Failure to Treat Life-Threatening Ventricular Tachyarrhythmias in Contemporary Implantable Cardioverter–Defibrillators

Implications for Strategic Programming

See Editorial by Krainski and Birgersdotter-Green

BACKGROUND: In clinical trials, manufacturer-specific, strategic programming of implantable cardioverter–defibrillators (ICDs), including faster detection rates, reduces unnecessary therapy but permits therapy for ventricular tachycardia/ventricular fibrillation (VF). Present consensus recommends a generic rate threshold between 185 and 200 beats per minute, which exceeds the rate tested in clinical trials for some manufacturers. In a case series, we sought to determine the relationship between programmed parameters and failure of modern ICDs to treat VF.

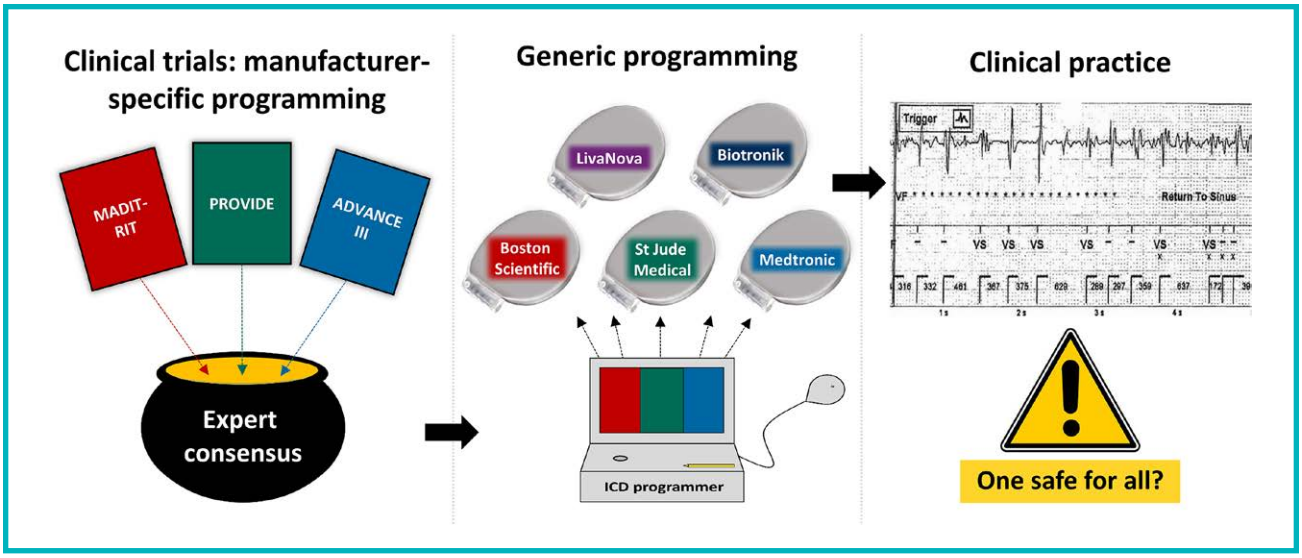
METHODS AND RESULTS: We reviewed cases in which normally functioning ICDs failed to deliver timely therapy for VF from April 2015 to January 2017 at 4 institutions. Of 10 ambulatory patients, 5 died from untreated VF, 4 had cardiac arrests requiring external shocks, and 1 was rescued by a delayed ICD shock. VF did not satisfy programmed detection criteria in 9 patients (90%). Seven of these patients had slowest detection rates that were consistent with generic recommendations but not tested in a peer-reviewed trial for their manufacturer's ICDs. Manufacturer-specific factors interacted with fast detection rates to withhold therapy, including strict VF episode termination rules, enhancements to minimize T-wave oversensing, and features that restrict therapy to regular rhythms in ventricular tachycardia zones. Untreated VF despite recommended programming accounted for 56% of sudden deaths and 11% of all deaths during the study period.

CONCLUSIONS: Complex and unanticipated interactions between manufacturer-specific features and generic programming can prevent therapy for VF. More data are needed to assess the risks and benefits of translating evidence-based detection parameters from one manufacturer to another.

Anna Margrethe Thøgersen, MD, DMSc
Jacob Moesgaard Larsen, MD, PhD
Jens Brock Johansen, MD, PhD
Moeen Abedin, MD
Charles D. Swerdlow, MD

Correspondence to: Charles D. Swerdlow, MD, Cedars-Sinai Heart Institute, Cedars-Sinai Medical Center, 414 N Camden Dr, Ste 1100, Beverly Hills, CA 90210. E-mail swerdlow@ucla.edu

Key Words: consensus ■ primary prevention ■ secondary prevention ■ shock ■ ventricular fibrillation



WHAT IS KNOWN

- In clinical trials, manufacturer-specific, strategic programming of implantable cardioverter–defibrillators (ICDs) reduces unnecessary therapy but permits therapy for ventricular tachycardia/fibrillation.
- Present guidelines provide generic programming recommendations. For some ICDs, these recommendations are extrapolated from evidence obtained using other manufacturer's ICDs with different sensing and detection features.

WHAT THE STUDY ADDS

- No patient with manufacturer-specific, programming validated in a clinical trial failed to receive an initial, timely shock for ventricular fibrillation.
- Most patients who did not receive timely ventricular fibrillation shocks had ICDs programmed consistent with guidelines extrapolated from evidence obtained using another manufacturer's ICDs with different sensing and detection features.
- More data are needed to assess both the benefits and risks of applying generic programming recommendations to specific ICDs in which these recommendations have not been validated clinically.

Reliable sensing and detection of ventricular fibrillation (VF) and rapid, life-threatening ventricular tachycardia (VT) was a challenge for early implantable cardioverter–defibrillators (ICDs). Manufacturers responded with improved technology; in this century, reports of failure to treat life-threatening VT or VF have been rare and limited to one[1–4] or a few patients.[5,6]

In the last decade, investigators focused on preventing unnecessary ICD therapies by strategic programming, including faster detection rates, longer detection times, discriminators for supraventricular tachycardia (SVT), and enhancements to prevent oversensing.[7] Clinical studies[8–13] report that strategic programming reduces unnecessary therapies without withholding therapy for life-threatening VT/VF. Each study used ICDs from a single manufacturer. Programmed parameters were strictly controlled within each study, but they varied among studies. The 2015 HRS/EHRA/APHRS/SOLAECE Consensus Statement on Optimal ICD Programming and Testing[7] (Consensus Statement) provides generic programming recommendations. For some ICDs, these recommendations are necessarily extrapolated from evidence obtained using another manufacturer's ICDs with different sensing and detection features. In a series of cases, we sought to determine the reasons that contemporary ICD systems failed to deliver therapy for life-threatening VT/VF in the era of strategic programming.

METHODS

Patient Selection

The 10 patients were ambulatory, expected to live >1 year, and did not have an acute illness. They met these criteria: (1) a shock for life-threatening VT/VF was either not delivered or delayed significantly, resulting in death or a major adverse event. For simplicity, we refer to failure to deliver timely therapy. (2) The ICD system functioned normally. (3) VT/VF detection and therapies were programmed ON. (4) The amplitude of sinus-rhythm R waves exceeded 5 mV at implant and follow-up. Index events occurred from April 2015 to January 2017. No patient who met the inclusion criteria was excluded. Patients 1 to 8 were programmed and followed at 1 of the 4 participating

institutions; patients 9 and 10 were programmed and followed at a community hospital; they were brought to a participating institution for tertiary care during their index events. To estimate completeness of inclusion, we reviewed all deaths and resuscitated cardiac arrests in ICD patients during the study period at the 2 institutions that tracked these data. This study was approved by the Institutional Committees on Human Research at the authors' institutions.

ICD Programming: Compliance With Recommendations

The Consensus Statement[7] provides 32 generic recommendations for tachycardia detection. Its online Appendix B provides programming examples that may be considered manufacturer-preferred values.

We reviewed programming for compliance or noncompliance with both generic and manufacturer-preferred recommendations that influence detection of VT/VF, including rate threshold and SVT discriminators. Programmed sensitivity and duration also influence detection; but, in all study patients, sensitivity was nominal and noncompliant durations were shorter than recommended, increasing rather than decreasing the likelihood of VT/VF detection.

The Consensus Statement recommends programming the slowest rate threshold between 185 and 200 beats per minute for primary prevention and ≤200 beats per minute for secondary prevention (but at least 10 beats per minute below the clinical VT rate),[7] independent of whether this rate defines a VT or VF zone. For each manufacturer, Appendix B provides both a single, preferred rate threshold and a range of acceptable rate thresholds that are within guidelines. For primary prevention patients, preferred rate thresholds vary from 185 to 188 beats per minute; the range of acceptable thresholds extends from the preferred value to 200 beats per minute. For some ICDs, the Consensus Statement and its Appendix B permits more restrictive programming than tested in clinical trials,[8–13] restricting therapy to faster rates.

RESULTS

Table 1 summarizes patient demographics. Table I in the Data Supplement shows device and implant data. Table 2 shows programmed parameters. One column indicates whether rate threshold programming complied with the generic recommendations of the Consensus Statement (consensus recommendations) and by extension was within guidelines as determined by Appendix B. A second column indicates whether the rate threshold equaled Appendix B's preferred threshold for the specific manufacturer. Table 3 summarizes manufacturer-specific features that contributed to failure to deliver timely shocks.

