

# Analysis of Implantable Cardioverter Defibrillator Therapy in the Antiarrhythmics Versus Implantable Defibrillators (AVID) Trial

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**ICD Therapy in AVID. Introduction:** The implantable cardioverter defibrillator (ICD) is commonly used to treat patients with documented sustained ventricular tachycardia (VT) or ventricular fibrillation (VF). Arrhythmia recurrence rates in these patients are high, but which patients will receive a therapy and the forms of arrhythmia recurrence (VT or VF) are poorly understood.

**Methods and Results:** The therapy delivered by the ICD was examined in 449 patients randomized to ICD therapy in the Antiarrhythmics Versus Implantable Defibrillators (AVID) Trial. Events triggering ICD shocks or antitachycardia pacing (ATP) were reviewed for arrhythmia diagnosis, clinical symptoms, activity at the onset of the arrhythmia, and appropriateness and results of therapy. Both shock and ATP therapies were frequent by 2 years, with 68% of patients receiving some therapy or having an arrhythmic death. An appropriate shock was delivered in 53% of patients, and ATP was delivered in 68% of patients who had ATP activated. The first arrhythmia treated in follow-up was diagnosed as VT (63%), VF (13%), supraventricular tachycardia (18%), unknown arrhythmia (3%), or due to ICD malfunction or inappropriate sensing (3%). Acceleration of an arrhythmia by the ICD occurred in 8% of patients who received any therapy. No physical activity consistently preceded arrhythmias, nor did any single clinical factor predict the symptoms of the arrhythmia.

**Conclusion:** Delivery of ICD therapy in AVID patients was common, primarily due to VT. Inappropriate ICD therapy occurred frequently. Use of ICD therapy as a surrogate endpoint for death in clinical trials should be avoided. (*J Cardiovasc Electrophysiol*, Vol. 14, pp. 940-948, September 2003)

*antiarrhythmic drugs, Antiarrhythmics Versus Implantable Defibrillators (AVID) Trial, antitachycardia pacing, arrhythmic death, implantable cardioverter defibrillator, sudden cardiac death, ventricular fibrillation, ventricular tachycardia*

## Introduction

As the implantable cardioverter defibrillator (ICD) has become the treatment of choice for patients with serious ventricular arrhythmias, including sustained ventricular tachycardia (VT) and cardiac arrest due to ventricular fibrillation (VF), ICD use has increased dramatically.<sup>1-7</sup> Despite this increase in the rate of ICD implantation, there is a paucity of information regarding the frequency and types of tachycardia re-

currences, incidence and outcome of therapies delivered by ICDs, clinical correlates of tachycardia recurrences, symptoms during tachycardia, and the frequency of inappropriate device discharges.

The Antiarrhythmics Versus Implantable Defibrillators (AVID) Trial evaluated therapy for patients who had survived VF or sustained hemodynamically unstable VT by randomizing the treatment to either an antiarrhythmic drug or an ICD.<sup>1</sup> The AVID Trial provided an opportunity to evaluate ICD function and clinical outcome of patients treated with ICDs because of the large number of patients treated with ICDs, the comprehensive follow-up, and the use of ICDs with sophisticated diagnostic capabilities.

The aim of this study was to evaluate the incidence and characteristics of arrhythmia events that triggered ICD therapy. The types and frequency of arrhythmias prompting therapy were analyzed and the outcomes of therapy were classified. The degree of concordance of arrhythmia diagnosis

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between the local Principal Investigator and the ICD Therapy Events Committee of AVID also was determined.

### Methods

The study population consisted of patients in the AVID Trial who were randomized to receive an ICD, had a device implanted, and were discharged alive from initial hospital admission. The study was a multicenter clinical trial, and the protocol was approved by each institution's Institutional Review Board. Written informed consent was obtained from each patient. Five hundred seven patients were randomized to receive an ICD; 492 patients actually had an ICD implanted and were discharged alive from the hospital. ECGs documenting the index arrhythmia type, when available, were retained at the local site. The arrhythmia classification (VT or VF) was reviewed for accuracy at site visits performed at each of the clinical sites but was not reviewed by the committee that reviewed the ICD therapy.

ICDs were interrogated at least every 3 months and when clinically appropriate because of delivery of therapy. At every 3-month follow-up visit or when prompted by ICD therapy, details of each episode of tachycardia were recorded, up to a maximum of five episodes. Unless evidence of intervening stable rhythm was available, any therapy delivered within 5 minutes of another was considered to be related to the same tachycardia episode. The date and time of each episode, the programmed minimum heart rate for any detection of VT or VF, and the status of activation of antitachycardia pacing (ATP) were recorded. For each episode, the patient was asked to recall the activity at the onset of the arrhythmia and the worst symptom experienced during the arrhythmia. The local Principal Investigator and/or Coordinator also recorded the number of therapies used for each episode (ATP, low energy shocks [ $\leq 10$  J], high-energy shocks, and external cardioversion or defibrillation) and whether the patient perceived the therapy. The Principal Investigator then made a diagnosis of the arrhythmia based upon all available data.

