Heart Rhythm Disorders

Inappropriate Implantable Cardioverter-Defibrillator Shocks

Incidence, Predictors, and Impact on Mortality

Johannes B. van Rees, MD,* C. Jan Willem Borleffs, MD,* Mihály K. de Bie, MD,*
Theo Stijnen, PhD,† Lieselot van Erven, MD, PhD,* Jeroen J. Bax, MD, PhD,*
Martin J. Schalij, MD, PhD*

Leiden, the Netherlands

Objectives   The purpose of this study was to assess the incidence, predictors, and outcome of inappropriate shocks in implantable cardioverter-defibrillator (ICD) patients.

Background   Despite the benefits of ICD therapy, inappropriate defibrillator shocks continue to be a significant drawback. The prognostic importance of inappropriate shocks outside the setting of a clinical trial remains unclear.

Methods   From 1996 to 2006, all recipients of defibrillator devices equipped with intracardiac electrogram storage were included in the current analysis and clinically assessed at implantation. During follow-up, the occurrence of inappropriate ICD shocks and all-cause mortality was noted.

Results   A total of 1,544 ICD patients (79% male, age 61 ± 13 years) were included in the analysis. During the follow-up period of 41 ± 18 months, 13% experienced ≥1 inappropriate shocks. The cumulative incidence steadily increased to 18% at 5-year follow-up. Independent predictors of the occurrence of inappropriate shocks included a history of atrial fibrillation (hazard ratio [HR]: 2.0, p < 0.01) and age younger than 70 years (HR: 1.8, p = 0.01). Experiencing a single inappropriate shock resulted in an increased risk of all-cause mortality (HR: 1.6, p = 0.01). Mortality risk increased with every subsequent shock, up to an HR of 3.7 after 5 inappropriate shocks.

Conclusions   In a large cohort of ICD patients, inappropriate shocks were common. The most important finding is the association between inappropriate shocks and mortality, independent of interim appropriate shocks.   (J Am Coll Cardiol 2011;57:556–62) © 2011 by the American College of Cardiology Foundation

Ventricular tachycardia (VT), deteriorating to ventricular fibrillation (VF) is responsible for an estimated one third of all cardiovascular mortality worldwide (1–3). Several important clinical trials have shown that the implantable cardioverter-defibrillator (ICD) provides a substantial and significant reduction in mortality in survivors of sudden cardiac arrest and high-risk patients with cardiovascular disease (4–9). Despite proven survival benefits, ICD treatment still has drawbacks, one of the most important being shocks delivered for causes other than potentially life-threatening VT or VF. These inappropriate shocks are painful, psychologically disturbing, and potentially arrhyth-

mogenic (10–13). Recently, a subgroup analysis of 2 major ICD clinical trials reported on the prognosis of ICD shocks and raised concern by establishing an association between inappropriate shocks and increased mortality (14,15). However, extrapolating these results to ICD recipients into everyday or routine clinical practice is difficult because these clinical trials comprised a selected population. Therefore, we analyzed a large population of ICD patients with long-term follow-up outside the setting of a clinical trial to evaluate the occurrence of inappropriate ICD shocks, to identify potential predictive parameters for inappropriate shocks, and to assess the impact of inappropriate shocks on long-term outcome.

Methods

Patient population. Since 1996, all patients who received an ICD at the Leiden University Medical Center were recorded in the departmental Cardiology Information System (EPD-vision, Leiden University Medical Center). For the current analysis, all ICDs implanted up to 2006 were

included to ensure a minimum in follow-up duration. Eligibility for ICD treatment was determined in accordance with the international guidelines and included patients with sustained VT and patients with a severely depressed left ventricular ejection fraction, regardless of previous ventricular arrhythmia (16–18). As a result of advancing guidelines, the eligibility has changed over time.

To retrieve accurate information about the origin and classification (i.e., appropriate vs. inappropriate) of ICD shocks, only recipients of ICDs equipped with intracardiac electrogram storage were included in the current analysis. Baseline characteristics were collected to identify potential predictors of inappropriate shocks. In addition, the effect of inappropriate shocks on mortality was assessed.

Device implantation and programming. All defibrillator systems were implanted in the pectoral region. During the implant procedure, testing of sensing and pacing threshold and defibrillation threshold was performed. The systems used were manufactured by Biotronik (Berlin, Germany), Medtronic (Minneapolis, Minnesota), Boston Scientific (Natick, Massachusetts), and St. Jude Medical (St. Paul, Minnesota).