Of the 8 patients who underwent implant testing, all had reliable sensing and detection of VF (maximum delay 1 s). Overall, 5 patients died of untreated VF, 4 patients required external defibrillation, and 1 patient was rescued by the ICD after aborted shocks. There was no evidence of a primary cause of cardiac arrest (eg, acute myocardial infarction, pulmonary embolus) in the 5 survivors or 3 patients who died after prolonged resuscitation. The flow chart in Figure 1 summarizes reasons for failure to deliver VF therapy.

Programming Consistent With Generic Consensus Recommendations (Cases 1 to 8)

In cases 1 to 8, rate thresholds complied with generic consensus recommendations; and SVT-VT discriminators complied with manufacturer preferences in Appendix B.[7]

Premature VF Episode Termination (Cases 1 and 2)

In 2 cases, ICDs detected VF, but the device-defined VF episode terminated prematurely because of intermittent undersensing.

Case 1

A 66-year-old man with a primary prevention St. Jude Medical ICD had VF that was detected rapidly and defibrillated with a single shock. His physician found no change in clinical status and made no changes in programming or medication. Two months later, the patient had a witnessed, out-of-hospital cardiac arrest. Paramedics defibrillated him from VF 13 minutes after collapse. Spontaneous circulation returned, but he died of anoxic encephalopathy.

Analysis. Figure 2 shows that the stored electrogram (EGM) began with monomorphic VT slower than the programmed VT detection interval (315 ms, 190 beats per minute); this VT degenerated to VF. The ICD detected VF, but terminated the device-defined VF episode prematurely (Return to Sinus), aborting the shock because it undersensed VF EGMs. After this, the ICD neither detected VF nor stored EGMs before paramedics performed external defibrillation. The shock would have been delivered if the VT interval had been programmed to the clinically validated value of 333 ms (180 beats per minute)[12] rather than the manufacturer-preferred value (Consensus Statement Appendix B[7]; Figure 2 and Figure I in the Data Supplement).

Case 2

A 76-year-old male with a secondary prevention St. Jude Medical ICD for out-of-hospital VF in 2008 presented with syncope in 2015.

Analysis. Figure 3 shows that premature episode termination occurred for the initiating VT because antitachycardia pacing slowed the VT to 318 to 332 ms (180–189 beats per minute) below the rate threshold of

Table 1. Clinical Data

Case	Age, y	Sex	Heart Disease	LVEF	NYHA Class	Indication	β Blocker	Antiarrhythmic
1	66	M	CAD	0.30	2	1°→2° (VF)	Y	Amiodarone
2	76	M	CAD	0.40	1	2° (VF)	Y	N
3	62	M	CAD	0.25	2	1°	Y	N
4	79	M	CAD	0.20	3	1°→2° (VT)	Y	N
5	41	M	CAD	0.18	3	1°	Y	N
6	87	M	CAD	0.35	2	1°	Y	N
7	75	M	CAD	0.20	3	2° (VF)	Y	N
8	67	M	NICM	0.45	2	2° (VF)	Y	N
9	14	M	Vasospastic MI	0.35	2	1°→2° (VT)	N	Amiodarone
10	44	M	NICM	0.20	3	1°→2° (VT)	Y	Amiodarone Mexiletine

1° indicates primary prevention for implantable cardioverter–defibrillator (ICD), 2° indicates secondary prevention for ICD, 1°→2° indicates primary prevention indication at implant with a subsequent VT or VF requiring ICD therapy. CAD indicates coronary artery disease; LVEF, left ventricular ejection fraction; M, male; MI, myocardial infarction; N, no; NICM, nonischemic cardiomyopathy; NYHA, New York Heart Association; VF, ventricular fibrillation; VT, ventricular tachycardia; and Y, yes.

300 ms (200) beats per minute. This episode would not have terminated prematurely if the VT interval had been programmed to the clinically validated value of 333 ms (180 beats per minute).[12] VT then degenerated to VF.

Three VF episodes terminated prematurely because of undersensing. It is likely that sensing enhancements designed to prevent T-wave oversensing[14] contributed to undersensing VF (Figure II in the Data Supplement).

Table 2. Programmed Parameters

Case	Sensitivity (mV)	Sensing Enhancements	Monitor (beats per minute/ms)	VT/VT1 (beats per minute/ms); Duration	FVT/VT2 (beats per minute/ms); Duration	VF (beats per minute/ms); Duration	Programmed Rate Threshold Consistent with†		
							Clinical Evidence	Generic Range	Manufacturer-Preferred Value
1	0.5*	LFA, Decay Delay 60 ms, Threshold Start 50%, SecureSense	OFF	OFF	190/315*; 24 intervals	250/240*; 12 intervals	No (VT2 and VF)[12]	Yes	VT2: No VF: Yes
2	0.3	Decay Delay 60 ms, Threshold Start 62.5%	OFF	OFF	200/300*; 30 intervals	240/250*; 12 intervals	No (VT2 and VF)[12]	Yes	VT2: No VF: Yes
3	0.3	None	150/400; 32 intervals	OFF	OFF	200/300*; 30/40 intervals	No (VF)[8–10,13]	Yes	No
4	0.5*	LFA, Decay Delay 60 ms, Threshold Start 50%, SecureSense	OFF	OFF	200/300*; 18 intervals	250/240*; 12 intervals	No (VT2 and VF)[12]	Yes	VT2: No VF: Yes
5	0.3	T-wave rejection, RV lead noise, LIA	Monitor 150/400; 44 intervals	OFF	188/320*; 40 intervals	200/300*; 18/24 intervals	No (VF) [8–10,13]	Yes	No (FVT, VF)
6	0.3	T-wave rejection, RV lead noise, LIA	OFF	150/400; 32 intervals	200/300*; 30/40 intervals	230/261*; 30/40 intervals	No (VF)[8–10,13]	Yes	No
7	0.8	None	OFF	150/400*; 26 intervals	182/330*; 22 intervals	231/260*; 18/24 intervals	No data	Yes	Yes
8	0.6	None	160/375; 30 s	OFF	200/300*; 5 s	250/240; 2.5 s	Yes[11]	Yes	No
9	0.5*	LFA, Decay Delay 60 ms; Threshold Start 50%; SecureSense	169/355; 18 intervals	OFF	200/300*; 30 intervals	250/240*; 18 intervals	No[12]	No	VT2: No VF: Yes
10	0.3	T-wave rejection, RV lead noise, LIA	167/360; 32 intervals	OFF	200/300*; 30/40 intervals	240/250*; 30/40 intervals	No (FVT, VF)[8–10,13]	No	No (FVT, VF)

FVT indicates fast VT zone; LFA, low-frequency attenuation filter; LIA, Lead Integrity Alert; RV, right ventricular; VF, ventricular fibrillation; and VT, ventricular tachycardia.
*Values indicate sensing thresholds and detection rate thresholds not tested in clinical trials.
†Clinical Evidence denotes values programmed in referenced peer-reviewed clinical trials. Generic Range denotes recommended range in Consensus Statement. Manufacturer-preferred value denotes value indicated in the Consensus Statement.

Table 3. Causes of Failure of Timely VF Therapy

Case	Recommended Programming	ICD Response to Clinical Arrhythmia		Root Cause of Failure to Treat Clinical VT/VF	Additional Factors
		VT (Cycle Length)	VF		
1	Yes	No therapy (395–345 ms)	No therapy	VT: Rate VF: Premature episode termination; rate and duration	Features to prevent T-wave oversensing*
2	Yes	270–320 ms	Therapy delay >1 min	Premature episode termination	Features to prevent T-wave oversensing*
3	Yes	No therapy (300–320 ms)	No therapy	VT/VF: Rate and duration	
4	Yes	…	No therapy	Rate and duration	Features to prevent T-wave oversensing
5	Yes	No therapy (310–350 ms)	No therapy	VT: Rate, Consecutive interval counting VF: Rate and duration	
6	Yes	…	No therapy	VF: Rate and duration	Consecutive interval counting (VT zone)
7	Yes	No therapy (344–375 ms)	Therapy delay 14 min	VT: Onset VF: Rate and stability	Onset and stability discriminators
8	Yes	No therapy (375–345 ms)	No therapy after 6th shock	VT: Rate VF: Postshock undersensing, rate and duration	
9	No	No therapy (345–360 ms)	No therapy	VT: Rate VF: Rate and duration	Features to prevent T-wave oversensing*
10	No	No therapy (300–330 ms)	Therapy delay 9 min	VT: Rate VF: Rate and duration	

ICD indicates implantable cardioverter–defibrillator; VF, ventricular fibrillation; and VT, ventricular tachycardia.
*Decay Delay, Threshold Start, low-frequency attenuation (LFA) filter.

VF Never Detected (Cases 3 to 7)

In 4 cases, the ICD did not detect the index episode of VF.

Case 3

A 62-year-old man with a primary prevention Medtronic cardiac resynchronization therapy ICD died suddenly and unexpectedly in his bedroom. A Lead Integrity Alert[15] was triggered by double-counted EGMs and transmitted to a remote monitoring network.

