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Impact of accelerated ventricular tachyarrhythmias on mortality in patients with implantable cardioverter-defibrillator therapy

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ABSTRACT

Background: Anti-tachycardia pacing (ATP) and shock delivery may induce or accelerate tachyarrhythmias in patients with implantable cardioverter-defibrillator (ICD). We investigated the incidence, triggers and impact on mortality of accelerated ventricular tachyarrhythmias.
Methods: Database analysis concerning ventricular tachyarrhythmias accelerated by ATP or shock in 1275 ICD patients (age at implantation 59.7 ± 14.0 years; 81% male).
Results: Within a mean follow-up period of 5.3 ± 4.0 years, intracardiac electrograms were available in 1170 patients (91.8%). Overall 157 episodes of accelerated ventricular tachyarrhythmias were found in 100 of 1170 patients (8.5%). Termination of tachyarrhythmias was achieved by shock delivery in 153 episodes (96.8%). Triggers of accelerated tachyarrhythmias were appropriate ATP in 139 (88.5%) and inappropriate ATP in 14 (8.9%), as well as appropriate and inappropriate shocks in 2 (1.3%) episodes, respectively. Chronic heart failure was significantly correlated with the occurrence and recurrence of acceleration ($p<0.001$). Patients with accelerated ventricular tachyarrhythmia and subsequent shock therapy revealed higher all-cause mortality (*HR* 1.760; *95% CI* 1.286–2.410; $p<0.001$) as well as higher cardiac mortality (*HR* 2.555; *95% CI* 1.446–4.513; $p=0.001$). The correlation between acceleration and all-cause mortality was independent of left ventricular function (*HR* 2.076; *95% CI* 1.633–2.639; $p<0.001$).
Conclusions: Ventricular ATP with arrhythmia acceleration and subsequent shock delivery is a frequent and serious complication of ICD therapy that predominantly occurs in patients with reduced left ventricular function. Finally, occurrence of accelerated ventricular tachyarrhythmias was associated with increased all-cause mortality.

1. Introduction

Ventricular anti-tachycardia pacing (ATP) terminates ventricular tachyarrhythmias in up to 89% in a painless and effective way [1,2]. However, anti-tachycardia pacing (ATP) and shock delivery may induce or accelerate ventricular tachyarrhythmias in patients with implantable cardioverter-defibrillator (ICD) therapy [1–10].

Currently, little is known about the trigger mechanisms and the complications of ventricular tachyarrhythmias accelerated by ATP or shock. This retrospective analysis investigates the incidence, as well as the triggers and the clinical outcome of accelerated tachyarrhythmias of ICD therapy in the everyday practice of a high volume center.

2. Methods

2.1. Definition and management of accelerated ventricular tachyarrhythmias

Ventricular tachycardia (VT) and ventricular fibrillation were summarized as ventricular tachyarrhythmia. The cut off cycle length for differentiation between *slow* and *fast VT* was 300 ms (Table 1). This standard program was developed over the years for the majority of ICD patients, except for patients with channelopathies or previously documented slower VT, for example. Anti-tachycardia pacing and shock therapy were defined as *ICD interventions*. Acceleration of VT and induction of ventricular arrhythmias by appropriate ICD interventions were summarized as *accelerated ventricular tachyarrhythmia*. This was defined as a decrease > 10% in ventricular cycle length after delivery of an ICD intervention (Fig. 1). The latter were defined as *inappropriate* when they were not triggered by ventricular tachyarrhythmias.

Including all ICD with biventricular pacing, anti-tachycardia pacing was delivered exclusively from the right ventricular lead. Patterns of ATP comprise *burst pacing* with a constant cycle length, and different *ramp pacings* with either continuous or discontinuous shortening of the cycle length.

Depending on the underlying trigger, recurrence of accelerated tachyarrhythmia may be avoided by re-programming of parameters concerning detection of ventricular tachycardia as well as coupling intervals and patterns of ATP (Table 1).

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Table 1
Standard programming of implantable cardioverter-defibrillator.