Defibrillators were programmed as follows: ventricular arrhythmia faster than 150 beats/min was monitored by the device without consequent defibrillator therapy (zone 1). Ventricular arrhythmias faster than 188 beats/min were initially attempted to be terminated with 2 bursts of anti-tachycardia pacing and, after continuation of the arrhythmia, with defibrillator shocks (zone 2). In the case of a ventricular arrhythmia faster than 210 beats/min, device shocks were the initial therapy (zone 3). Furthermore, atrial arrhythmia detection was set to >170 beats/min with supraventricular tachycardia discriminators enabled. In all devices, stability and sudden onset algorithms were activated to reduce the occurrence of inappropriate shocks (19). Moreover, additional discriminators were activated in dual-chamber ICDs and cardiac resynchronization therapy defibrillators (20,21). Settings were adapted only when clinically indicated (i.e., hemodynamic well-tolerated VT at high rate, VT in the monitor zone).

Follow-up. In the Dutch health care system, the implanting center is responsible for the device follow-up, which is performed every 3 to 6 months after implantation. At every follow-up, device storage was checked for delivered therapy (appropriate/inappropriate). Adjudication of the delivered therapy was performed by a trained electrophysiologist.

An inappropriate shock was defined as an episode, starting with a shock not delivered for VT or VF and ending if sinus rhythm was redetected by the ICD. Consequently, it was possible that multiple inappropriate shocks occur within 1 episode. If a subsequent episode started within 5 min after the previous episode ended, it was not considered as a new episode. Furthermore, the cause of an inappropriate shock was categorized into supraventricular tachycardia (including atrial fibrillation [AF]), sinus tachycardia, or abnormal sensing.

Patients with missing data for more than 6 months were considered lost to follow-up.

Statistical analysis. Continuous variables were presented as mean ± SD and categorical variables as number and percentage. Cumulative event rates were calculated by using the Kaplan-Meier method and log-rank test, in which patient death and device replacement were considered censoring events. Causes of inappropriate shocks for the different device types were compared using the chi-square test. Predictors of inappropriate shocks were determined by the method of Cox proportional hazards regression. First, univariate analysis was performed, containing all baseline variables and interim appropriate shocks. Subsequently, all variables with a p value <0.10 were included in the multivariate analysis. A p value <0.25 was considered as statistically significant for the multivariate regression. To examine differences in the occurrence of inappropriate shocks per time span of ICD implantations, patients were divided into 2 groups by the median calendar year of ICD implantations. A log-rank test was used to compare the cumulative event rates between both groups.

The relationship between inappropriate shocks and all-cause mortality was assessed using a Cox proportional hazard model with first inappropriate shock or multiple inappropriate shocks (≤5 shocks) as a time-dependent covariate, adjusting for commonly used predictors of all-cause mortality (history of AF, age older than 70 years [22], New York Heart Association (NYHA) functional class higher than II, renal clearance <90 ml/min [determined with the Cockroft-Gault formula] [23], QRS duration >120 ms, use of β-blockers [22], and interim appropriate shocks [15]).

Interim appropriate shocks were defined as appropriate ICD shocks before an inappropriate ICD shock and considered time-dependent covariates in analyses for prediction of inappropriate shocks as well as for prediction of all-cause mortality. The calculated relationship was presented as a hazard ratio (HR) with a 95% confidence interval (CI).

The statistical software program SPSS version 16.0 (SPSS, Inc., Chicago, Illinois) was used for statistical analysis. A p value <0.05 was considered significant, with the exception of multivariate analyses.

Results

Patient population. From 1996 to 2006, 1,658 patients received an ICD system with intracardiac electrogram technology according to the international guidelines (16–18). One hundred fourteen patients (7%) were lost to follow-up. The remaining 1,544 patients (93%) constituted the patient population. Of these patients (79% men, average age 61 ± 13 years), 56% received an ICD for primary prevention and

Abbreviations and Acronyms

AF = atrial fibrillation

CI = confidence interval

HR = hazard ratio

ICD = implantable cardioverter-defibrillator

NYHA = New York Heart Association

VF = ventricular fibrillation

VT = ventricular tachycardia

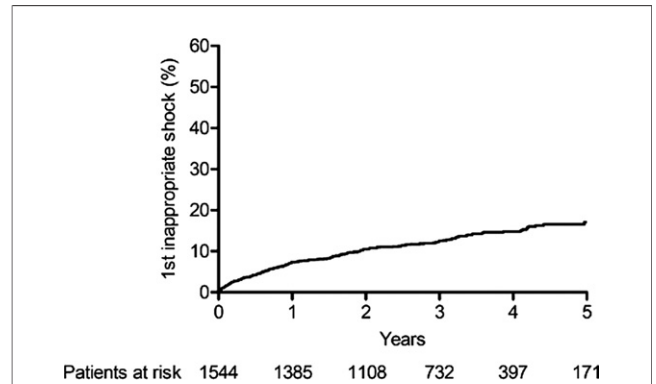| Table 1	Baseline Characteristics of Patient Population (n = 1,544)	
Clinical parameters		
Age (yrs)	61 ± 13	
Male	1,220 (79)	
Primary prevention	865 (56)	
Ischemic heart disease	988 (64)	
Left ventricular ejection fraction	35 ± 16%	
QRS duration (ms)	125 ± 35	
NYHA functional class III or IV	510 (33)	
History of AF	355 (23)	
History of smoking	818 (53)	
Diabetes	293 (19)	
Medication		
Beta-blockers (without sotalol)	787 (51)	
Sotalol	216 (14)	
Statins	880 (57)	
Diuretics	942 (61)	
ACE inhibitors/AT antagonists	1,112 (72)	
Ca antagonists	154 (10)	
Amiodarone	309 (20)	
Devices		
Single-chamber ICD	188 (12)	
Dual-chamber ICD	819 (53)	
CRT-D	537 (35)	