Analysis. Figure 4 and Figure III in the Data Supplement show transmitted EGMs. In each Figure, Panel 1 shows the onset of monomorphic VT as a device-defined nonsustained episode, triggered by intervals that are transiently shorter than the VF detection interval of 300 ms. EGMs from multiple nonsustained episodes over the next 46 minutes show that VT slowed to cycle length 290 to 330 ms and degenerated to polymorphic VT/VF. Monomorphic VT would have been detected with a clinically validated VF interval of 330 ms (182 beats per minute)[8,9]; transmitted data are insufficient to determine whether detection would have occurred with the validated value of 320 ms (188 beats per minute).[10,13]

Case 4

A 79-year-old man with a primary prevention St. Jude Medical cardiac resynchronization therapy ICD had monomorphic VT with cycle length 260 to 280 ms in December 2016 that was detected and treated in the VT zone (240–300 ms). In January 2017, he had a witnessed cardiac arrest while sitting in a chair. Cardiopulmonary resuscitation was performed until paramedics arrived 9 minutes later and defibrillated him from polymorphic VT/VF to sinus rhythm (Figure IVA in the Data Supplement). He died despite pro-

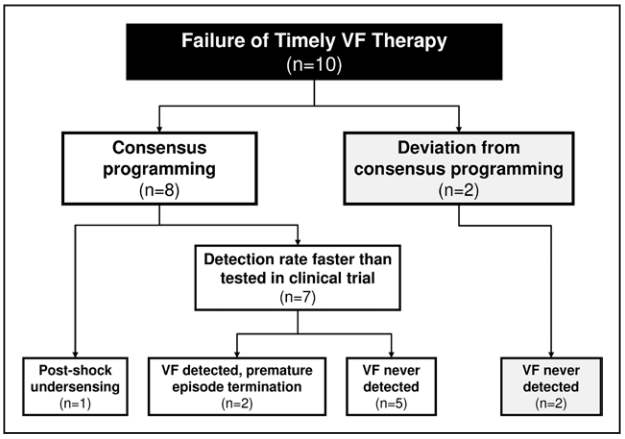


Figure 1. Flow chart summarizes implantable cardioverter–defibrillator (ICD) programming and reasons for failure to deliver timely ventricular fibrillation (VF) therapy.

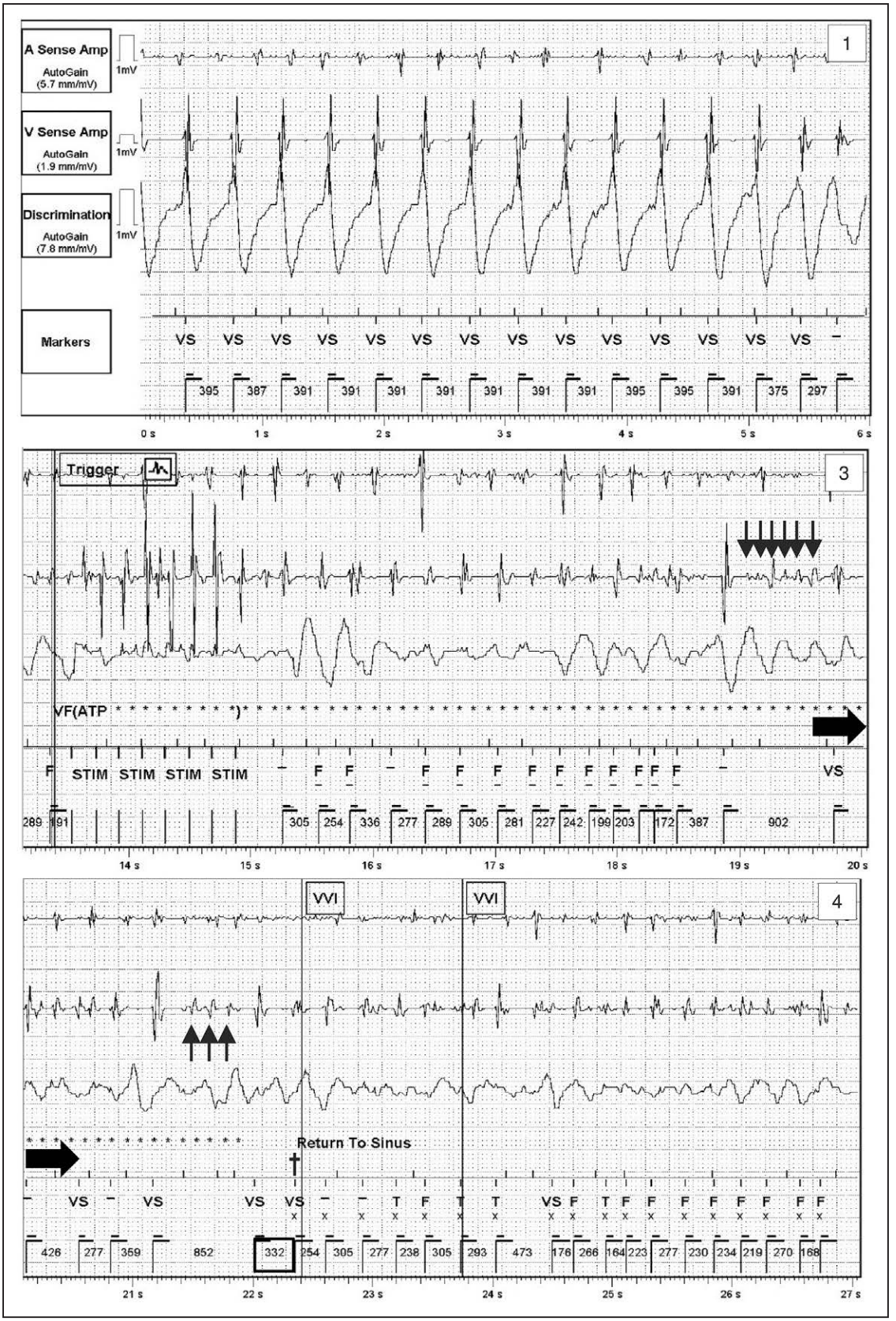


Figure 2. Case 1. Stored electrogram (EGM) displays 3 of 4 continuous panels showing filtered atrial EGM (A Sense Amp), filtered right ventricular (RV) sensing EGM (V Sense Amp), shock EGM (RV coil Can, discrimination), dual-chamber markers, ventricular intervals in ms, and timeline in s (Figure I in the Data Supplement).
Panel 1 shows ongoing monomorphic ventricular tachycardia (VT) at cycle length of 387 to 395 ms, slower than (*Continued*)

longed resuscitation. During resuscitation, he had 3 episodes of monomorphic VT that the ICD detected and treated.

Analysis. Figure IVB in the Data Supplement shows the first of 3 similar episodes. Each persisted for an unknown duration with cycle length slower than the VT interval (300 ms) before accelerating into the VT zone. The subsequent stored VTs suggest that untreated VF may have begun with VT slower than the detection interval and that this VT degenerated to VF, which was undersensed.

Case 5

A 41-year-old man suffered an arrhythmic cardiac arrest on in-hospital telemetry, the night after elective implantation of a primary prevention Medtronic ICD. He had no metabolic abnormalities, and he received no antiarrhythmic drugs. After resuscitation, he required inotropic support and underwent heart transplantation 6 weeks later.

Analysis. Figure 5A shows that initial episode of low-frequency VF did not fulfill the programmed detection criteria for either VF (18/24 intervals shorter than 300 ms) or VT (40 consecutive intervals,[16] 300–319 ms). Double counting triggered the Lead Integrity Alert,[15] which extended the number of intervals to detect VF to 30 of 40. After external defibrillation, monomorphic VT occurred and degenerated to polymorphic VT with cycle length 310 to 350 ms (Figure VB in the Data Supplement). This required a second external defibrillation (Figure 5C Panel 2). High-frequency VF recurred a 2 s later (Figure 5C Panel 3; Figure V in the Data Supplement).

Case 6

An 87-year-old man with complete heart block and a primary prevention Medtronic cardiac resynchronization therapy ICD had a cardiac arrest while sleeping. His caregiver called 911. Paramedics found him in VF and defibrillated him to pulseless electric activity, but he did not regain spontaneous circulation. The ICD transmitted a Lead Integrity Alert.

Analysis. The transmitted EGMs in Figure VI in the Data Supplement show VF with undersensing that never fulfilled the detection criteria for VF (30/40 intervals shorter than 300 ms). Further, detection of VT did not occur despite a slow VT interval (400 ms) because Medtronic uses consecutive interval counting in the VT zone. Undersensing or entrance block caused occasional device-measured intervals slower than the VT interval, which repeatedly reset the VT count to 0 (Figure VI in the Data Supplement).

Case 7

A 75-year-old man with long-standing atrial fibrillation had an ICD implanted in 1994 for out-of-hospital VF and upgraded in 2011 to a Biotronik cardiac resynchronization therapy ICD. In 2015, his electrophysiologist increased the VT detection interval to 400 ms after the patient had suspected arrhythmic syncope. One month later, he had a witnessed cardiac arrest followed by immediate cardiopulmonary resuscitation. Paramedics found him in VF and defibrillated him to pulseless electric activity. He died after a prolonged resuscitation including repetitive sequences of VF.