	Slow VT zone	Fast VT zone	VF zone
Cycle length (ms)	375–300	300–250	<250
Anti-tachycardia therapy	1) Burst ATP 2) Ramp ATP	1) Burst ATP 2) Ramp ATP 3) Shock	Shock *(burst-before-shock if available)*
ATP coupling interval (%)	80–85	78–81	*Not applicable*

ATP, anti-tachycardia pacing; VF, ventricular fibrillation; VT, ventricular tachycardia.

2.2. Endpoints

First, we aimed to investigate the incidence and trigger mechanisms of accelerated ventricular tachyarrhythmias. Furthermore, we focused on all-cause and cardiac mortality in these patients.

2.3. Patient population

Within an observation period of 21 years, overall 1275 patients received an ICD in our institution. Data processing was based on a computerized database for quality management of ICD patients, which was closed for final analysis by the end of 2010. Over the years, the indications for implantation of ICD varied in dependence on the guidelines for the prevention of sudden cardiac death and ventricular arrhythmias, last updated in 2006 [11]. Implantation for primary prevention of sudden cardiac death was indicated in 20.1% (Table 2).

The authors of this manuscript have certified that they comply with the principles of ethical publishing in the International Journal of Cardiology.

2.4. ICD implantation and follow-up

The decision for a single- or a dual-chamber ICD depended on the presence of concomitant pacing indications. Until 2008, ICD implantation was performed with defibrillation threshold testing in conscious sedation; at least a 10 Joule defibrillation safety margin (20–25 J, depending on device type) had to be achieved for protocol satisfaction. Programmed shock energy was constant for each patient. After 2008, defibrillation threshold testing before ICD implantation was abandoned completely. Patients were followed in the outpatient department 6 weeks and 6 months after implantation, then regularly every 6 months, as well as in case of symptomatic ICD therapies. All stored intracardiac electrocardiograms of ICD interventions were analyzed by two cardiologists.

2.5. Statistics

Data were expressed as frequencies or percentages for discrete variables and as mean ± standard deviation for continuous variables. Comparisons between groups were made using the chi-square test for categorical variables, and the Student *t* test for continuous variables, when normally distributed. Statistical significance was considered if $p<0.05$. Cox proportional hazard models were performed to determine independent predictors of all-cause mortality: predefined cardiovascular risk factors (left ventricular ejection fraction<40%, coronary artery disease, ischemic or non-ischemic heart failure, atrial fibrillation or flutter, and age) as well as accelerated ventricular tachyarrhythmia were included in the multivariable analyses. A Kaplan–Meier analysis with the log-rank test was used to determine the all-cause mortality according to accelerated ventricular tachyarrhythmias.

3. Results

3.1. Population

Baseline characteristics of all 1275 patients are summarized in Table 2. In this collective, chronic heart failure was defined as a reduced left ventricular ejection fraction (LVEF)<40%, as assessed by transthoracic echocardiography or cardiac scintigraphy with technetium. Within a mean follow-up period of 5.3 ± 4.0 years, intracardiac electrograms were documented in 1170 patients (91.8%). Overall, 157 episodes of accelerated ventricular tachyarrhythmias were detected in 100 of 1170 patients (8.5%). These patients predominantly had ischemic chronic heart failure (50%), followed by non-ischemic chronic heart failure (27%), coronary artery disease without heart failure (17%), idiopathic ventricular tachyarrhythmias (5%), and long QT syndrome (1%). Chronic heart failure with a left ventricular ejection fraction<40% showed a significant correlation with accelerated ventricular tachyarrhythmias (77% vs. 23%; $p<0.001$). Accordingly, there was a significant difference in left ventricular ejection fraction between patients with and without occurrence of acceleration (29.9 ± 13.5 vs. 34.8 ± 15.0; $p=0.007$).