The entire ICD interrogation printout, including available electrograms, and the clinical data were forwarded to the Clinical Trial Center for review by the ICD Therapy Events Committee. The event was reviewed by a member of the Events Committee who also recorded the following: status of activation of ATP (if available), availability of electrograms, longest detection interval for VT or VF, cycle length of the detection zone, QRS morphology change from sinus rhythm, morphology (monomorphic or polymorphic) of the rhythm, mean cycle length, regularity of rhythm prior to first documented therapy, number of attempts at ATP and the result of ATP (effective, ineffective, acceleration, inappropriate, or unknown), number of low-energy and/or high-energy shocks and the result of shocks (effective, ineffective, acceleration, inappropriate, or unknown), and the classification of the first rhythm at the beginning of therapy and the worst rhythm during the sequence of therapies. The hierarchy of treated rhythms, starting with the worst, was as follows: VF, VT, atrial fibrillation, other supraventricular tachycardia, and sinus tachycardia.

If device malfunction resulted in delivery of a therapy, the rhythm triggering the therapy was defined as "inappropriate." Therapy delivered for supraventricular arrhythmias (including atrial fibrillation, atrial flutter, and sinus tachycardia) also was defined as "inappropriate."

Arrhythmia diagnosis was not based on rigid arrhythmia definitions. Specifically, the local Principal Investigator and the Events Committee reviewer based their diagnoses on characteristics such as the abruptness of onset of the arrhythmia, the morphology of the electrogram of the arrhythmia compared to the morphology of the electrogram of normal rhythm, the rate, the regularity of the arrhythmia, and the mode of termination. The arrhythmia was not defined by arbitrary ICD detection zones or by any predefined cycle length criteria. Clinical information, such as symptoms during the event, could also be considered by the reviewer in making a diagnosis. ICD events that occurred after the common termination date for ICD data collection of September 1, 1997, were excluded, and follow-up was censored at September 1, 1997. For events reviewed by the Events Committee, their diagnosis was considered to be final. For events not reviewed by the Events Committee (primarily those for which the ICD printouts could not be retrieved), the Principal Investigator's diagnosis was final.

For comparison of diagnostic accuracy between the Principal Investigator and Events Committee, each episode that had occurred by September 1, 1997, and for which an ICD printout was available (78% of the total) was reviewed by a member of the ICD Events Committee. If a conclusive arrhythmia diagnosis could not be made with ease, the episode was reviewed by the entire Events Committee. If the diagnosis was still uncertain, the rhythm was called "unknown." During the course of the study, 106 events (7%) were cycled through the Events Committee review process twice to assess congruency of diagnoses. Cases were chosen randomly but were weighted to include more examples of events with discrepancies between the Principal Investigator and Events Committee reviewer. For 77 of these events, the Principal Investigator and the Events Committee member had agreed on the diagnosis; 29 were events for which there was a disagreement. The Events Committee reviewer was unaware that the arrhythmia was being reviewed a second time, and a single event was never reviewed twice by the same Events Committee reviewer.

All ICD therapies were evaluated to identify and characterize those elements in the patients' histories that might predict subsequent arrhythmic events.

### Statistical Analysis

Baseline comparisons were evaluated using Chi-square or Student's *t*-test, where appropriate. Time to therapy was measured from the date of ICD implant to the date of each type of arrhythmia. A patient could have multiple arrhythmia types recorded. Comparisons of time to therapy were made using the Kaplan-Meier estimation and log rank statistics.

### Results

During the course of the AVID Trial, which lasted for more 4 years, ICD technology both improved and became more complex. Table 1 outlines the ICD systems that were implanted in 492 patients. The qualifying arrhythmia was VF in 216 patients and VT in 276. Review of the qualifying arrhythmia resulted in a change in arrhythmia type in only 3 patients. In 5 patients, death occurred before the device could be implanted; in 4 patients death occurred after implantation but before hospital discharge, and in 6 patients an antiarrhythmic drug was substituted for the ICD (due to

**TABLE 1**  
ICD Systems Implanted/Programmed Therapies

	Qualifying Arrhythmia For AVID		
	Total [N (%)]	VT [N (%)]	VF [N (%)]
N	492	276	216
ICD memory			
Measured average rate, no individual RR intervals	43 (9)	12 (4)	31 (14)
R-R intervals only, no electrograms	88 (18)	52 (19)	36 (17)
R-R intervals and electrograms	361 (73)	212 (77)	149 (69)
Therapy available			
Shock only	45 (9)	13 (5)	32 (15)
Shock and ATP	447 (91)	263 (95)	184 (85)
ATP on	149 (33)	131 (50)	18 (10)
ATP off	259 (58)	118 (45)	141 (77)
ATP variably on/off	36 (8)	12 (5)	24 (13)
ATP not reported	3 (1)	2 (1)	1 (1)
Maximum programmed detection interval (msec)	339 ± 51	351 ± 53	324 ± 42

ATP = antitachycardia pacing; ICD = implantable cardioverter defibrillator; VF = ventricular fibrillation; VT = ventricular tachycardia.

implantation difficulties in 4 patients and withdrawal of patient consent for the ICD in 2 patients). Average follow-up to September 1, 1997 was 22 ± 12 months. During follow-up, 2,057 episodes of ICD therapy were reported, 1,612 of which were reviewed by the Events Committee.

The percentage of the devices implanted that had the capability of stored electrograms increased over the course of the trial. Forty-three percent of ICDs implanted in the first year of the study had stored electrograms, 71% in the second year, and 100% of those implanted in the third and fourth years. Corresponding percentages for ICDs with stored electrograms and R-R intervals are 7%, 64%, 98%, and 100%. However, even in the more advanced ICD models, it was common that only a limited number of therapies could be retrieved with corresponding electrograms, commonly the most recent 4 or 5 episodes of arrhythmia. Earlier electrograms were deleted from the memory of the device prior to the interrogation if more than 4 or 5 episodes occurred between interrogations; therefore, it often was impossible to retrieve detailed information about the older events.