Analysis. Relevant ICD parameters include detection intervals consistent with recommended secondary prevention programming (VT1: 400 ms, VT2: 330 ms, VF: 260 ms) and nominal values of single-chamber SVT-VT discriminators: Onset at 20% and Stability at 24 ms.[7,17] Stored EGMs at the time of collapse recorded monomorphic VT at cycle length 375 to 344 ms in the VT

Figure 2 Continued. the programmed VT detection interval of 315 ms. The rhythm becomes polymorphic at 6 s (end of Panel 1) and then degenerates to VF, which is detected at 13.4 s (beginning of Panel 3). The ICD delivers antitachycardia pacing (ATP, STIM markers, 13.4–14.9 s) while charging (line of small asterisks, 13.4–21.8 s). However, at 22.4 s (Panel 4), the ICD classifies the rhythm as sinus, aborting the shock and resetting VT and ventricular fibrillation (VF) counters to 0 (Return to Sinus marker). Markers denote intervals classified (binned) in the Sinus zone (VS), VT zone (T), or VF zone (F). Intervals are not binned (–) in any zone if zones differ for the index interval and its average with preceding 3 intervals.[14] Return to Sinus occurs when a programmable number of consecutive classified (binned) intervals are slower than the slowest detection interval. In this case, Return to Sinus was programmed to the nominal value of 5 intervals (range 3–7 intervals). Subsequently, clinical polymorphic VT/VF did not satisfy the programmed number of intervals to detection VT (24 intervals shorter than 315 ms) or VF (12 intervals shorter than 240 ms). Undersensing of low-amplitude VF EGMs after high-amplitude VF EGMs was critical in erroneous premature termination of the device-defined VF episode and aborting the shock. Arrows in Panel 3 denote that 6 sequential VF EGMs are not sensed after a high amplitude because EGM amplitude decreases faster than dynamically adjusting sensitivity can adapt. Features to prevent T-wave oversensing may also have contributed to undersensed EGMs. Signals with comparably low amplitude were sensed reliably toward the end of Panel 2 (Figure I in the Data Supplement). The final undersensing event occurs at 21.2 s (Panel 4) after 3 sequentially undersensed EGMs with amplitude 0.91 to 1.1. mV (third upward arrow). Undersensing these EGMs results in a device-defined ventricular interval of 852 ms (VS marker). The subsequent EGM is sensed accurately with an interval of 332 ms (black box), resulting in the fifth consecutive binned, VS interval (†) and premature episode termination. However, if VT detection had been programmed to clinically tested value of 333 ms, the 332 ms interval would have been unclassified (–), and premature episode termination would not have occurred. Because the ICD completed charging during the 852 ms interval (end of line of asterisks), it would have delivered the shock synchronous with the EGM ending the 254 ms interval after the † EGM (first binned VT or VF interval after charging). STIM indicates ventricular antitachycardia pacing; VS, ventricular sensed event; and VVI, ventricular demand pacing.

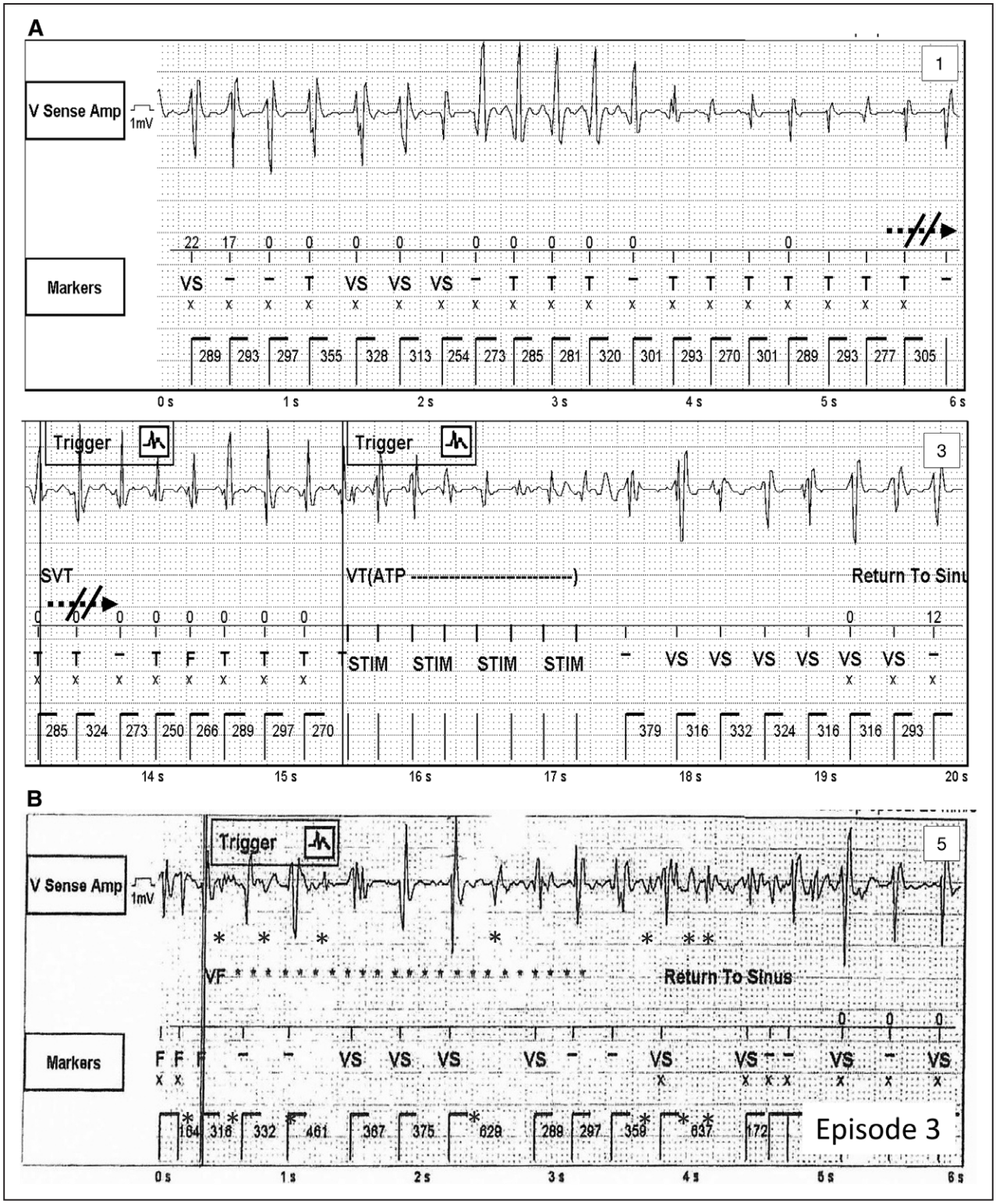


Figure 3. Case 2. Stored electrograms (EGMs) display filtered right ventricular (RV) dedicated bipolar sensing EGM (V Sense Amp), ventricular markers, ventricular intervals in ms, and timeline in s.

These multiple device-defined episodes were recorded during a single clinical ventricular tachycardia/ventricular fibrillation (VT/VF) episode. **A**, Monomorphic VT. Discontinuous Panels 1 and 3 show that VT begins an unknown time before the recording. The VT cycle length straddles the Sinus VT boundary of 300 ms so that multiple intervals in Panel 2 remain unclassified. VT is detected at 15.4 s in Panel 3 (VT(ATP—-…)) and antitachycardia pacing (ATP) is delivered immediately (STIM markers). After ATP, VT slows to 318 to 332 ms in the Sinus zone, resulting in episode termination (Return to Sinus; **B**) VF. The next stored EGM recorded about a minute later showed detection of VF. It is likely that the monomorphic VT degenerated (*Continued*)

zone that did not fulfill the Onset criterion and was thus classified as SVT (Figure 6A). The stored EGM in Figure 6B was recorded 13 minutes later and shows VF. Because of intermittent undersensing, the calculated ventricular cycle length (276 ms) was in the VT2 zone, so the Stability algorithm was applied and determined that the rhythm was irregular. Thus, the ICD classified VF as SVT and withheld therapy (Figure 6).

Postshock Undersensing (Case 8)

Case 8

A 67-year-old man underwent Boston Scientific ICD implantation with an integrated bipolar lead after out-of-hospital VF. One month later, he suffered a witnessed cardiac arrest. Paramedics arrived 12 minutes later and defibrillated VF after a long resuscitation. With prolonged hospitalization, the patient recovered completely and underwent VT ablation.

Analysis. Figure VII in the Data Supplement shows monomorphic VT that degenerated to VF, which was detected and defibrillated to sinus rhythm. This initiated a repetitive sequence of recurrent VF followed by successful defibrillation. However, the amplitude of the sensed EGMs decreased progressively in successive postshock recurrences of VF until they were undersensed consistently and VF remained undetected (Figure VII in the Data Supplement).

Deviation From Consensus Programming (Cases 9 to 10)

In case 9, the VT interval was set to 300 ms after apparently successful ablation of slower VT; the patient presented with VT slower than 300 ms and subsequent undersensed VF (Figure VIII in the Data Supplement). In case 10, the VT detection interval was not increased after antiarrhythmic drug treatment was changed (Figure IX in the Data Supplement; Data Supplement).