Values shown are mean ± SD or n (%).

ACE = angiotensin-converting enzyme; AF = atrial fibrillation; AT = angiotensin; CRT-D = cardiac resynchronization therapy defibrillator; ICD = implantable cardioverter-defibrillator; NYHA = New York Heart Association.
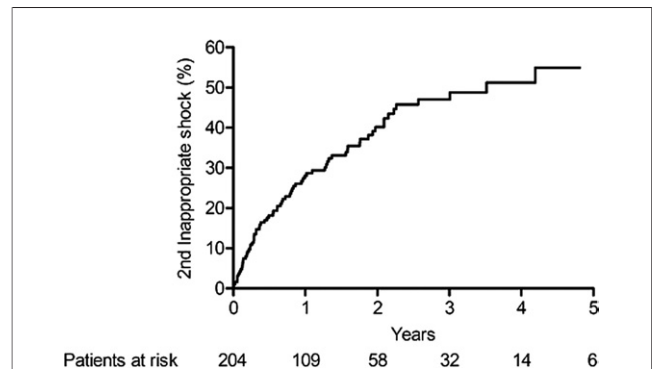

Figure 1 First Inappropriate Device Shock

Kaplan-Meier curve for the occurrence of first inappropriate implantable cardioverter-defibrillator shock.

64% had ischemic heart disease. Baseline patient characteristics are summarized in Table 1.

Incidence of inappropriate shocks. During the follow-up period of 41 ± 18 months, 204 of 1,544 patients (13%) experienced a total of 665 inappropriate ICD shocks. The average time from implantation to first inappropriate shock was 17 ± 16 months. The cumulative event rate for first inappropriate shocks was 7% (95% CI: 6% to 9%) at 1 year, 13% (95% CI: 11% to 14%) at 3 years, and 18% (95% CI: 15% to 20%) at 5 years (Fig. 1). A second inappropriate shock was experienced by 73 of 204 patients (36%) with an average time from first to second shock of 11 ± 11 months. The cumulative event rate for a second inappropriate shock was 28% (95% CI: 22% to 34%) at 1-year follow-up, 49% (95% CI: 40% to 58%) at 3-year follow-up, and 55% (95% CI: 44% to 66%) at 5-year follow-up (Fig. 2).

Predictors of inappropriate shocks. To determine specific clinical parameters predicting the occurrence of inappropriate device discharges, the univariate Cox model disclosed that age younger than 70 years (HR: 1.7, 95% CI: 1.1 to 2.3; $p < 0.01$), history of AF (HR: 2.0, 95% CI: 1.5 to 2.7; $p < 0.01$), nonischemic heart disease (HR: 1.3, 95% CI: 1.0 to 1.8; $p = 0.04$), nonuse of statins (HR: 1.4, 95% CI: 1.0 to 1.8; $p = 0.03$), and interim appropriate shocks (HR: 1.6, 95% CI: 1.0 to 2.7; $p = 0.04$) were independent predictors of inappropriate shocks (Table 2). By multivariate analysis,

age younger than 70 years (HR: 1.8, 95% CI: 1.3 to 2.5; $p < 0.01$), history of AF (HR: 2.0, 95% CI: 1.5 to 2.7; $p < 0.01$), no statin use (HR: 1.3, 95% CI: 1.0 to 1.7; $p = 0.10$), and interim appropriate shocks (HR: 1.6, 95% CI: 1.0 to 2.6; $p = 0.06$) were predictors of the occurrence of inappropriate shocks.

Period of ICD implantation. To explore whether differences over time could be observed in the occurrence of inappropriate shocks, 2 ICD patient groups were designated according to the median of calendar years of ICD implantations (May 2004). The first group underwent ICD implantation from 1996 to May 2004 and comprised 772 patients. The cumulative event rate for first inappropriate shock was 7% (95% CI: 5% to 9%) at 1 year, 10% (95% CI: 7% to 12%) at 2 years, and 11% (95% CI: 9% to 14%) at 3 years. The second group consisted of 772 patients who received an ICD system from May 2004 to 2006. The cumulative event rate for first inappropriate shock was 8% (95% CI: 6% to 10%) at 1 year, 12% (95% CI: 9% to 14%) at 2 years, and 14% (95% CI: 11% to 16%) at 3 years (Fig. 3).