3.2. Electrophysiological aspects of accelerated tachyarrhythmia

Triggers of accelerated ventricular tachyarrhythmia were appropriate ATP in 139 (88.5%), inappropriate ATP in 14 (8.9%), as well as appropriate and inappropriate shocks in 2 episodes (1.3% each) respectively. Seven out of 100 patients had more than one trigger for accelerated tachyarrhythmias. Shock delivery was the only trigger in three patients. In overall 573 patients with documented ATP (49% of our collective), 97 patients (17%) revealed accelerated ventricular tachyarrhythmias. Despite tailored re-programming of ATP parameters (listed in Table 1), 31 patients (31%) had recurrent episodes of accelerated tachyarrhythmia. Recurrence of acceleration was also significantly correlated to chronic heart failure (81% vs. 19%; $p<0.001$).

Neither the initial cycle length of accelerated ventricular tachyarrhythmias (322 ± 60 ms), nor the coupling intervals of ATP (79 ± 3%) did correlate with acceleration. Concerning the incidence of acceleration, there was no statistical significant difference between monomorphic and polymorphic VT, as well as between VT with initially slow (49.5%) and VT with initially fast (50.5%) tachycardia cycle length (363 ± 59 ms vs. 283 ± 22 ms, $p<0.001$). Acceleration was more often related to *burst* than to *ramp* ATP (77% vs. 23%, $p<0.001$), which is explained by our standard program (Table 1).

Termination of accelerated tachyarrhythmias was achieved by *shock delivery* in 153 of 157 episodes (96.8%) in 99 patients, with an average of 1.94 shocks per episode (overall 297 shocks). Within this group, 24 patients (i.e. 2% of all 1170 patients) experienced a shock exclusively after an episode of acceleration. Patients with acceleration had significantly more shocks than patients with shock experience without acceleration (12.0 ± 12.7 vs. 6.8 ± 10.6 shocks per patient; $p<0.001$). When disregarding all shocks delivered after acceleration, patients with acceleration and preserved left ventricular function experienced as many shocks as patients with chronic heart failure and shock therapy without acceleration (6.5 ± 9.5 vs. 6.4 ± 8.5 shocks per patient). There was no significant difference in the incidence of acceleration between single-chamber, dual-chamber and biventricular ICD devices (55/700 vs. 36/372 vs. 9/98 patients, respectively; i.e. 7.9% vs. 9.7% vs. 9.2%; $p=$ n.s.). The mean time to the first episode of acceleration was 2.8 ± 3.1 years, with a wide range between 3 days and 16.2 years.

3.3. Mortality

All-cause mortality was 31.4% (367 of 1170 patients), whereas cardiac mortality was documented in 7.3% (85 of 1170 patients). Patients with a LVEF<40% showed a significantly higher mortality (243 vs. 124 patients; i.e. 35.3% vs. 25.7%; $p<0.001$), and mortality was associated with a significantly lower LVEF as well (29.5 ± 13.4% vs. 36.9 ± 15.1%; $p<0.001$). Multivariable analysis revealed the following predictors of all-cause mortality: LVEF<40%, age and accelerated ventricular tachyarrhythmias (Table 3). Furthermore, all-cause mortality was significantly higher in the 512 patients with shock experience than in the 658 patients without shock delivery (186 vs. 181 patients; i.e. 36.3% vs. 27.5%; $p=0.002$). All-cause mortality was statistically not different between patients with either only appropriate or only inappropriate shocks (33.4% vs. 29.7%; $p=$ n.s.). In particular, shock experience was associated with a higher *cardiac* mortality (46 vs. 39 patients; i.e. 9.0% vs. 5.9%; $p=0.046$).

When compared to patients without acceleration, patients with accelerated ventricular tachyarrhythmias revealed higher all-cause mortality (*HR* 1.760; *95% CI* 1.286–2.410; $p<0.001$; Fig. 2), as well as higher cardiac mortality (*HR* 2.555; *95% CI* 1.446–4.513; $p=0.001$). When compared to patients with ATP alone, patients with ATP and subsequent acceleration also revealed higher all-cause mortality (47/98 vs. 139/413 patients; i.e. 48% vs. 33.6%; $p<0.001$). Indeed, acceleration was an independent predictor of mortality in patients with documented ATP (Table 4). As displayed in Table 5, acceleration of ventricular tachyarrhythmias with subsequent shock therapy had a