Completeness of the Data Set

No patient who met the study criteria was knowingly excluded. We reviewed all cardiac arrests and other deaths in ICD patients during the study period at the 2 institutions that tracked these data. These institutions contributed 8 of 10 cases, including 3 of the 4 cardiac arrest cases and all 5 fatal cases. There were no other resuscitated cardiac arrests during the study period. Of 47 total decedents during the study period, 9 died suddenly. In addition to the 5 study patients who died, 2 patients died of pulseless electric activity, 1 patient with a fractured defibrillation lead died of VF that was detected but not defibrillated, and 1 patient died suddenly without postmortem ICD interrogation (Table II in the Data Supplement). Thus, failure to detect VF despite recommended programming was responsible for 5 of 8 adjudicated sudden deaths (62%), 56% of total sudden deaths, and 11% of all deaths in ICD patients.

DISCUSSION

We present a series of contemporary ICD patients who did not receive timely VF shocks. Our principal finding is that, in most patients, ICD programming deviated from values validated in manufacturer-specific, clinical trials,[8–13] which form the evidence base for the Consensus Statement,[7] but they complied with more restrictive, generic recommendations of the Consensus Statement. Failure to detect VF despite generically recommended programming was the most common cause of sudden death at the 2 centers that tracked these data. These data suggest that differences in sensing and detection methods among manufacturers may limit the applicability of generic programming recommendations.

Prior Studies: Programming Sensing and Detection of VT/VF

In the last decade, randomized clinical trials[9–12] and prospective observational studies[8,13] in primary prevention patients found that faster rate thresholds of 180 to 200 beats per minute and longer durations of at least 6 to 12 s reduce unnecessary shocks[8–13] and may reduce mortality.[18] Programmed parameters were tightly controlled within each study using ICDs from a single manufacturer, but varied among studies using different manufacturers' ICDs. Importantly, studies report no deaths from untreated VT/VF. Programmed, slowest rate thresholds were 182 to 188 beats per minute for Medtronic ICDs[8–10,13] (VF zone), 180 beats per minute for St. Jude ICDs[12] (VT zone), and 200 beats per minute for Boston Scientific ICDs[11] (VF zone). Data on strategic programming of secondary prevention patients are limited to subgroup analyses of 1 randomized[19] and 1 observational study,[13] each using Medtronic ICDs; these data support programming 188 beats per minute if the clinical VT is faster than this rate.

Figure 3 Continued. to VF in the interval between the 2 recordings. Figure IIB in the Data Supplement shows sequential VF episodes 1 to 3 in which VF detection criteria were met, but shocks were aborted because of undersensing that caused premature episode termination. Figure 3B displays only episode 3 (Panel 5). The mV calibration marker shows that VF EGMs have relatively high base peak amplitudes of 5 to 10 mV for larger EGMs and 1 to 2 mV for most undersensed EGMs. Asterisks denote selected undersensed EGMs that contributed to premature episode termination because of combined effects of highly variable EGM amplitudes, fast programmed detection interval, the high programmed Threshold Start of 62.5%, and the programmed Decay Delay of 60 ms (Figure X in the Data Supplement). STIM indicates ventricular antitachycardia pacing; SVT, supraventricular tachycardia; and VS, ventricular sensed event.

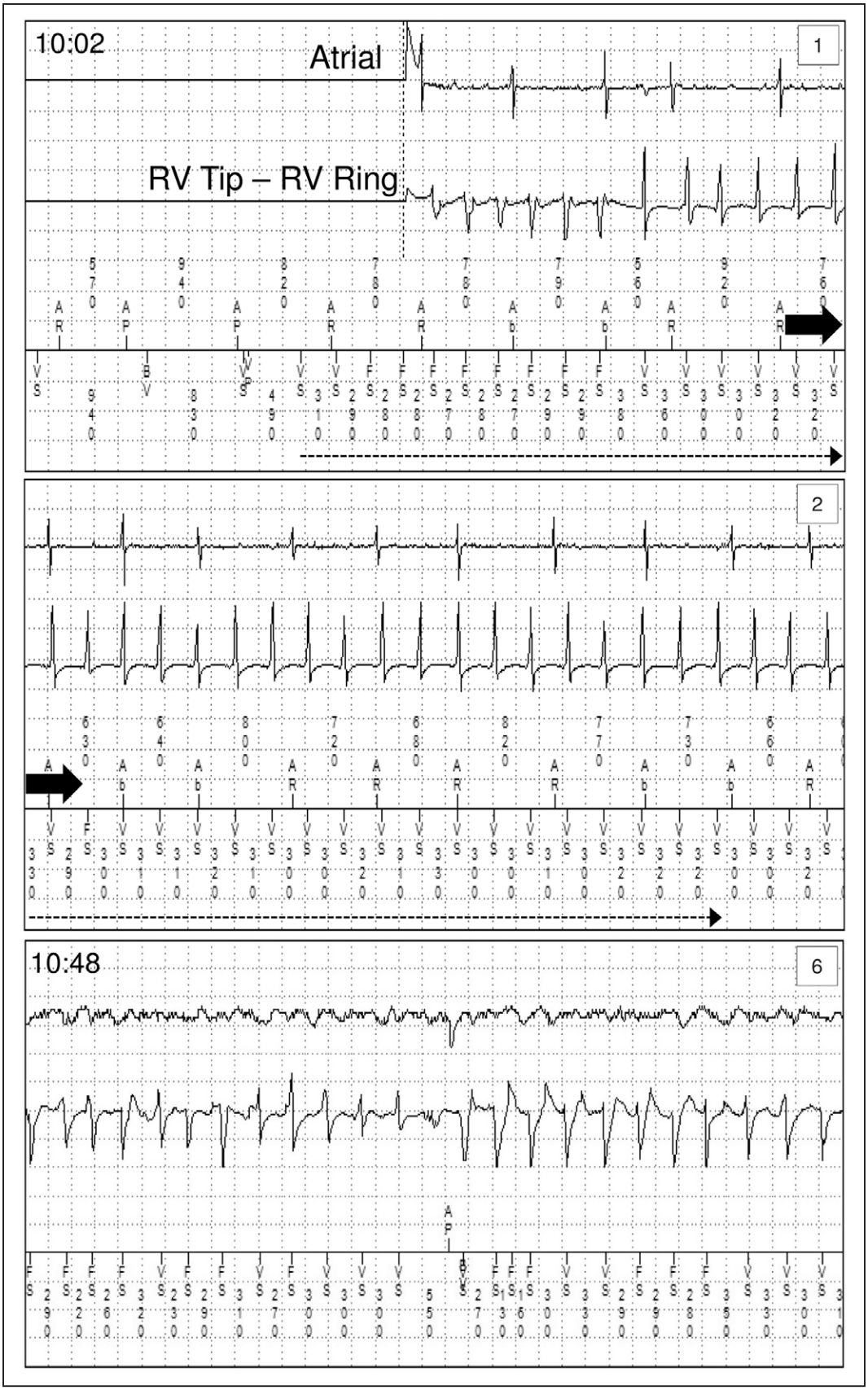


Figure 4. Case 3. Electrograms (EGMs) and interval plot transmitted with Lead Integrity Alert.
Atrial, right ventricular (RV) wide-band filtered sensing channel (RV Tip-RV Ring), and dual-chamber marker channel are shown. Panel 1, Onset of monomorphic ventricular tachycardia (VT) at 10:02. Event storage is triggered by the 8 intervals (*Continued*)

The Consensus Statement[7] relied on this evidence to develop generic programming recommendations including a range of reasonable heart rate cutoffs that are inclusive of those proven in good-quality trials. Its online Appendix B provides manufacturer-preferred examples intended to best approximate the recommended behaviors for each available ICD model.

Present Study

In contrast to clinical trials[8–13] in which no patient died from untreated VT/VF with manufacturer-specific programming, we report patients with adverse outcomes. Overall, failure of VF to satisfy programmed detection criteria was critical in 9 of our 10 patients (90%, all but patient 8). Patients 1 to 8 had programming consistent with generic, Consensus Statement recommendations. However, in patients 1 to 6, programming was inconsistent both with manufacturer-specific, clinical trials and manufacturer-preferred values (online Appendix B). In patient 7, programming complied with manufacturer-preferred values, but these values had not been validated in a peer-reviewed, clinical study. Programming a detection rate validated clinically for the manufacturer's ICD would have resulted in prompt shocks for at least 4 other patients (1–3, 10); of these, patient 1 would not have received prompt shocks with manufacturer-preferred programming.

Our cases illustrate how variability of VF within patients necessitates a safety margin for detection: all 8 ICDs tested at implant detected VF reliably with the settings that failed to detect the index VF; 2 detected spontaneous VF or rapid VT before the index VF (cases 1, 4), and 1 detected VF after external defibrillation (case 5). Overall, failure of VF therapy accounted for 11% of deaths in ICD patients at institutions that tracked these data. In a postmortem series, Tseng et al[20] reported that similar failures accounted for 6% of deaths in ICD patients.

Interaction of Manufacturer-Specific Features With Generic Programming

Counting Methods, Detection Duration, and SVT Discriminators

Manufacturers use different methods to count ventricular intervals that satisfy rate criteria.[14,16,17,21] Each method tolerates slow intervals in the VF zone. However, Boston Scientific tolerates more slow intervals (40%) than Medtronic (25%) or Biotronik (33%); yet only Boston Scientific ICDs have been tested with a slowest detection rate of 200 beats per minute and only for durations less than about 5 s.[11] Patient 3 was programmed to 200 beats per minute using Medtronic counting for a longer duration (30/40 intervals) that was tested for slower rates of 182[10,13] or 188 beats per minute.[8,9] Therapy would have been delivered with a threshold of 182 beats per minute. Without a monitoring zone, we cannot determine whether therapy would have occurred with a threshold of 188 beats per minute. Similarly, we cannot determine whether validated programming would have resulted in prompt therapy in patients 4 and 5.