ATP was consistently activated throughout follow-up in 149 patients. Low-energy shock was programmed as initial therapy in 19% of patients, whereas 54% had high-energy shock programmed as the only therapy.

Because only average heart rate during an episode was available in 43 of the ICDs implanted, these 43 patients were eliminated from the detailed analysis that follows, leaving 449 patients in the study. Because the ICD used was a function of date of implantation and not of patient characteristics, these exclusions do not harm the validity of the overall analysis.

Table 2 outlines the characteristics of arrhythmia diagnosis, including all arrhythmias (not just those reviewed by the Events Committee), but including only the first of an arrhythmia type (e.g., if a patient had multiple episodes of VT, only the first was counted). VF tended to be irregular and polymorphic; VT was seldom either. Both VT and VF usually had a morphology change from baseline. Cycle lengths

overlapped greatly, although atrial fibrillation and supraventricular tachycardia were slower.

The summary of ICD therapies is given in Table 3A. An ICD shock was delivered to 45% of patients at 1 year and 62% of patients at 2 years, whereas ATP was delivered in 63% of patients with ATP on and activated at 1 year and 77% of such patients at 2 years. At least one episode of therapy, either ATP or shock, was delivered in 51% of patients at 1 year, censoring patients who died. The first arrhythmia treated in follow-up was VT in 63%, VF in 13%, supraventricular tachycardia in 18%, an unknown type of arrhythmia in 3%, and due to ICD malfunction or inappropriate sensing in 3%. Only 47% of patients at 1 year and 32% at 2 years had not received an ICD therapy and had not suffered arrhythmic death. Table 3B limits the analysis to patients whose ICDs had electrograms recorded and counts only the events reviewed by the Committee.

Figures 1–3 illustrate the time to any therapy (appropriate or inappropriate), time to first ATP, and time to first shock. In Figure 1, arrhythmic death was considered to be an endpoint as well. Of those patients receiving any therapy during the entire follow-up, 91% had at least one shock, and 89% of those patients with ATP turned on had at least one ATP. Many of the patients who received a therapy experienced multiple therapies during follow-up; 48% of patients with ATP programmed on (n = 89/185) received 3 or more different ATP therapy episodes, whereas 36% of patients with ATP turned on received 3 or more shocks. Among all patients, including those with ATP turned on, 41% had 3 or more episodes of ATP or shock during follow-up.

ATP was successful in treating VT 89% of the time, whereas low-energy shock was successful 83% of the time. Arrhythmic death was the outcome of 1% of all episodes treated by the ICD (19/2,057).

**TABLE 2**  
Characteristics of Arrhythmias During Follow-Up\*

	Diagnosed and Treated Arrhythmias in Follow-Up*			
	VT (N = 1,058)	VF (N = 139)	AF (N = 150)	SVT (N = 83)
Cycle length (msec)	314 ± 47	223 ± 39	342 ± 56	387 ± 54
Range	172–510	120–315	230–520	193–530
Morphologic change from baseline				
No	31 (7%)	1 (1%)	68 (97%)	54 (98%)
Yes	422 (93%)	78 (99%)	2 (3%)	1 (2%)
Unknown or missing	605	60	80	28
Polymorphic				
No	576 (97%)	0 (0%)	83 (98%)	61 (97%)
Yes	15 (3%)	98 (100%)	2 (2%)	2 (3%)
Unknown or missing	467	41	65	20
R-R irregularity				
No	745 (93%)	58 (47%)	25 (18%)	63 (93%)
Yes	54 (7%)	65 (53%)	117 (82%)	3 (5%)
Unknown or missing	259	16	8	17

\*First arrhythmia noted in an episode; reviewed by the Events Committee; percentages are based upon known data.

AF = atrial fibrillation; SVT = supraventricular tachycardia; VF = ventricular fibrillation; VT = ventricular fibrillation.

**TABLE 3A**  
Percentage of Patients Receiving Therapy or Experiencing Arrhythmic Death\*

	Total Population (n = 449)		Qualifying Arrhythmia for AVID			
			VT (n = 264)		VF (n = 185)	
	1 Year	2 Years	1 Year	2 Years	1 Year	2 Years
Shocks	45 ± 2	62 ± 3	55 ± 3	71 ± 3	33 ± 4	50 ± 4
Any appropriate shock	39 ± 2	53 ± 3	49 ± 3	63 ± 3	26 ± 3	39 ± 4
Low-energy shock	9 ± 1	15 ± 2	13 ± 2	24 ± 3	3 ± 1	4 ± 2
High-energy shock	43 ± 2	59 ± 3	51 ± 3	65 ± 3	33 ± 4	50 ± 4
ATP <sup>†</sup>	63 ± 4	77 ± 4	64 ± 5	79 ± 4	57 ± 12	68 ± 12
Any appropriate ATP	55 ± 4	68 ± 5	55 ± 5	70 ± 5	53 ± 13	53 ± 13
No therapy	47 ± 3	32 ± 3	36 ± 2	21 ± 3	63 ± 4	47 ± 4
Arrhythmic death	2 ± 1	5 ± 1	2 ± 1	3 ± 1	3 ± 1	8 ± 3

\*Estimated by method of Kaplan-Meier.

<sup>†</sup>Percentage of patients in whom ATP was available and activated, and the ICD date-stamped episode (n = 135 total; VT = 117, VF = 18).  
ATP = antitachycardia pacing; VF = ventricular fibrillation; VT = ventricular tachycardia.