Figure 2 Second Inappropriate Device Shock

Kaplan-Meier curve for the occurrence of second inappropriate implantable cardioverter-defibrillator (ICD) shock received after the first inappropriate ICD shock.

Table 2	Predictors of ≥1 Inappropriate Shocks					
	Univariate			Multivariate		
	HR	95% CI	p Value	HR	95% CI	p Value
Female	0.8	0.6–1.2	0.34			
Age <70 yrs	1.7	1.1–2.3	<0.01*	1.8	1.3–2.5	0.01
History of AF	2.0	1.5–2.7	<0.01*	2.0	1.5–2.7	<0.01
History of smoking	1.2	0.9–1.6	0.32			
Secondary indication for ICD	1.1	0.8–1.5	0.48			
Nonischemic heart disease	1.3	1.0–1.8	0.04*			
No statins at baseline	1.4	1.0–1.8	0.03*	1.3	1.0–1.7	0.09
Beta-blocker	0.8	0.6–1.1	0.22*			
NYHA functional class III to IV	1.0	0.7–1.3	0.96			
Interim appropriate shocks	1.6	1.0–2.7	0.04*	1.6	1.0–2.6	0.06

*Variable was included in multivariate analysis.
CI = confidence interval; HR = hazard ratio; other abbreviations as in Table 1.

In multivariate risk analysis, adjusted for baseline and interim variables (history of AF, age younger than 70 years, no statin use, and interim appropriate shocks), patients who received an ICD after May 2004, compared with before May 2004, tended to experience more inappropriate shocks (HR: 1.3, 95% CI: 1.0 to 1.8; p = 0.05).

Causes and differences between device types. The main cause of inappropriate shocks was misdiagnosis of supraventricular tachycardia, occurring in 155 of the 204 patients (76%). The mean ventricular cycle length at the time of a patient's first inappropriate shock for supraventricular tachycardia was 299 ± 39 ms and occurred predominantly in ICD program zone 2 (60%).

As can be seen in Table 3, comparison per device type did not show significant differences in the occurrence of inappropriate shocks. However, the cause of inappropriate shocks did differ between device types. Patients with a single-chamber ICD received significantly more shocks resulting from misdiagnosis of sinus tachycardia than patients with a dual-chamber ICD (24% vs. 8%, p = 0.02). Furthermore, patients with cardiac resynchronization therapy with a defibrillator tended to experience more inappropriate discharges due to abnormal sensing than ICD recipients with a single-chamber ICD (15% vs. 8%, p = 0.28).

Effect of inappropriate shocks on survival. A total of 298 patients (19%) died during the study follow-up. Compared with patients without inappropriate shocks, the occurrence of the first inappropriate shock tended to increase the risk of all-cause mortality (HR: 1.4, 95% CI: 1.0 to 2.0; p = 0.07). Adjustment for potential confounders (history of AF, age older than 70 years, NYHA functional class higher than II, renal clearance <90 ml/min, QRS duration >120 ms, beta-blocker use, and interim appropriate shocks) demonstrated that the occurrence of an initial inappropriate shock was related to a 60% increase in risk of mortality (HR: 1.6, 95% CI: 1.1 to 2.3; p = 0.01). Moreover, adjusted time-dependent mortality risk of subsequent inappropriate shocks had an HR of 1.4 (95% CI: 1.2 to 1.7, p < 0.01) per additional shock, up to an HR of 3.7 after experiencing 5 inappropriate shocks (Table 4).

Discussion

The main findings of the current study on the incidence, predictors, and outcome of inappropriate shocks can be summarized as follows: 1) the cumulative incidence of inappropriate shocks was 7% at 1-year follow-up, 13% at 3-year follow-up, and 18% at 5-year follow-up; 2) misdiagnosis of supraventricular tachycardia was the leading cause (76%) of inappropriate shocks; 3) age younger than 70 years, history of AF, no statin use, and interim appropriate shocks were predictors of inappropriate shocks; and 4) inappropriate shocks were associated with a higher risk of all-cause mortality.