In addition, counting methods for the VT zone vary among manufacturers. Medtronic ICDs count consecutive intervals.[16] During VF in patient 6, the VT count was repeatedly reset to 0 by intermittent, device-measured intervals slower than the VT interval, which occurred because of undersensing or entrance block. Biotronik ICDs use up/down counting.[17] In patient 7, VF with undersensing had a measured rate of 217 beats per minute (276 ms) in the VT2 zone. This constituted a problem because unvalidated, manufacturer-preferred programming of the Stability discriminator ≤231 beats per minute (260 ms) prevented detection of VF; Stability discriminators are of little value >200 beats per minute.

Episode Termination Rules

ICD-defined VT/VF episodes continue until the rhythm is classified as normal (sinus) based on (slow) rate and duration. Therapy is not delivered if the episode terminates prematurely. St. Jude Medical ICDs have the most sensitive episode termination rule.[14] Cases 1 and 2 show how it interacts with fast detection rates and occasional undersensing to withhold therapy after VF has been detected.

Enhancements to Minimize T-Wave Oversensing

St. Jude Medical sensing enhancements Decay Delay and Threshold Start[14] (Figure X in the Data Supplement) increase ventricular blanking and have been associated with VF undersensing.[1,20] The low-frequency attenuation filter may reduce the amplitude of VF EGMs more than the amplitude of sinus-rhythm EGMs because VF EGMs have lower frequency content than sinus-rhythm EGMs.[22] In the St. Jude Medical PROVIDE trial of strategic programming (Programming Implantable Cardioverter Defibrillators in Patients With Primary Prevention Indication to Prolong Time to First Shock),[12] the detection rate was 180 beats per minute; use of Decay Delay

Figure 4 Continued. shorter than the programmed ventricular fibrillation (VF) detection interval (300 ms FS markers). In Panel 2 (continuous with Panel 1), VT cycle length then slows to 290 to 330 ms in the Monitor zone. The end of the dotted horizontal line spanning Panels 1 and 2 indicates when VF would have been detected with a clinically validated detection interval of 330 ms (182 beats per minute). The corresponding Monitor zone interval lasted 35 min. Rapid nonsustained VT episodes were stored intermittently for 46 min until 10:48 AM (Figure V in the Data Supplement Panels 3 to 5). Panel 6, Last device-defined nonsustained episode. Ventricular intervals are denoted VS in the Sinus or Monitor zone, FS in the VF zone, BV for biventricular paced. Atrial markers denote pacing (AP, atrial paced event), blanking-period sensing (AB, sensed event in atrial blanking period), and refractory-period sensing (AR, sensed event in atrial refractory period).

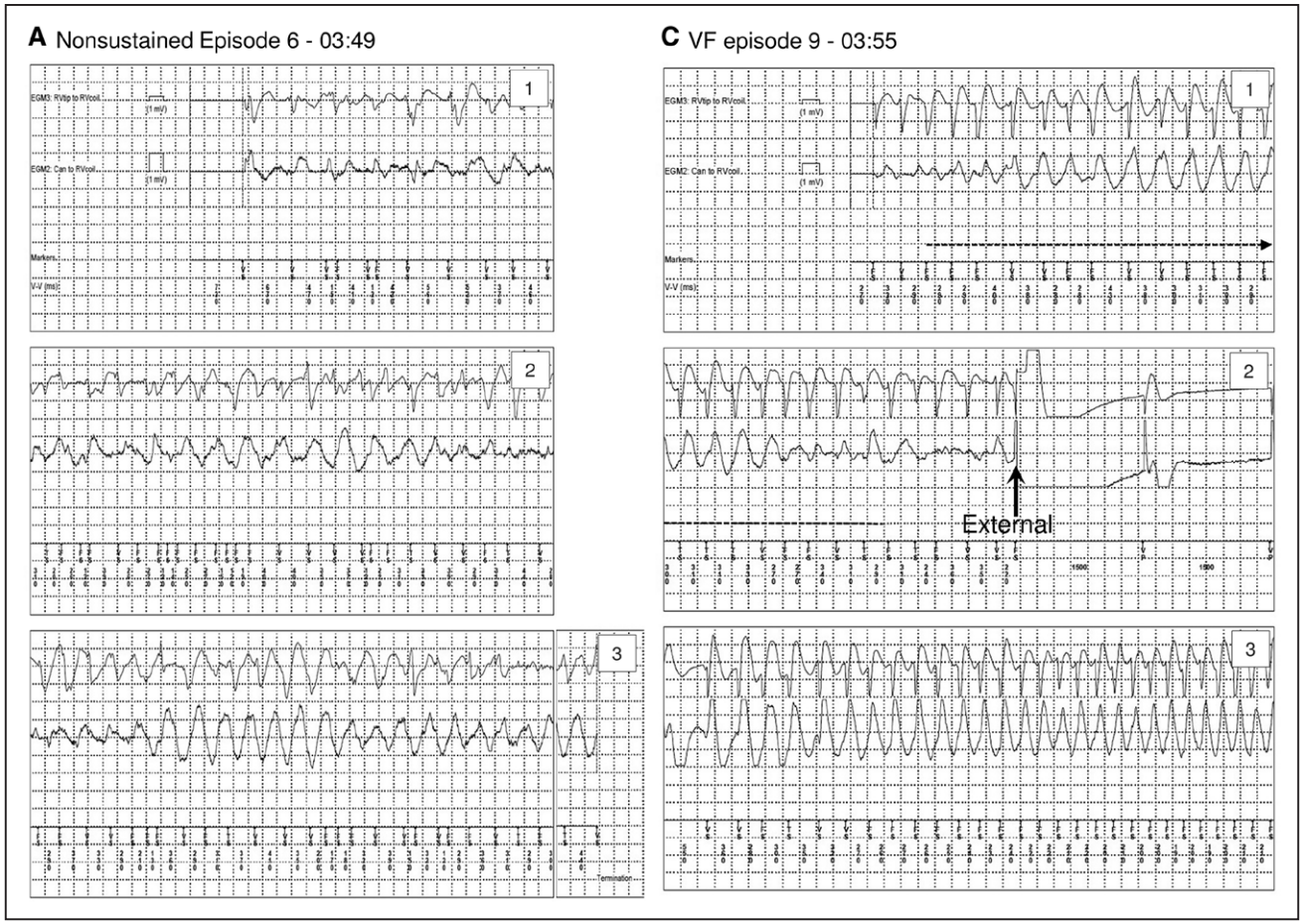


Figure 5. Case 5. Selected electrograms (EGMs) show right ventricular (RV) integrated bipolar EGM (RV Tip-RV Coil), shock EGM (Can-RV Coil), and ventricular markers.
The implantable cardioverter–defibrillator (ICD) did not record the onset of ventricular fibrillation (VF). It recorded the first device-defined, nonsustained episode (episode 1) at 03:48. **A**, Nonsustained episode 6 at 03:49 is the last episode recorded before the first external defibrillation. VF EGMs have a low-frequency content and do not fulfill the programmed detection criteria for either VF (18/24 intervals shorter than 300 ms) or ventricular tachycardia (VT; 40 consecutive intervals shorter than 320 ms). Intervals in the VT zone do not contribute to detection because consecutive interval counting causes each interval in the sinus zone (320 ms or greater) to reset the VT count to 0. Undetected recurrence of undetected monomorphic and polymorphic VT is shown in Figure VB in the Data Supplement. **C**, VF episode 9 at 03:55. Three continuous panels show polymorphic VT with cycle length 270 to 430 ms that does not satisfy interval/duration criteria for detection and requires a second external shock (Panel 2, up arrow). If the VF interval had been programmed to the clinically validated values of 320 or 330 ms, this polymorphic VT would have satisfied the programmed 18/24 intervals for detection of VF (end of dotted arrow in Panels 1 and 2). However, the Lead Integrity Alert[15] was activated incorrectly during Episode 5 when both oversensing criteria were fulfilled. This alert increased the number of intervals for VF detection to 30/40 during Episode 6 and subsequent episodes. After the shock, VT recurred following the second paced beat and immediately accelerated to VF. The frequency content of EGMs was higher during this VF than during the first VF or the polymorphic VT above. The ICD detected VF rapidly and defibrillated it with a single shock (Figure VC to VC in the Data Supplement Panels 4 to 6).

and Threshold Start were not controlled; and most ICDs predated the low-frequency attenuation filter. Thus, the interaction of these features with a detection rate of 200 beats per minute is untested.