Table 4 outlines the number of patients with each rhythm triggering ICD therapy and the number of episodes of each rhythm. Almost three times as many patients had VT treated as had VF treated. The vast majority (72%) of ventricular arrhythmias were VT. Only 9% of arrhythmias began as VF. The mean cycle length of ventricular tachycardia was 314 ± 47 msec, and the mean ventricular fibrillation cycle length was 223 ± 39 msec (Table 2). Similar data were seen if the analysis was limited to patients with ICDs having electrograms, with only reviewed episodes considered. A multivariate analysis was performed to identify factors predictive of therapy for VF in both the VT and VF subgroups. Variables considered included gender, age, left ventricular ejection fraction, history of myocardial infarction, remote history of VF, remote history of VT, history of atrial fibrillation, coronary artery disease, and history of congestive heart failure. For patients enrolling in AVID with an index arrhythmia of VF, the only predictor of subsequent VF was a history of atrial fibrillation (P = 0.001). For patients entering AVID with VT, the only predictor of VF in follow-up was male gender (P = 0.005).

Of note, 11% of patients had at least one episode classified as inappropriate therapy for atrial fibrillation, and 9% of patients had inappropriate therapy for supraventricular tachy-

cardia that triggered device therapy. Univariate analysis of patient characteristics revealed no differences between those receiving inappropriate therapy and those who did not, except that patients receiving inappropriate therapy were slightly younger (63 ± 11 years vs 66 ± 11 years, P < 0.03). Of the total 2,057 episodes, 15.8% were related to supraventricular arrhythmias.

Table 5 lists the frequency of worsening of an arrhythmia by ICD therapy. Only episodes from ICDs with electrograms and reviewed by the Events Committee are included because we believed that a more thorough review of these events was necessary. Each episode was counted separately (because a patient could have multiple episodes of a single arrhythmia reported). Only episodes initially classified as VT, supraventricular tachycardia, or atrial fibrillation were included. Acceleration occurred in 5% of all episodes. Importantly, delivery of a low-energy shock in this population did not result in acceleration to unstable VT or VF in any of the 61 low-energy shocks. Table 6 shows that the risk of acceleration with ATP was greater at higher rates of VT. Paradoxically, ATP success also was greater with the faster VT episodes.

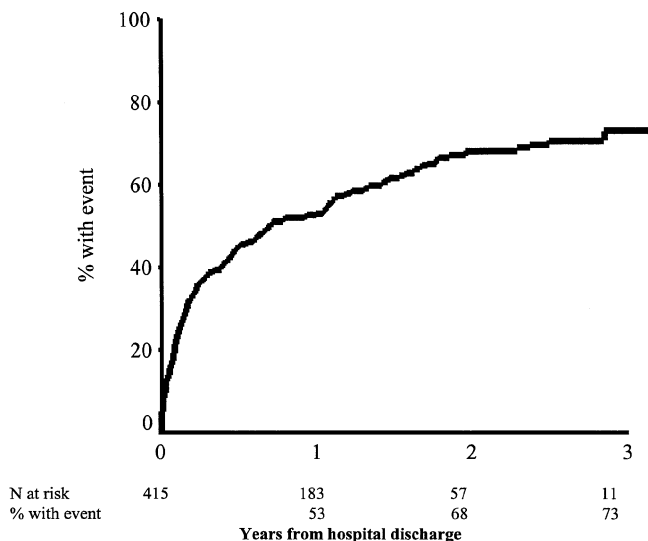
Table 7 shows the activity, as reported by the patient, that was associated with an arrhythmia, and includes all arrhythmias reported, whether or not reviewed by the Events

**TABLE 3B**  
Percentage of Patients Receiving Therapy or Experiencing Arrhythmic Death\*—Patients with ICDs Having Electrograms, Includes Reviewed Episodes Only

	Total Population (n = 361)		Qualifying Arrhythmia for AVID			
			VT (n = 212)		VF (n = 149)	
	1 Year	2 Years	1 Year	2 Years	1 Year	2 Years
Shocks	41 ± 3	55 ± 3	50 ± 4	64 ± 4	29 ± 4	41 ± 5
Any appropriate shock	35 ± 3	46 ± 3	44 ± 4	57 ± 4	22 ± 4	31 ± 4
Low-energy shock	7 ± 1	12 ± 2	11 ± 2	17 ± 3	2 ± 1	2 ± 1
High-energy shock	39 ± 3	52 ± 3	47 ± 4	60 ± 4	29 ± 4	41 ± 5
ATP <sup>†</sup>	61 ± 5	71 ± 5	64 ± 5	74 ± 5	40 ± 13	52 ± 15
Any appropriate ATP	48 ± 5	56 ± 5	50 ± 5	59 ± 6	33 ± 12	33 ± 12
No therapy	52 ± 3	37 ± 3	40 ± 4	26 ± 4	68 ± 4	53 ± 5
Arrhythmic death	2 ± 1	4 ± 1	2 ± 1	2 ± 1	2 ± 1	7 ± 3

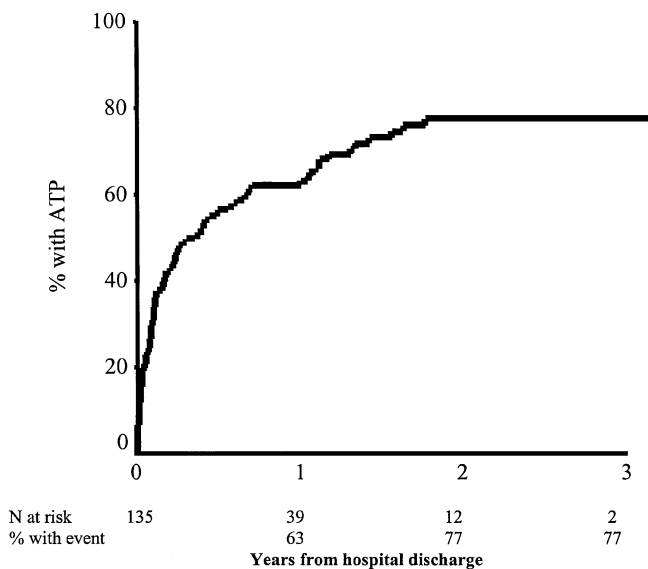
\*Estimated by method of Kaplan-Meier.

