) fibrillation zone tachyarrhythmic episodes was lower than the ≈93% value reported for similar patients with comparable DFTs (12,24,25), and even below that described with monophasic shocks (26). In addition, we observed an overall antitachycardia pacing success rate of only 60% compared with a reported success rate of 92% to 97% in patients similar to ours (12,24–26).

Despite the statistical nature of defibrillation success (27), a purely random basis for all the first-shock therapy failures in this series is unlikely given the low implant DFTs, the high proportion of patients known to have received appropriate and successful ICD therapies (before death) and the one to three normal premortem VF tests in our study group. Conceivably, some first-shock failures might have been due to a subthreshold programmed energy, because in 43% of the patients the programmed first defibrillation shock voltage was only marginally greater, and in some cases equal to or lower than the implant DFT, not in keeping with the recommended "safety margin" (28). Under ordinary conditions, the DFT for an epicardial system is expected to remain stable over time (29). The increased frequency of first-shock failures in our series, therefore, implicates dynamic factors that subacutely or acutely altered adversely the energy requirement for terminating VT or VF, as suggested by premortem worsening CHF in 40% of our patients and preterminal symptoms suggestive of ischemia in one-third of witnessed SDs.

Potential mechanisms of SD patients with ICDs. Although the ultimate rhythm in patients dying suddenly with (or without) an ICD is expected to be asystole or EMD, such an outcome can arise directly as an initial, pacing-unresponsive bradyarrhythmia, or indirectly as the sequel to one or more VT or VF events. Acute EMD (without antecedent VT or VF) can occur on a primary cardiac (e.g., acute MI) or noncardiac basis (e.g., massive pulmonary embolism). Interpretation of VT or VF in the SD setting is more complex. Clearly, an acute pathophysiologic derangement, such as ischemia, can trigger VT or VF; in some cases, however, even if VT or VF so initiated is promptly detected and treated appropriately by the ICD ("effective" therapy), asystole or EMD can follow (2–5,18,19). Moreover, rapidly recurrent VT or VF events can, despite successful treatment, lead to eventual mechanical failure either from repeated bouts of myocardial hypoperfusion or from potentially harmful effects of defibrillating shocks on ventricular function in chronically failing myocardium (30,31), as suggested by the markedly reduced baseline LVEF (mean 0.25) in the present patient group compared with the

Table 3. Continued

Summary of ICD Therapy Outcome for Most Recent (≤11) Tachyarrhythmic Episodes				
			Final Tachy Therapy#	
Success of First Therapy§	No. of Episodes‖ Requiring ≥2 Successive Shocks	Maximal Successive No. of Shocks¶ (and Time [s]) to Redetect SR	Tachy Morphology (CL [ms])	Successful
1/1	0	1 (<10)		
8/11	2	3 (30–40)	VF (<250)	Yes
2/5	0			
7/8	(1)	6 (≥630–640)	PVT (300)	Yes
0/1	0			
11/11	0	1 (10–20)	VF (<250)	Yes
4/11	4	3 (25–35)		
1/4	2 (1)	5 (65–75)	PVT (320)	No
0/3	0			
(2/2)	0	1 (30–40)	PVT (300)	Inappropriate SRD
7/9	2	6 (≥630–640)	PVT (260)	Yes
0/2	0			
3/5	(1)	6 (≥630–640)	PVT (280)	Yes
NA	NA	NA	PVT (240)	Aborted Spontaneously
8/10				
2/3	(1)	6 (≥630–640)	PVT (<250)	Aborted spontaneously**
1/1	0	1 (5–15)	VF (<250)	Yes
7/7	0	1 (5–15)	MVT (400)	Yes
1/1	0	1 (<10)	MVT (250)	Yes
4/4	0	1 (15–25)	VT (300)	Aborted spontaneously**
1/11	7	3 (95–105)	VF (<250)	Aborted spontaneously**

*Excluding patient nos. 7 and 8, who did not have postmortem device interrogation. Patient numbers correspond to those listed in Table 1. †Numeric values represent shock voltage for cardioversion (Tach zone) or defibrillation (Fib zone). ‡Shocks delivered for tachyarrhythmias in either Tach or Fib zone. §Denominator refers to the number of first therapy attempts (≤11) in either Tach or Fib zone. Value in parentheses reflects Fib therapy after failed ATP. ‖Number in parentheses denotes episodes after failed ATP and/or low energy cardioversion. ¶For a given tachyarrhythmic episode; time refers to duration from delivery of the first therapy to redetection of "sinus rhythm" for a given tachyarrhythmic episode (therapy duration); 630 to 640 s is the maximal time reported even if the actual duration is greater. #For the most recent (final) tachyarrhythmic episode; successful outcome of delivered therapy is based on documented (from data log and stored electrogram) termination of final tachyarrhythmic episode. **Penultimate (within seconds of final) stored electrogram showed appropriate and successful therapies. ATP = antitachycardia pacing; CL = cycle length; Fib = fibrillation; MVT = monomorphic ventricular tachycardia; PVT = polymorphic ventricular tachycardia; SRD = sinus redetection; SR = sinus rhythm or any rhythm at a rate less than the programmed tachycardia detection rate; Tach = tachycardia; Tachy = tachyarrhythmia; other abbreviations as in Table 1.

≈0.30 to 0.35 range typical of patients in large ICD series (12,13,26).

Submaximal first-shock energies for VF and, more importantly, a lower than 100 V (~10 J) first-shock safety margin, as programmed in 86% and 43%, respectively, of our cases of tachyarrhythmia-associated SD (Table 3) may be sufficient under relatively stable laboratory testing conditions but may be inadequate during acute pathophysiologic changes.

Study limitations. The complexities of clarifying the nature of "terminal" events associated with SD are well known (32,33) and may not be clarified in the case of the ICD recipient dying suddenly (7,33). Despite availability of event markers and time-stamped stored electrograms, there often remain uncertainties about the precise timing of the fatal event. Moreover, autopsies were performed in only three of our patients. A higher autopsy rate might have provided additional insight into the mechanisms of SD in our patient group; for instance, evidence for some acute events would help to explain both the immediate cause of death (in some cases noncardiac [7]) and the reduced effectiveness of initial ICD therapies. In addition, the present series involved epicardial lead systems only and devices from a single manufacturer; however, there are no reasons to suspect device-specific differences in the final event(s), although with the current widespread use of transvenous lead systems, ICD lead failures might play a larger role in the cause of SD in the future (20–23,34).

Conclusions. The present study suggests that, by and large, SD in patients with ICD reflects acute myocardial mechanical deterioration, with "incidental" tachyarrhythmias or bradyarrhythmias that, though effectively treated by the device, may still lead to death. However, whether or not the already remarkably low SD rate in device-treated patients can be further reduced ultimately would depend on the mechanism(s) of SD in ICD recipients. The possibility that some cases of SD in patients with ICDs might be preventable merits continued investigation.

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Appendix

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