Additional Factors

Patients 8 to 10 illustrate known mechanisms of withholding VF therapy. In patient 8, postshock undersensing of VF occurred after repetitive shocks through an integrated bipolar lead.[23] Patient 9 was considered cured of VT after ablation, so his ICD was set to primary prevention parameters; in studies of VT ablation, detection rates have not been reprogrammed after VT was rendered noninducible. Case 10 emphasizes the importance of reprogramming the detection rate when antiarrhythmic drugs are added.[7]

Role of Preceding Monomorphic VT in Withholding VF Therapy

Untreated monomorphic VT initiated polymorphic VT/VF in 7 of the 8 patients in whom we could determine the

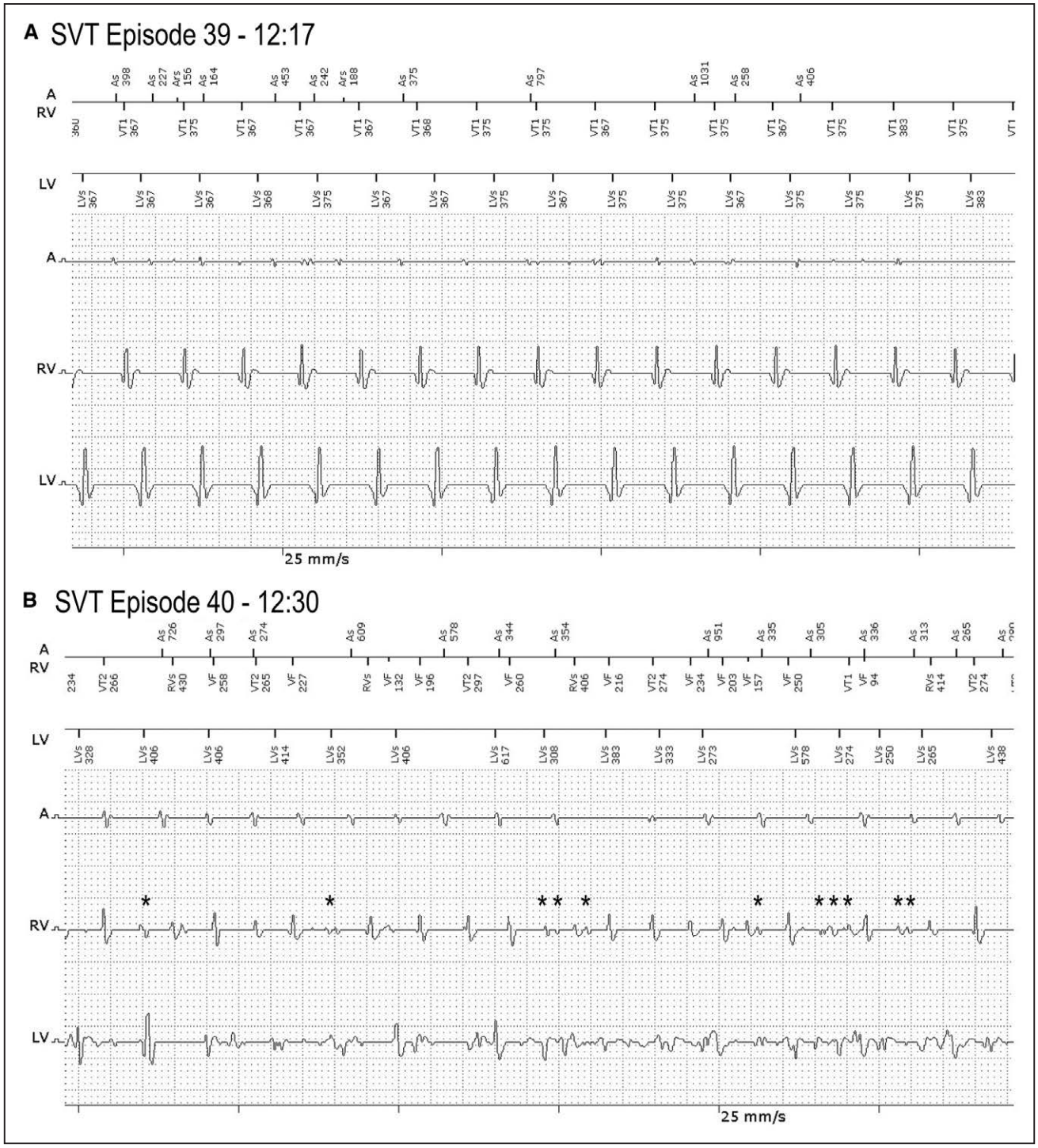


Figure 6. Case 7. Electrograms (EGMs) from 2 device-defined supraventricular tachycardia (SVT) episodes (device lifetime device episodes No. 39 and 40) recorded during cardiac arrest.

Each panel shows markers, atrial EGM, right ventricular (RV) dedicated bipolar EGM, and left ventricular (LV) bipolar EGM. **A**, Monomorphic ventricular tachycardia (VT) with cycle length 367 to 383 ms in the VT 1 zone. The atrial EGM confirms atrioventricular (A-V) dissociation with additional far-field R waves. This VT began during maximum rate sensor-driven pacing (not shown) and had a measured Onset of 19%, less than the 20% required to be classified as VT. **B**, Ventricular fibrillation (VF) with intermittent undersensed EGMs (asterisks). Most undersensed EGMs results from high-amplitude EGMs after low-amplitude EGMs faster than dynamic sensitivity can adjust. Thus, the device measured a cycle length 276 ms, in the VT2 zone. The measured Stability of 148 ms exceeded both the nominal (programmed) value of 24 ms and the manufacturer recommended value of 40 ms required for classification as VT2.

initiating rhythm. In at least 4 of these patients, clinically validated, manufacturer-specific programming would have treated VT before it degenerated to VF. Further, VF that arises from prolonged VT may be difficult to detect or treat. Although low-frequency VF has been considered an agonal rhythm, metabolic changes during VT may produce de novo, low-frequency VF (patients 3, 7, and 9) because of local conduction block or hyperkalemia, resulting in long device-detected intervals because of undersensing or entrance block.[6] Patient 5's first recorded rhythm was low-frequency VF, but recurrence of high-frequency VF promptly after the first defibrillation indicates that the presenting VF was not an agonal rhythm. In addition, prolonged VT may cause metabolic changes that facilitate early postshock recurrence of VT/VF (eg, catecholamine release, patients 4, 5, 7–9).

Clinical Implications

VF detection algorithms must be robust against device-detected intervals slower than the rate threshold to compensate for undersensing, entrance block, or detection restrictions applied in VT zones. Both fast detection rates and enhancements that facilitate undersensing increase the fraction of such device-detected, slow intervals. When devices measure slow intervals, strict counting methods and the Stability discriminator reduce sensitivity for detecting VF in VT zones; sensitive episode termination rules reduce the likelihood that VF therapy will be delivered once VF is detected; and long detection times enhance both effects. Finally, fast detection rates may increase the likelihood that VT will not be detected until it degenerates to low-frequency VF, which may be difficult to detect.

Ideally, programming should deliver all life-saving ICD therapy but no unnecessary therapy. Practically, the programmer's dilemma is to balance the risks of failure to treat VF with the risks of inappropriate therapies. Although evidence-based, manufacturer-specific programming may withhold necessary therapy, the absence of deaths from untreated VF in the 6414 patients in strategic programming groups of clinical trials[8–13] places a low, upper bound on the likelihood of such events.

Our cases illustrate how complex and unanticipated interactions between manufacturer-specific features and generic rate thresholds can withhold therapy for VF. Programming manufacturer-preferred values enumerated in Appendix B might have prevented some, but not all, treatment failures. No patient with manufacturer-specific, programming validated in a clinical trial failed to receive an initial, timely shock for VF. Thus indirectly, our study supports the recommendation of the Consensus Statement[7] (Section 23) encouraging programming ICDs to manufacturer-specific therapies of proven benefit; we recommend such programming even if Appendix B permits programming to other values. Our study identifies risk associated with programming recommendations extrapolated from evidence obtained using another manufacturer's ICDs with different sensing and detection features; however, we cannot provide alternative recommendations and do not advocate abandonment of any recommendations of the Consensus Statement.

Limitations

We did not compare adverse outcomes using evidence-based manufacturer-specific programming and more restrictive, generic programming. Although such generic programming accounted for 62% of adjudicated sudden deaths in ICD patients at institutions that tracked outcomes, our series of cases is too small for definitive conclusions.

Even if manufacturer-specific, evidence-based programming is available for an ICD, programming more restrictive values permitted by the Consensus Statement Appendix B may further reduce unnecessary therapies and thus further reduce morbidity beyond the reduction provided by evidence-based programming. However, the low rate of unnecessary therapy in evidence-based clinical trials places a low upper bound on the incremental benefit of such programming.

Conclusions

Given the rarity of failure to treat VF with evidence-based, manufacturer-specific programming, failures of generic programming constitute a readily preventable cause of sudden death. More data are needed to assess both the benefits and risks of applying generic programming recommendations to specific ICDs in which these recommendations have not been validated clinically.

AFFILIATIONS

From the Department of Cardiology, Aalborg University Hospital, Denmark; Department of Cardiology, Odense University Hospital, Denmark (J.B.J.); Paul L. Foster School of Medicine, Texas Tech University Health Science Center, El Paso (M.A.); and Cedars-Sinai Heart Institute, Cedars-Sinai Medical Center, Los Angeles, CA (C.D.S.).

ACKNOWLEDGMENTS

We are grateful to Sylvain Ploux, MD, for his critical review of this article.

DISCLOSURES

Dr Abedin is a consultant to St. Jude Medical. Dr Swerdlow is a consultant to Medtronic and has received speaking hono-

raria from Medtronic and Boston Scientific. The other authors report no conflicts.