<sup>†</sup>Percentage of patients in whom ATP was available and activated, and the ICD date-stamped episode (n = 118 total; VT = 102, VF = 16).  
ATP = antitachycardia pacing; VF = ventricular fibrillation; VT = ventricular tachycardia.

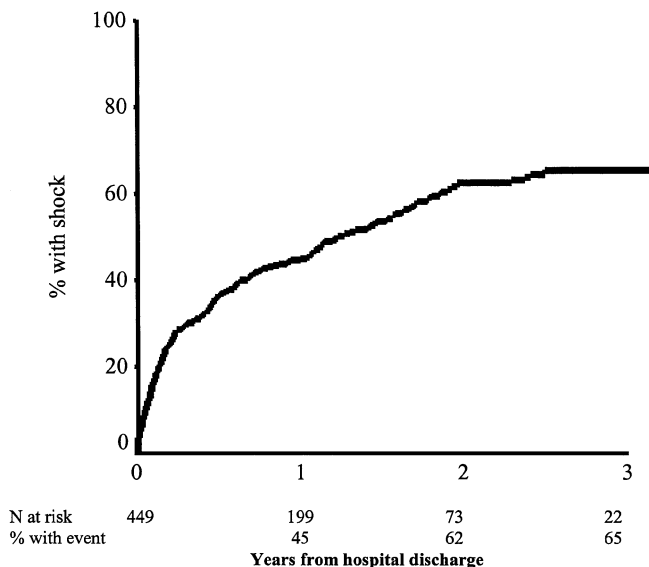


**Figure 1.** Time to any therapy or arrhythmic event in patients (N = 415) with implantable cardioverter defibrillators (ICDs) that date-stamp all therapy episodes. Arrhythmic events include arrhythmic death, sustained ventricular arrhythmias, and antitachycardia pacing or shock from the ICD. Patients are censored at noncardiac or nonarrhythmic cardiac deaths.

Committee. Most arrhythmias, both VF and VT, occurred during sedentary activity or sleep, with only occasional episodes associated with moderate or heavy exercise. Therapy was relatively less common during sleep, with 9% of reported episodes of VT/VF occurring during what is probably 25% to 33% of an average patient's day. However, VF episodes occurred during sleep 19% of the time. Limited, moderate, or heavy exercise accounted for 17% of all reported appropriate therapies where activity was known, which is a higher proportion of events relative to the percentage of time spent exercising in this relatively sedentary population. Importantly, therapy was delivered while the patient was driving



**Figure 2.** Time to first antitachycardia pacing (ATP) therapy in patients (N = 135) with ATP activated and with implantable cardioverter defibrillators (ICDs) that date-stamp ATP episodes. Patients are censored at any death.



**Figure 3.** Time to first shock therapy in patients (N = 449) with implantable cardioverter defibrillators (ICDs) that date-stamp shock episodes. Patients are censored at any death.

only five times during the trial, and two of these treatments were administered for supraventricular tachycardia. Of interest was the frequent inability of patients to remember the activity (unknown category) at the time of arrhythmia and therapy (39% of all episodes).

The most common symptoms associated with VT were palpitations, dizziness, dyspnea, and chest pain. Approximately 10% of patients reported presyncope or syncope. These more serious symptoms were associated with only slightly faster, more irregular, and more polymorphic arrhythmias (Table 8). There were no clinical characteristics that reliably predicted a particular symptom at the time of VT.

Table 9 illustrates the concordance of diagnosis between the Principal Investigator and the ICD Events Committee in the 1,612 episodes of ICD therapy reviewed by the Events Committee (of the total 2,057 episodes reported during AVID). All arrhythmia episodes are included in Table 9, that is, a patient frequently is represented more than once in different cells. Considering all categories of arrhythmias, the Principal Investigator and the Events Committee agreed on 1,099 (68%) of 1,612 episodes. Atrial fibrillation was frequently misclassified: agreement occurred on 70 (49%) of 144 episodes. The Principal Investigator classified 36 of the atrial fibrillation episodes as VT. Important differences between the Principal Investigator and the ICD Events Committee that would affect fundamental analyses related to VT/VF occurred in 295 (18%) of 1,612 episodes. Misclassifying VF as VT and VT as VF accounted for many of the discrepancies. When they agreed that an arrhythmia was ventricular, there was concordance in the distinction between VT and VF in 971 (89%) of 1,095 episodes. They agreed on 56 (40%) of 139 events ultimately diagnosed as VF and 915 (85%) of 1,081 events ultimately classified as VT. Both the Principal Investigator and the Events Committee reviewer frequently used the diagnosis of "unknown." Excluding all events where a diagnosis of "unknown" was made (such a diagnosis demands further review by an expert committee), then practical agreement was achieved in 1,214 (92%) of 1,310 of all events.

