Appropriate Therapy But Not Inappropriate Shocks Predict Survival in Implantable Cardioverter Defibrillator Patients

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ABSTRACT

Background: Inappropriate implantable cardioverter defibrillator (ICD) shocks have been linked to a worse clinical outcome due to direct myocardial injury.

Hypothesis: The occurrence of ventricular tachyarrhythmia indicating progression of the underlying heart disease, but not the ICD shock itself, has prognostic impact in clinical routine.

Methods: In a retrospective study, 1117 recipients of an ICD were analyzed with respect to appropriate and inappropriate therapies and survival.

Results: During a mean follow-up of 2.92 years, appropriate therapy occurred in 27.7% and 54.0% of patients who had received an ICD for primary and secondary prevention of sudden cardiac death (SCD), respectively ($P < 0.0001$). Inappropriate shock therapy occurred in 15.0% and 25.4% of patients who had received an ICD for primary and secondary prevention of SCD, respectively ($P = 0.122$). Appropriate ICD therapy had a strong impact on overall survival ($P < 0.0001$), and this association was found both in primary ($P < 0.0001$) and secondary ($P = 0.002$) prevention of SCD. Inappropriate ICD shocks had no impact on total mortality, neither in primary nor secondary prevention of SCD.

Conclusions: Inappropriate shocks do not affect survival, in strong contrast to appropriate ICD therapy. Our study does not support the hypothesis that shock therapy in itself worsens clinical outcome. However, it confirms that appropriate ICD therapy is a warning sign and should prompt physicians to consider additional treatment strategies.

Introduction

Treatment with an implantable cardioverter defibrillator (ICD) improves survival in patients with increased risk for sudden cardiac death (SCD).^{1–3} However, both appropriate^{4,5} and inappropriate⁶ defibrillator shocks have been linked to poor clinical prognosis, possibly by causing direct myocardial injury or because they indicate disease progression.⁷ In this study, we retrospectively analyzed 1117 patients with respect to appropriate and inappropriate ICD therapies and survival.

Methods

Study Population

Baseline characteristics of the cohort (1117 ICD recipients from the University Clinic of Innsbruck, Austria, and from

the University Clinic of Zürich, Switzerland) are shown in Table 1. The underlying heart disease was coronary artery disease in 606 of the patients (54.3%), dilated cardiomyopathy in 337 (30.2%), arrhythmogenic right ventricular dysplasia in 31 (2.8%), hypertrophic cardiomyopathy in 29 (2.6%), idiopathic ventricular tachycardia (VT) or ventricular fibrillation (VF) in 26 (2.3%), noncompaction cardiomyopathy in 25 (2.2%), valvular heart disease in 24 (2.1%), congenital heart disease in 12 (1.1%), Brugada syndrome in 9 (0.8%), long QT syndrome in 6 (0.5%), recurrent coronary vasospasm causing ventricular tachyarrhythmia in 4 (0.4%), cardiac sarcoidosis in 3 (0.3%), a cardiomyopathy due to Lamin mutation in 2 (0.2%), a restrictive cardiomyopathy including amyloidosis in 2 (0.2%), and short QT syndrome in 1 (0.1%). The patients were routinely followed every 6 months, and appropriate or inappropriate ICD therapies were analyzed by telemetry. Appropriate ICD therapy was defined as either antitachycardia pacing, cardioversion, or defibrillation of VT or VF by analysis of the stored

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Table 1. Baseline Characteristics of Patients

Characteristic, n (%)	All Patients (n = 1117)	Primary Prevention (n = 441, 39.5%)	Secondary Prevention (n = 676, 60.5%)
Male	909 (81.4)	356 (80.7)	553 (81.8)
Ischemic etiology	606 (54.3)	220 (49.9)	386 (57.1)
NYHA >II	403 (36.1)	230 (52.2)	173 (25.6)
QRS >120 ms	552 (49.4)	257 (58.3)	295 (43.6)
LVEF <30%	633 (56.7)	355 (80.5)	278 (41.1)
GFR <60 mL/ min/1.73 m ²	478 (42.8)	207 (46.9)	271 (40.1)
AF	419 (37.5)	154 (34.9)	265 (39.2)
Age >70 y	216 (19.3)	67 (15.2)	149 (22.0)
Device type			
Single chamber	582 (52.1)	187 (42.4)	395 (58.4)
Dual chamber	275 (24.6)	60 (13.6)	215 (31.8)
CRT-D	260 (23.3)	194 (44.0)	66 (9.8)
Abbreviations: AF, atrial fibrillation; CRT-D, cardiac resynchronization therapy with an ICD; GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association functional class; QRS, QRS complex.			

electrograms. Any ICD shock therapy not delivered for VT or VF was defined as inappropriate.