FOOTNOTES

Received April 1, 2017; accepted July 14, 2017.

The Data Supplement is available at http://circep.ahajournals.org/lookup/suppl/doi:10.1161/CIRCEP.117.005305/-/DC1.

Circ Arrhythm Electrophysiol is available at http://circep.ahajournals.org.

REFERENCES

1. Michaud J, Horduna I, Dubuc M, Khairy P. ICD-unresponsive ventricular arrhythmias. *Heart Rhythm*. 2009;6:1827–1829. doi: 10.1016/j.hrthm.2009.06.005.
2. Lee IO, Ukena C, Böhm M, Buob A, Neuberger HR. Underdetection of ventricular tachycardia by an implantable cardioverter-defibrillator due to a locally prolonged arrhythmia cycle length. *Clin Res Cardiol*. 2013;102:923–925. doi: 10.1007/s00392-013-0606-x.
3. Anguera I, Sabaté X, Sugrañes G, Cequier A. Fatal undersensing of ventricular fibrillation due to intermittent high-amplitude R waves. *Pacing Clin Electrophysiol*. 2012;35:e284–e286. doi: 10.1111/j.1540-8159.2011.03270.x.
4. Chin A, Healey JS, Ribas CS, Nair GM. Delayed AICD therapy and cardiac arrest resulting from undersensing of ventricular fibrillation in a subject with hypertrophic cardiomyopathy-a case report. *Indian Pacing Electrophysiol J*. 2015;15:121–124. doi: 10.1016/j.ipej.2015.07.009.
5. Barold SS, Kucher A, Nägele H, Buenfil Medina JC, Brodsky M, Van Heuverswyn FE, Stroobandt RX. Dissimilar ventricular rhythms: implications for ICD therapy. *Heart Rhythm*. 2013;10:510–516. doi: 10.1016/j.hrthm.2012.12.004.
6. Montgomery JA, Kanagasundram AN, Clair WK, Rottman JN, Crossley GH. Sudden cardiac death despite a functional cardioverter-defibrillator: the case for early and aggressive therapy for ventricular tachycardia in selected patients. *J Cardiovasc Electrophysiol*. 2016;27:120–124. doi: 10.1111/jce.12867.
7. Wilkoff BL, Fauchier L, Stiles MK, Morillo CA, Al-Khatib SM, Almendral J, Aguinaga L, Berger RD, Cuesta A, Daubert JP, Dubner S, Ellenbogen KA, Mark Estes NA III, Fenelon G, Garcia FC, Gasparini M, Haines DE, Healey JS, Hurtwitz JL, Keegan R, Kolb C, Kuck KH, Marinskis G, Martinelli M, McGuire M, Molina LG, Okumura K, Proclemer A, Russo AM, Singh JP, Swerdlow CD, Teo WS, Uribe W, Viskin S, Wang CC, Zhang S. 2015 HRS/EHRA/APHRS/SOLAECE expert consensus statement on optimal implantable cardioverter-defibrillator programming and testing. *Heart Rhythm*. 2016;13:e50–e86. doi: 10.1016/j.hrthm.2015.11.018.
8. Wilkoff BL, Williamson BD, Stern RS, Moore SL, Lu F, Lee SW, Birgersdotter-Green UM, Wathen MS, Van Gelder IC, Heubner BM, Brown ML, Holloman KK; PREPARE Study Investigators. Strategic programming of detection and therapy parameters in implantable cardioverter-defibrillators reduces shocks in primary prevention patients: results from the PREPARE (Primary Prevention Parameters Evaluation) study. *J Am Coll Cardiol*. 2008;52:541–550. doi: 10.1016/j.jacc.2008.05.011.
9. Gasparini M, Menozzi C, Proclemer A, Landolina M, Iacopino S, Carboni A, Lombardo E, Regoli F, Biffi M, Burrone V, Denaro A, Boriani G. A simplified biventricular defibrillator with fixed long detection intervals reduces implantable cardioverter defibrillator (ICD) interventions and heart failure hospitalizations in patients with non-ischaemic cardiomyopathy implanted for primary prevention: the RELEVANT [Role of long dEtection window programming in patients with LEft VentriculAr dysfunction, Non-ischemic eTiology in primary prevention treated with a biventricular ICD] study. *Eur Heart J*. 2009;30:2758–2767. doi: 10.1093/eurheartj/ehp247.
10. Gasparini M, Proclemer A, Klersy C, Kloppe A, Lunati M, Ferrer JB, Hersi A, Gulaj M, Wijfels MC, Santi E, Manotta L, Arenal A. Effect of long-detection interval vs standard-detection interval for implantable cardioverter-defibrillators on antitachycardia pacing and shock delivery: the ADVANCE III randomized clinical trial. *JAMA*. 2013;309:1903–1911. doi: 10.1001/jama.2013.4598.
11. Moss AJ, Schuger C, Beck CA, Brown MW, Cannom DS, Daubert JP, Estes NA III, Greenberg H, Hall WJ, Huang DT, Kautzner J, Klein H, McNitt S, Olshansky B, Shoda M, Wilber D, Zareba W; MADIT-RIT Trial Investigators. Reduction in inappropriate therapy and mortality through ICD programming. *N Engl J Med*. 2012;367:2275–2283. doi: 10.1056/NEJMoa1211107.
12. Saeed M, Hanna I, Robotis D, Styperek R, Polosajian L, Khan A, Alonso J, Nabutovsky Y, Neason C. Programming implantable cardioverter-defibrillators in patients with primary prevention indication to prolong time to first shock: results from the PROVIDE study. *J Cardiovasc Electrophysiol*. 2014;25:52–59. doi: 10.1111/jce.12273.
13. Auricchio A, Schloss EJ, Kurita T, Meijer A, Gerritse B, Zweibel S, AlSmadi FM, Leng CT, Sterns LD; PainFree SST Investigators. Low inappropriate shock rates in patients with single- and dual/triple-chamber implantable cardioverter-defibrillators using a novel suite of detection algorithms: PainFree SST trial primary results. *Heart Rhythm*. 2015;12:926–936. doi: 10.1016/j.hrthm.2015.01.017.
14. Zdarek J, Israel CW. Detection and discrimination of tachycardia in ICDs manufactured by St. Jude Medical. *Herzschrittmacherther Elektrophysiol*. 2016;27:226–239. doi: 10.1007/s00399-016-0455-1.
15. Swerdlow CD, Gunderson BD, Ousdigian KT, Abeyratne A, Sachanandani H, Ellenbogen KA. Downloadable software algorithm reduces inappropriate shocks caused by implantable cardioverter-defibrillator lead fractures: a prospective study. *Circulation*. 2010;122:1449–1455. doi: 10.1161/CIRCULATIONAHA.110.962407.
16. Brown ML, Swerdlow CD. Sensing and detection in Medtronic implantable cardioverter defibrillators. *Herzschrittmacherther Elektrophysiol*. 2016;27:193–212. doi: 10.1007/s00399-016-0450-6.
17. Brüggemann T, Dahlke D, Chebbo A, Neumann I. Tachycardia detection in modern implantable cardioverter-defibrillators. *Herzschrittmacherther Elektrophysiol*. 2016;27:171–185. doi: 10.1007/s00399-016-0449-z.
18. Scott PA, Silberbauer J, McDonagh TA, Murgatroyd FD. Impact of prolonged implantable cardioverter-defibrillator arrhythmia detection times on outcomes: a meta-analysis. *Heart Rhythm*. 2014;11:828–835. doi: 10.1016/j.hrthm.2014.02.009.
19. Kloppe A, Proclemer A, Arenal A, Lunati M, Martìnez Ferrer JB, Hersi A, Gulaj M, Wijffels MC, Santi E, Manotta L, Mangoni L, Gasparini M. Efficacy of long detection interval implantable cardioverter-defibrillator settings in secondary prevention population: data from the Avoid Delivering Therapies for Nonsustained Arrhythmias in ICD Patients III (ADVANCE III) trial. *Circulation*. 2014;130:308–314. doi: 10.1161/CIRCULATIONAHA.114.009468.
20. Tseng ZH, Hayward RM, Clark NM, Mulvanny CG, Colburn BJ, Ursell PC, Olgin JE, Hart AP, Moffatt E. Sudden death in patients with cardiac implantable electronic devices. *JAMA Intern Med*. 2015;175:1342–1350. doi: 10.1001/jamainternmed.2015.2641.
21. Zanker N, Schuster D, Gilkerson J, Stein K. Tachycardia detection in ICDs by Boston Scientific: algorithms, pearls, and pitfalls. *Herzschrittmacherther Elektrophysiol*. 2016;27:186–192. doi: 10.1007/s00399-016-0454-2.
22. Swerdlow CD, Asirvatham SJ, Ellenbogen KA, Friedman PA. Troubleshooting implanted cardioverter defibrillator sensing problems I. *Circ Arrhythm Electrophysiol*. 2014;7:1237–1261. doi: 10.1161/CIRCEP.114.002344.
23. Natale A, Sra J, Axtell K, Akhtar M, Newby K, Kent V, Geiger MJ, Brandon MJ, Kearney MM, Pacifico A. Undetected ventricular fibrillation in transvenous implantable cardioverter-defibrillators. Prospective comparison of different lead system-device combinations. *Circulation*. 1996;93:91–98.