Incidence. In major randomized clinical trials, the occurrence of inappropriate ICD therapy (i.e., anti-tachycardia pacing and shocks) is well assessed, ranging from 10% to 24% over 20 to 45 months of follow-up (24). However, lower incidences were

Patients at risk (≤ May, 2004)	772	701	647	596
Patients at risk (> May, 2004)	772	694	498	224
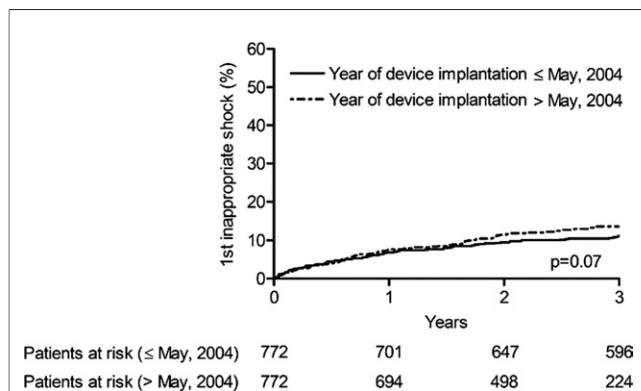
Figure 3   **First Inappropriate Shock Comparing Time Periods of ICD Implantation**

Kaplan-Meier curve for the occurrence of first inappropriate implantable cardioverter-defibrillator (ICD) shock in patients who received an ICD before May 2004 **(solid line)** and in patients who received an ICD after May 2004 **(dashed line)**.

Table 3	Causes of Inappropriate Shocks			
	Total (n = 1,544)	Single-Chamber ICD (n = 188)	Dual-Chamber ICD (n = 819)	CRT-D (n = 537)
Patients with ≥1 inappropriate shock	204 (13)	29 (15)	122 (15)	53 (10)
Rhythm misdiagnosis				
Supraventricular tachycardia	155 (76)	19 (65)	96 (79)	40 (75)
AF	92 (45)	14 (48)	55 (45)	23 (43)
Other than AF	63 (31)	5 (17)	41 (34)	17 (32)
Abnormal sensing	25 (12)	2 (8)	15 (12)	8 (15)
Sinus tachycardia	22 (11)	7 (24)	10 (8)	5 (10)
Unclassified	2 (1)	1 (3)	1 (1)	0 (0)

Values shown are n (%).
Abbreviations as in Table 1.

reported when assessing inappropriate shocks only, such as 9% in the AVID (Antiarrhythmics versus Implantable Defibrillators) trial (15) and 11.5% in the MADIT II (Multicenter Automatic Defibrillator Implantation Trial II) (25), both reported during 2-year follow-up. The current analysis demonstrated a comparable cumulative event rate of 10% at 2-year follow-up and showed that this incidence steadily increased to 18% at 5-year follow-up. In addition, more than one-half of the patients who received a single inappropriate shock experienced another one within the 5-year follow-up.

Predictors. Because more than one-half of all inappropriate shocks are due to misdiagnosis of AF, several studies found a history of AF was the most significant baseline clinical predictor of inappropriate shocks (15,26–31). Then again, these studies showed less consistency in identifying other predictors. For instance, Hreybe et al. (27) demonstrated patients with severe symptomatic heart failure (NYHA functional classes III and IV) to be at increased risk of inappropriate shocks, whereas Nanthakumar et al. (28) demonstrated NYHA functional class I as an independent predictor of inappropriate shocks. Furthermore, other predictors included the absence of coronary artery disease, use of β-blockers, ICD device type, history of smoking, no

statin use, younger age, and increased diastolic blood pressure (15,26,27,29,31).

In the current study, multivariate analysis demonstrated that ICD recipients with a history of AF have a significantly higher risk of inappropriate shocks (HR: 2.0, p < 0.01). Additionally, the present study showed that age younger than 70 years independently predicted the occurrence of inappropriate shocks (HR: 1.8, p < 0.01). Most likely, this is due to the fact that 23% of all inappropriate shocks were caused by abnormal sensing and sinus tachycardia, both associated with younger age (32).

The large cohort and long follow-up assessed in the current analysis might provide more accurate identification of predictors of inappropriate shocks than that proposed in previous studies.

Prevention of inappropriate shock over time. Ever since the first implantation, ICDs are under constant development to improve treatment of tachyarrhythmias and decrease adverse events. Advanced algorithms, multiple sensing leads, and improved device programming should reduce the occurrence of inappropriate shock (19–21). Interestingly, the current study did not confirm this theory. Patients who received their ICD system after May 2004, compared with before May 2004, did

Table 4	Predictors of All-Cause Mortality					
	Univariate			Multivariate		
	HR	95% CI	p Value	HR	95% CI	p Value
Baseline variables						
History of atrial fibrillation*	1.3	1.0–1.7	0.11	1.4	1.0–1.7	<0.01
Age >70 yrs*	2.7	2.2–3.4	<0.01	1.9	1.5–2.5	<0.01
NYHA functional class >II*	2.0	1.6–1.5	<0.01	1.5	1.1–1.9	0.03
Renal clearance <90 ml/min*	2.7	2.0–3.7	<0.01	1.7	1.2–2.4	0.02
QRS duration >120 ms*	2.0	1.6–2.5	<0.01	1.4	1.1–1.8	0.02
No use of beta-blockers*	1.3	1.0–1.7	0.01			
Interim events						
Inappropriate shock	1.4	1.0–2.0	0.07	1.6	1.1–2.3	0.01
Per inappropriate shocks (≤5)†	1.3	1.1–1.6	<0.01	1.4	1.2–1.7	<0.01
Interim appropriate shocks*	2.5	1.9–3.3	<0.01	1.6	1.2–2.1	<0.01