**TABLE 4**  
Rhythm Triggering ICD Therapy

	All Reported Events		Patients with ICDs Having Electrograms; Reviewed Episodes Only	
	No. of Patients (%)	No. of Episodes (%)	No. of Patients (%)	No. of Episodes (%)
Ventricular fibrillation	77 (17%)	178 (9%)	47 (13%)	117 (10%)
Ventricular tachycardia	209 (47%)	1,475 (72%)	140 (39%)	820 (70%)
Atrial fibrillation	51 (11%)	192 (9%)	38 (11%)	112 (10%)
Other supraventricular tachycardia	42 (9%)	134 (7%)	32 (9%)	88 (7%)
Otherwise inappropriate	13 (3%)	23 (1%)	12 (3%)	22 (2%)
Unknown	30 (7%)	55 (3%)	13 (4%)	17 (1%)

For the 106 episodes that were reviewed twice by the Events Committee, there was concordance of diagnosis between the two in 86 (81%) of 106 cases. Of 86 arrhythmias classified as VF or VT by at least one reviewer, 74 were diagnosed as VF, VT, or by both (86%). Complete agreement on VF was present in 7 cases and on VT in 63 cases.

**Discussion**

The present study documents that ICD therapies are common in patients who have a history of life-threatening ventricular arrhythmias (survivors of VF or patients who have experienced sustained VT with serious hemodynamic compromise). The ICD improves survival compared with antiarrhythmic drugs,<sup>1,2</sup> and approximately 68% of patients receive an ATP or shock therapy within 2 years after device implantation. This incidence of ICD therapy is consistent with other reports of ICD therapy.<sup>7-13</sup> Unlike many previous reports of ICD therapies, the high percentage of devices in the present study with retrievable R-R interval and electrogram data permitted a more precise analysis and diagnosis of events triggering ICD therapy. As might be expected in this population, the first rhythm detected and treated was most commonly VT, even among those patients in whom the initial clinical tachycardia was VF. Only 9% of all arrhythmic episodes began as VF. These findings of VT and VF recurrences are consistent with reported data from cardiac arrest survivors treated with ICDs<sup>14,15</sup> but document more frequent VF recurrence com-

pared to a population of patients with prior healed myocardial infarction and VT or VF.<sup>16</sup> These differences in VT/VF recurrence probably are related to differences in patient population. The AVID Trial population reported here includes a heterogeneous group of patients with both VT and VF presentations; studies restricted to patients with prior myocardial infarction would be expected to have a preponderance of monomorphic VT.

Whereas inappropriate sensing, ICD malfunction, and electrode failures rarely triggered ICD therapy in the AVID patients, atrial fibrillation and other supraventricular tachycardias were responsible for attempted therapy in 22% of patients and 16% of all treated episodes. Despite the use of ICDs with detection enhancements for diagnosing supraventricular tachycardia in this study, this rate of inappropriate therapy for supraventricular tachycardia (including atrial fibrillation) is comparable to previous reports of inappropriate therapy in 13% to 39% of patients.<sup>12,17-20</sup> The continued problem of VT/VF therapy delivered for supraventricular tachycardias may reflect a reluctance to activate detection enhancements until problems with supraventricular tachycardia are documented. The potential for underdetection of VT or VF has been raised, resulting in delay or suppression of therapy when these algorithms are activated.<sup>21,22</sup> It is possible that dual-chamber ICD detection algorithms may help to obviate these problems.

Symptoms reported by patients preceding ICD therapy varied from none to syncope. Approximately one third of all patients with ICD therapy reported no symptoms preceding delivery of therapy, whereas <10% of patients reported presyncope or syncope. As might be expected, patients who reported severe symptoms were more likely to have a documented rapid ventricular tachyarrhythmia that had a polymorphic pattern. This range of clinical symptoms

**TABLE 5**  
Acceleration of Arrhythmia by ICD Therapy—Patients with ICDs Having Electrograms, Includes Reviewed Episodes Only

	Therapy Resulting in Acceleration			
	Total Episodes [N (%)]	ATP [N (%)]	Shock	
			Low-Energy [N (%)]	High-Energy [N (%)]
VT to unstable VT	12/755 (2)	12/525 (2)	0/50 (0)	0/263 (0)
VT to VF	27/755 (4)	17/525 (3)	0/50 (0)	10/263 (4)
SVT to VT	4/79 (5)	1/66 (2)	0/2 (0)	3/40 (8)
SVT to VF	4/79 (5)	4/66 (6)	0/2 (0)	0/40 (0)
AF to VT	2/102 (2)	2/67 (3)	0/9 (0)	0/50 (0)
AF to VF	1/102 (1)	0/67 (0)	0/9 (0)	1/50 (2)
Total	50/936 (5)	36/658 (5)	0/61 (0)	14/353 (4)

AF = atrial fibrillation; ATP = antitachycardia pacing; SVT = supraventricular tachycardia; VF = ventricular fibrillation; VT = ventricular tachycardia.

**TABLE 6**  
Success of ATP in Patients with ICDs Having Electrograms, Includes Reviewed Episodes Only

	Cycle Length of VT			
	>400 msec (N = 95)	400–360 msec (N = 162)	359–320 msec (N = 187)	<320 msec (N = 192)
Result of ATP				
Success	39%	62%	83%	84%
No effect	59%	35%	12%	9%
Acceleration	2%	3%	4%	7%

ATP = antitachycardia pacing; VT = ventricular tachycardia.