Statistical Analysis

Categorical data are presented as absolute numbers with percentages; continuous parameters are shown as mean $\pm$ SD. Kaplan-Meier curves and log-rank test were used to compare incidence of appropriate and inappropriate ICD therapy and their effect on survival in primary and secondary prevention ICD patients. Follow-up started after implantation of the device and ended at appropriate or inappropriate ICD therapy, death, or latest follow-up examination. Two-sided *P* values <0.05 were considered statistically significant. All statistical analyses were conducted using SPSS 17.0 statistical software (SPSS Inc., Chicago, IL).

Results

Incidence and Prognostic Implications of Appropriate and Inappropriate ICD Therapies

Overall mortality was 22.1% (247 out of 1117 patients) and did not differ between patients who had their ICD implanted for primary or secondary prevention (*P* = 0.515; Figure 1A). During a mean follow-up of 2.92 years, appropriate ICD therapy occurred in 27.7% and 54.0% of ICD patients in primary and secondary prevention, respectively (*P* < 0.0001; Figure 1B). Inappropriate shock therapy occurred in 21.0% of all patients (15.0% and 25.4% in

Figure 1. Kaplan-Meier curves showing overall survival (A), incidence of appropriate ICD therapy (B), and incidence of inappropriate ICD shocks (C) in ICD recipients, stratified to primary or secondary prevention of SCD. Abbreviations: ICD, implantable cardioverter defibrillator; SCD, sudden cardiac death.

primary and secondary prevention, respectively (*P* = 0.122; Figure 1C). The rhythm triggering inappropriate therapy was categorized as atrial fibrillation or flutter in 138

(A)

(B)

(C)

- no appropriate ICD therapy
- appropriate ICD therapy

Figure 2. Kaplan-Meier curves showing that appropriate ICD therapy affects survival (A). This association was found in all ICD recipients, regardless of whether the device had been implanted for primary (B) or secondary (C) prevention of SCD. Abbreviations: ICD, implantable cardioverter defibrillator; SCD, sudden cardiac death.

patients (12.4%), supraventricular tachycardia including sinus tachycardia in 45 patients (4.0%), or inappropriate sensing in 52 patients (4.6%). Lead dysfunction occurred in 16.5% of all patients during follow-up.

(A)

(B)

(C)

- no inappropriate ICD therapy
- inappropriate ICD therapy

Figure 3. Kaplan-Meier curves showing that inappropriate ICD shocks have no impact on total mortality. This lack of association (A) was found in all ICD recipients, regardless of whether the device had been implanted for primary (B) or secondary (C) prevention of SCD. Abbreviations: ICD, implantable cardioverter defibrillator; SCD, sudden cardiac death.

Appropriate ICD therapies had a strong impact on overall survival ($P < 0.0001$; Figure 2A), and this association was found both in primary ($P < 0.0001$; Figure 2B) and secondary ($P = 0.002$; Figure 2C) prevention of SCD. Inappropriate ICD therapies had no impact on overall

survival ($P = 0.615$; Figure 3A), neither in primary ($P = 0.427$; Figure 3B) nor secondary ($P = 0.813$; Figure 3C) prevention of SCD.

Discussion

Our retrospective study of 1117 ICD recipients clearly confirmed that the occurrence of appropriate ICD therapy is associated with a markedly increased risk of death, as recently shown in the Multicenter Automatic Defibrillator Implantation Trial-II (MADIT-II) or the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT).^{4,5} However, as both MADIT-II and SCD-HeFT were primary prevention trials, our study is the first to show such an association in patients who had received an ICD for secondary prevention of SCD. Therefore, appropriate ICD therapies should be regarded as a warning sign and a marker of disease progression. It should prompt physicians to consider additional treatment-strategies, such as optimization of neurohumoral medication, revascularization in ischemic cardiomyopathy, cardiac resynchronization therapy in the presence of broad QRS complexes, or evaluation for heart transplantation in selected patients.

In contrast to reports from MADIT-II or SCD-HeFT, inappropriate shocks had no impact on survival in our cohort.^{5,6} The reason for this discrepancy is unclear. However, this finding does not support the concept that ICD shocks have adverse effects on ventricular function causing direct myocardial injury. Accordingly, shocks cannot be linked to generally increased total mortality, regardless of whether they have been delivered appropriately or inappropriately.

Conclusion

Our study does not confirm the hypothesis that shock therapy in itself worsens clinical outcome as has been reported, as shown in patients receiving inappropriate shocks. In contrast, appropriate ICD therapy is a warning sign and a marker of disease progression resulting in increased mortality. Although reducing inappropriate shocks in ICD patients is an important clinical issue to improve quality of life and prolong duration of battery function, our findings suggest that such interventions will not improve prognosis.

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