*Adjusted in multivariate analysis for single inappropriate shock. †In multivariate analysis, adjusted for all baseline variables and for interim appropriate shocks.
Abbreviations as in Tables 1 and 2.

not experience fewer inappropriate shocks (Fig. 3). In addition, multivariate analysis, adjusted for baseline and interim variables, even showed that these patients were at increased risk of experiencing inappropriate shocks. The most plausible explanation for this paradox is found within the evolving guidelines, which intermittently change ICD patient population from mostly secondary prevention patients to mostly primary prevention patients. In general, primary prevention patients are in poor cardiac condition (33), which could result in higher risk and prevalence of AF—the strongest predictor of the occurrence of inappropriate shocks. Hence, the increasing number of primary prevention patients could downgrade the effect of advanced ICD technology in reducing the occurrence of inappropriate shock.

Single-chamber ICDs versus dual-chamber ICDs versus cardiac resynchronization therapy defibrillators. With supraventricular arrhythmias as the principal cause of inappropriate shocks, one might hypothesize that additional sensing information would improve discrimination between supraventricular tachyarrhythmias and ventricular tachyarrhythmias to prevent inappropriate therapy. Therefore, in theory, dual-chamber ICDs should perform better than single-chamber ICDs. However, in the literature, there are doubts regarding the performance of devices with extra sensing/pacing leads compared with single-chamber ICDs. Theuns et al. (34) performed a prospective, randomized study to evaluate the performance of tachyarrhythmia detection algorithms in single- and dual-chamber ICDs, but did not find a significant reduction in the number of inappropriate arrhythmia classifications. Other studies found similar results (20,35,36). In contrast, a randomized trial conducted by Friedman et al. (37) demonstrated a small but significant reduction of inappropriate supraventricular tachyarrhythmias detection (8.6%) when using optimized programmed dual-chamber ICDs compared with single-chamber ICDs. These findings were supported by Soundarraj et al. (29).

In the present study, no significant differences were observed in the incidence of inappropriate shocks when comparing the 3 different device types.

Long-term outcome. Recent subgroup analysis of the MADIT II and the SCD-HeFT (Sudden Cardiac Death In Heart Failure Trial) found an association between increased mortality risk and ICD shocks, irrespective of appropriateness (14,15). For appropriate shocks, this association is explicable because patients who receive appropriate shocks also have VT or VF due to progressively deteriorating cardiac condition. In contrast, it was unforeseen that this association also applied to inappropriate shocks.

The present study confirmed this finding in routine clinical practice, outside the setting of a clinical trial, by demonstrating a significant correlation between inappropriate shocks and death. Moreover, the risk of all-cause mortality increased per delivered inappropriate shock; up to an HR of 3.7 after experiencing 5 inappropriate shocks.

One might postulate different explanations for the increased risk of death, including: 1) myocardial injury resulting in deterioration of left ventricular ejection fraction; 2) increased anxiety and depression associated with increased mortality; and 3) the indirect result of AF, being the leading mechanism for inappropriate shocks and also associated with an increased risk of mortality (38–40). From the current study, it is difficult to favor one explanation over another. However, various studies have supported the first explanation because they found increased markers for myocardial damage after uncomplicated ICD testing at implantation, implying cardiac tissue damage due to these high-voltage electrical discharges (38,41,42).

When comparing the results of the subgroup analysis of the MADIT II and SCD-HeFT with the current study, a notable difference was seen in the risk of all-cause mortality after experiencing an inappropriate shock (HR: 2.2 vs. HR: 2.0 vs. HR: 1.6, respectively). This difference could be explained if one assumed that (inappropriate) ICD shocks indeed cause myocardial tissue injury. In addition, ICD patients with poor cardiac condition and left ventricular function have less reserve to withstand extra cardiac damage. Therefore, inappropriate shocks will have more adverse consequences in a population with reduced cardiac function, as assessed in the MADIT II and SCD-HeFT (5,14).

Overall, it remains difficult to state that the higher risk of death was indeed caused by inappropriate ICD shocks, but so far, 3 large independent studies demonstrated an adverse relationship between ICD shocks and patient survival.