**TABLE 7**  
Activity Associated with Arrhythmias During Follow-Up

Type of Arrhythmia in Follow-Up	Activity						
	Sleeping [N (%)]	Sedentary/Awake [N (%)]	Limited Exercise [N (%)]	Moderate Exercise [N (%)]	Heavy Exercise [N (%)]	Driving [N (%)]	Unknown [N (%)]
All therapies	157 (8)	734 (36)	253 (12)	59 (3)	37 (2)	5 (0)	812 (39)
All VT/VF	142 (9)	606 (37)	201 (12)	41 (2)	17 (1)	3 (0)	643 (39)
VT	109 (7)	529 (36)	185 (13)	36 (2)	15 (1)	2 (0)	599 (41)
VF	33 (19)	77 (43)	16 (9)	5 (3)	2 (1)	1 (1)	44 (25)
Atrial fibrillation	5 (3)	70 (36)	23 (12)	11 (6)	10 (5)	0 (0)	73 (38)
Other SVT	5 (4)	42 (31)	16 (12)	7 (5)	10 (7)	2 (1)	52 (39)
Inappropriate	3 (13)	9 (39)	7 (30)	0 (0)	0 (0)	0 (0)	4 (17)
Unknown/other	2 (4)	7 (13)	6 (11)	0 (0)	0 (0)	0 (0)	40 (73)

SVT = supraventricular tachycardia; VF = ventricular fibrillation; VT = ventricular tachycardia.

preceding device therapy has been reported previously<sup>9,18,23,24</sup> and reinforces the importance of objective rhythm diagnosis utilizing device diagnostics rather than clinical symptoms to document VT or VF recurrence. Reliable predictors of symptoms associated with the arrhythmia in follow-up were absent.

Most arrhythmias were not precipitated by any specific physical activity, although exercise was associated with increased arrhythmia frequency. Arrhythmias during sleep were less common than expected. The onset of arrhythmias while driving was extremely rare, with only 5 episodes resulting in therapy. This low incidence of symptomatic episodes during driving has been noted previously and supports recommendations regarding ICD patients and the operation of motor vehicles.<sup>25-27</sup>

In 90% of the ICDs implanted in the AVID Trial, therapy options included high-energy shocks, low-energy shocks, and ATP. Among the patients who had ATP activated, it was quite successful, particularly for the more rapid VTs. The overall ATP success rate has been reported in smaller ICD populations,<sup>10,12,28,29</sup> but the success for rapid VT is in the AVID Trial is higher than previously reported. Furthermore, the risk of acceleration is relatively low. Thus, ATP seems to be underutilized, both in this study and in general clinical practice. Many patients in our study potentially could have benefited from activation of ATP, and some shocks would have been avoided. Likewise, low-energy shocks were infrequently used but were generally successful. Although the use of ATP and low-energy shocks diminishes the symptoms associated with high-energy shocks, potentially preserves battery life, and

**TABLE 8**  
Correlates of Most Severe Symptoms Experienced by a Patient During ICD Therapy for VT\*

	Symptoms					
	No Symptoms (N = 101)	Palpitations, Diaphoresis, Anxiety, Fatigue (N = 47)	Nausea, Dizziness, Dyspnea, Chest pain (N = 62)	Near-Syncope (N = 24)	Syncope (N = 9)	Unknown (N = 92)
<b>Patient Characteristics</b>						
Age (years; $\pm$ SD)	66 $\pm$ 11	66 $\pm$ 9	65 $\pm$ 11	67 $\pm$ 10	69 $\pm$ 6	67 $\pm$ 10
Sex						
Male (%)	90	75	84	79	78	80
Female (%)	10	26	16	21	22	20
Qualifying arrhythmia						
VT (%)	84	89	86	88	44	84
VF (%)	16	11	15	13	56	16
Ejection fraction (%; $\pm$ SD)	29 $\pm$ 10	28 $\pm$ 10	31 $\pm$ 11	29 $\pm$ 08	23 $\pm$ 9	29 $\pm$ 11
History of prior VF (%)	4	9	5	13	11	2
History of prior sustained VT (%)	20	21	29	25	11	22
History of atrial fibrillation/flutter	25	32	24	8	22	24
History of CHF (%)	50	40	55	50	78	50
History of unexplained syncope (%)	19	9	15	20	11	11
History of MI (%)	79	85	73	75	56	79
Organic cardiac disease <sup>†</sup>						
CAD (%)	87	96	81	92	78	90
Other (%)	28	21	31	25	33	23
<b>Rhythm Characteristics</b>						
Cycle length (msec)	310 $\pm$ 50	308 $\pm$ 57	303 $\pm$ 45	282 $\pm$ 38	269 $\pm$ 41	311 $\pm$ 50
Polymorphic (%) <sup>‡</sup> (unknown)	8 (35)	4 (40)	6 (44)	8 (50)	20 (44)	2 (42)
R-R irregularity (%) <sup>‡</sup> (unknown)	5 (19)	11 (19)	8 (18)	6 (29)	25 (11)	8 (17)

\*Each patient is listed once, classified by the worst symptom during any VT.

<sup>†</sup>More than one disease could be listed per patient.

<sup>‡</sup>Percentage of reported analyses.

CAD = coronary artery disease; CHF = congestive heart failure; MI = myocardial infarction; VF = ventricular fibrillation; VT = ventricular tachycardia.