Study limitations. The current study used prospectively collected data from a single-center ICD registry. Because ICDs were implanted over a 10-year period, evolving and expanding guidelines for the implantation of ICDs, device programming, and pharmacological treatment of arrhythmias could have created a heterogeneous population. Furthermore, we attempted to control for potential confounders using multivariate statistical with time-dependent covariate analysis. However, the influence of potentially included unknown confounders could not be ruled out.

Conclusions

The current study demonstrates that in an ICD patient cohort, outside the setting of a clinical trial, inappropriate shocks occur in 13% of ICD recipients, mainly due to misdiagnosis of supraventricular tachycardia. Clinical predictors of inappropriate shocks were younger age, history of AF, no statin use, and interim appropriate shocks. Finally, inappropriate shocks were associated with a higher risk of all-cause mortality, which increased per delivered inappropriate shock and was independent of interim appropriate shocks.

Reprint requests and correspondence: Dr. Martin J. Schalij, Department of Cardiology, Leiden University Medical Center, Albinusdreef 2, 2333 ZA Leiden, the Netherlands. E-mail: m.j.schalij@lumc.nl.

REFERENCES

1. Myerburg RJ, Kessler KM, Castellanos A. Sudden cardiac death: epidemiology, transient risk, and intervention assessment. Ann Intern Med 1993;119:1187–97.
2. Huikuri HV, Castellanos A, Myerburg RJ. Sudden death due to cardiac arrhythmias. N Engl J Med 2001;345:1473–82.
3. Josephson M, Wellens HJ. Implantable defibrillators and sudden cardiac death. Circulation 2004;109:2685–91.
4. The Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. N Engl J Med 1997;337:1576–83.
5. Moss AJ, Zareba W, Hall WJ, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. N Engl J Med 2002;346:877–83.
6. Bardy GH, Lee KL, Mark DB. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. N Engl J Med 2005;352:225–37.
7. Buxton AE, Lee KL, Fisher JD, Josephson ME, Prystowsky EN, Hafley G. A randomized study of the prevention of sudden death in patients with coronary artery disease. Multicenter Unsustained Tachycardia Trial Investigators. N Engl J Med 1999;341:1882–90.
8. Moss AJ, Hall WJ, Cannom DS, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. Multicenter Automatic Defibrillator Implantation Trial Investigators. N Engl J Med 1996;335:1933–40.
9. Kadish A, Dyer A, Daubert JP, et al. Prophylactic defibrillator implantation in patients with nonischemic dilated cardiomyopathy. N Engl J Med 2004;350:2151–8.
10. Mark DB, Anstrom KJ, Sun JL, et al. Quality of life with defibrillator therapy or amiodarone in heart failure. N Engl J Med 2008;359:999–1008.
11. Prudente LA. Phantom shock in a patient with an implantable cardioverter defibrillator: case report. Am J Crit Care 2003;12:144–6.
12. Schron EB, Exner DV, Yao Q, et al. Quality of life in the antiarrhythmics versus implantable defibrillators trial: impact of therapy and influence of adverse symptoms and defibrillator shocks. Circulation 2002;105:589–94.
13. Vollmann D, Luthje L, Vonhof S, Unterberg C. Inappropriate therapy and fatal proarrhythmia by an implantable cardioverter-defibrillator. Heart Rhythm 2005;2:307–9.
14. Poole JE, Johnson GW, Hellkamp AS, et al. Prognostic importance of defibrillator shocks in patients with heart failure. N Engl J Med 2008;359:1009–17.
15. Daubert JP, Zareba W, Cannom DS, et al. Inappropriate implantable cardioverter-defibrillator shocks in MADIT II: frequency, mechanisms, predictors, and survival impact. J Am Coll Cardiol 2008;51:1357–65.
16. Epstein AE, DiMarco JP, Ellenbogen KA, et al. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices). J Am Coll Cardiol 2008;51:e1–62.
17. Gregoratos G, Abrams J, Epstein AE, et al. ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/NASPE Committee to Update the 1998 Pacemaker Guidelines). J Am Coll Cardiol 2002;40:1703–19.
18. Zipes DP, Camm AJ, Borggrefe M, et al. ACC/AHA/ESC 2006 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: a report of the American College of Cardiology/American Heart Association Task Force and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death). J Am Coll Cardiol 2006;48:e247–346.
19. Higgins SL, Lee RS, Kramer RL. Stability: an ICD detection criterion for discriminating atrial fibrillation from ventricular tachycardia. J Cardiovasc Electrophysiol 1995;6:1081–8.