**TABLE 9**  
Concordance of Principal Investigator and Events Committee Diagnosis\*

		Principal Investigator Diagnosis							Total
		VF	VT	AF	SVT	Inappropriate	Unknown Rhythm	Other	
ICD Events Committee Diagnosis	VF	56	73	2	0	0	8	0	139
	VT	51	915	10	6	0	96	3	1081
	AF	1	36	70	12	1	24	0	144
	SVT	2	28	6	27	0	16	2	81
	Inappropriate	0	0	2	0	4	4	1	11
	Unknown rhythm	9	92	9	9	1	28	5	153
	Other	2	0	0	0	0	1	0	3
	<b>Total</b>	121	1144	99	54	6	177	11	1612

AF = atrial fibrillation; SVT = supraventricular tachycardia; VF = ventricular fibrillation; VT = ventricular tachycardia.

results in more rapid delivery of therapy, such therapy has been found to be potentially proarrhythmic due to acceleration of stable tachycardias to more rapid and unstable VT and VF.<sup>28-30</sup> In the present study, acceleration was relatively infrequent, occurring in approximately 8% of patients and <5% of all arrhythmia episodes. This incidence is consistent with previous reports and confirms in this larger population of ICD patients the safety of both ATP therapy and low-energy shocks for VT. In this study population, low-energy shocks did not result in acceleration to unstable VT or VF in any of the 93 low-energy shock deliveries for spontaneous VT. This finding contrasts with a previous report by Bardy et al.,<sup>30</sup> who found acceleration of induced VT in 21% of patients at the time of device implantation. The absence of acceleration by low-energy shocks in the present study documents the safety and efficacy of low-energy shocks for therapy of clinical spontaneous VT. Of some concern was the acceleration of SVT to VT or VF in 10% of episodes. Previous reports have also noted a similar frequency of this problem.<sup>12,31,32</sup>

Clinically, difficulties in diagnosing arrhythmias from the limited information provided by R-R intervals or electrograms has been recognized.<sup>18,33</sup> Although many studies have reported diagnoses of tachycardias triggering device therapy, few have defined criteria for specific tachycardias or described the process by which diagnoses are made.<sup>10,15,18</sup> In the present study, an Events Committee was established at initiation of the trial to review ICD therapy episodes rigorously and to define mechanisms triggering such activity. This review process would also assess the concordance of the Events Committee's diagnosis with that which the Principal Investigator assigned at the time the patient was seen and the ICD was interrogated. Our study evaluated the ease of diagnosis of an event that triggers an ICD therapy. In approximately 10% of the episodes reviewed by the Events Committee, a definitive diagnosis could not be assigned to the arrhythmic event. For the entire 1,612 reviewed episodes, perfect concordance of diagnosis between the Principal Investigator and the Events Committee was 68.2%. However, practical agreement (correctly diagnosing an event as ventricular) was seen in 81.7%. If only the Principal Investigator reviewed the events and if those events diagnosed "unknown" by the Principal Investigator were excluded (because these obviously need to be more extensively reviewed), then the Principal Investigator would agree with an Events Committee in 92% of all events. These findings suggest that, for trials in which assigning an exact arrhythmia diagnosis to an ICD event is an important objective,<sup>34,35</sup> a review committee for

final diagnosis is needed only for the events identified by the Principal Investigator as an uncertain arrhythmia. Recent development of dual-chamber ICD arrhythmia detection algorithms may improve the diagnosis further.

Characteristics of arrhythmias were sought that would accurately make a better distinction between VT and VF. As expected, VF was associated with a shorter cycle length, but there was considerable overlap with the cycle lengths found for VT. Morphology itself was not particularly useful because both VT and VF characteristically showed changes from electrograms recorded during sinus rhythm. Polymorphic tachyarrhythmia electrograms accurately distinguished between VF and VT because VT only rarely has a polymorphic electrogram. Regularity of the R-R interval likewise was useful but was not helpful in distinguishing VF from atrial fibrillation.

### Study Limitations

Qualifying arrhythmias were not reviewed by the Committee, and not all were reviewed at site visits, so some qualifying arrhythmia classifications could have been incorrect. Only approximately one third of the patients had ATP activated, so the success of ATP may have been skewed by the population in which it was used. Not all events were reviewed by the Events Committee. None of the devices used in this study was a dual-chamber unit; therefore, AV relationships could not be analyzed for arrhythmia diagnosis. Detection enhancements that were available in these ICDs were not activated in any prescribed manner, and the programmed status of these enhancements was not recorded in any consistent manner for the Events Committee. ICD interrogation after death occurred only infrequently. Only 17 of the 72 patients who died on or before September 1, 1997, had ICD data reported from a death event. With respect to important device malfunction, these data might have been the most revealing.

### Conclusion

The AVID Trial demonstrates in patients who previously experienced life-threatening arrhythmias that therapies from the ICD are frequent. As expected, VT was the most common arrhythmia, but there was a significant incidence of non-VT events that triggered device therapy, despite the use of third-generation ICDs. Therapy for VT and VF, including ATP, was very successful in terminating these tachycardias with a low incidence of device proarrhythmia. ATP was underutilized,



and acceleration of a tachyarrhythmia was uncommon. Inappropriate therapy occurred frequently, but no clinical or electrophysiologic parameter predicted inappropriate therapy accurately. In this population, recurrence of VT and VF was not associated with any particular activity or symptom, although syncope was associated with more rapid and polymorphic tachycardia. The arrhythmia diagnosis made by the local Principal Investigator is generally correct and review by an Events Committee is unnecessary, except for episodes identified by the Principal Investigator as uncertain or confusing. Use of dual-chamber ICD detection algorithms may further improve arrhythmia diagnosis.

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