20. Kuhlkamp V, Dornberger V, Mewis C, Suchalla R, Bosch RF, Seipel L. Clinical experience with the new detection algorithms for atrial fibrillation of a defibrillator with dual chamber sensing and pacing. J Cardiovasc Electrophysiol 1999;10:905–15.
21. Burri H, Sunthorn H, Shah D, Lerch R. Optimization of device programming for cardiac resynchronization therapy. Pacing Clin Electrophysiol 2006;29:1416–25.
22. Goldenberg I, Vyas AK, Hall WJ, et al. Risk stratification for primary implantation of a cardioverter-defibrillator in patients with ischemic left ventricular dysfunction. J Am Coll Cardiol 2008;51:288–96.
23. Levey AS, Coresh J, Balk E, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Ann Intern Med 2003;139:137–47.
24. Germano JJ, Reynolds M, Essebag V, Josephson ME. Frequency and causes of implantable cardioverter-defibrillator therapies: is device therapy proarrhythmic? Am J Cardiol 2006;97:1255–61.
25. Klein RC, Raitt MH, Wilkoff BL, et al. Analysis of implantable cardioverter defibrillator therapy in the Antiarrhythmics Versus Implantable Defibrillators (AVID) trial. J Cardiovasc Electrophysiol 2003;14:940–8.
26. Bhavnani SP, Coleman CI, White CM, et al. Association between statin therapy and reductions in atrial fibrillation or flutter and inappropriate shock therapy. Europace 2008;10:854–9.
27. Hreybe H, Ezzeddine R, Barrington W, et al. Relation of advanced heart failure symptoms to risk of inappropriate defibrillator shocks. Am J Cardiol 2006;97:544–6.
28. Nanthakumar K, Dorian P, Paquette M, et al. Is inappropriate implantable defibrillator shock therapy predictable? J Interv Card Electrophysiol 2003;8:215–20.
29. Soundarraj D, Thakur RK, Gardiner JC, Khasnis A, Jongnarangsin K. Inappropriate ICD therapy: does device configuration make a difference. Pacing Clin Electrophysiol 2006;29:810–5.
30. Theuns DA, Klootwijk AP, Simoons ML, Jordaens LJ. Clinical variables predicting inappropriate use of implantable cardioverter-defibrillator in patients with coronary heart disease or nonischemic dilated cardiomyopathy. Am J Cardiol 2005;95:271–4.
31. Woo A, Monakier D, Harris L, et al. Determinants of implantable defibrillator discharges in high-risk patients with hypertrophic cardiomyopathy. Heart 2007;93:1044–5.
32. Kleemann T, Becker T, Doenges K, et al. Annual rate of transvenous defibrillation lead defects in implantable cardioverter-defibrillators over a period of >10 years. Circulation 2007;115:2474–80.
33. Ezekowitz JA, Armstrong PW, McAlister FA. Implantable cardioverter defibrillators in primary and secondary prevention: a systematic review of randomized, controlled trials. Ann Intern Med 2003;138:445–52.
34. Theuns DA, Klootwijk AP, Goedhart DM, Jordaens LJ. Prevention of inappropriate therapy in implantable cardioverter-defibrillators: results of a prospective, randomized study of tachyarrhythmia detection algorithms. J Am Coll Cardiol 2004;44:2362–7.
35. Deisenhofer I, Kolb C, Ndrepepa G, et al. Do current dual chamber cardioverter defibrillators have advantages over conventional single chamber cardioverter defibrillators in reducing inappropriate therapies? A randomized, prospective study. J Cardiovasc Electrophysiol 2001;12:134–42.
36. Al-Ahmad A, Wang PJ, Homoud MK, Estes NA III, Link MS. Frequent ICD shocks due to double sensing in patients with biventricular implantable cardioverter defibrillators. J Interv Card Electrophysiol 2003;9:377–81.
37. Friedman PA, McClelland RL, Bamlet WR, et al. Dual-chamber versus single-chamber detection enhancements for implantable defibrillator rhythm diagnosis: the detect supraventricular tachycardia study. Circulation 2006;113:2871–9.
38. Schluter T, Baum H, Plewan A, Neumeier D. Effects of implantable cardioverter defibrillator implantation and shock application on biochemical markers of myocardial damage. Clin Chem 2001;47:459–63.
39. Sherwood A, Blumenthal JA, Trivedi R, et al. Relationship of depression to death or hospitalization in patients with heart failure. Arch Intern Med 2007;167:367–73.
40. Borleffs CJ, van Rees JB, van Welsenes GH, et al. Prognostic importance of atrial fibrillation in implantable cardioverter-defibrillator patients. J Am Coll Cardiol 2010;55:879–85.
41. Allan JJ, Feld RD, Russell AA, et al. Cardiac troponin I levels are normal or minimally elevated after transthoracic cardioversion. J Am Coll Cardiol 1997;30:1052–6.
42. Hurst TM, Hinrichs M, Breidenbach C, Katz N, Waldecker B. Detection of myocardial injury during transvenous implantation of automatic cardioverter-defibrillators. J Am Coll Cardiol 1999;34:402–8.