Clinical course and prognostic relevance of antitachycardia pacing-terminated ventricular tachyarrhythmias in implantable cardioverter-defibrillator patients

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Aims
In patients with an implantable cardioverter-defibrillator (ICD), ICD shocks due to ventricular tachycardia (VT) or ventricular fibrillation (VF) have been associated with an increased mortality. It is not known whether patients with antitachycardia pacing (ATP)-terminated VT/VF episodes have a similar worse outcome. The aim of this study was to evaluate the clinical course and prognostic impact of ATP-terminated episodes on mortality in ICD patients.

Methods and results
A total of 1398 consecutive patients of the prospective single-centre ICD-registry Ludwigshafen who underwent an ICD implantation between 1992 and 2008 for primary or secondary prevention of sudden cardiac death were analysed. Patients treated with ATP were compared with patients with appropriate ICD shocks or patients without any appropriate ATP or ICD shock. During the median follow-up time of 6 years, 749 (54%) patients experienced 17,827 episodes of VT or VF which were terminated by ATP in 74% and by shock in 26% of patients. In approximately half (n = 321/749) of those patients with VT/VF, the first episode was terminated by ATP. In a multivariate analysis adjusted for different baseline confounding parameters, the occurrence of first ATP therapy was associated with a higher mortality rate [hazard ratio (HR) 2.60, 95% confidence interval (CI) 2.02–3.35]. When excluding all patients with appropriate ICD shocks first ATP therapy remained associated with a worse prognosis (HR 1.92, 95% CI 1.38–2.67).

Conclusions
In ICD patients, about three-fourths of ventricular arrhythmias are terminated by ATP. The occurrence of ATP-terminated episode is associated with an increased mortality rate.

Keywords
Antitachycardia pacing • Prognosis • Defibrillation • Implantable cardioverter-defibrillator

Introduction
Ventricular arrhythmias in implantable cardioverter-defibrillator (ICD) patients can be terminated either by shock or by antitachycardia pacing (ATP). Both are very common in ICD patients.1–5 It is well known that ICD shocks are associated with a worse outcome.3,4–7 In the SCD-HeFT study, ICD patients had a five-fold increase in risk of death after receiving an appropriate shock.1 Until now it is unclear whether termination of ventricular arrhythmias by ATP has a similar association with increased mortality in clinical practice. In the MADIT-RIT study, change of ICD programming towards fewer ICD shocks and ATP therapy resulted in reduction of all-cause mortality.5 A meta-analysis by Scott et al.8 proposed that the marked reduction of episodes of appropriate ATP therapy along with the reduction of inappropriate ICD therapy may contribute to the decrease in all-cause mortality seen with prolonged arrhythmia detection time. On the other hand, a recently published study of Bencardino et al.9 suggested that sustained ventricular arrhythmias per se have a negative impact on prognosis rather than the modality of ICD therapy.

While ICD shocks have a strong negative influence on quality of life,10 ATP-treated ventricular tachycardia (VT) is often asymptomatic and can be frequently detected during routine ICD controls.2 Ventricular tachycardia ablation or antiarrhythmic therapy is useful...
a tool to reduce the occurrence of VTs. Antitachycardia pacing-treated VTs could be a suitable target for VT ablation as those VTs are usually slower and hemodynamically more stable. But VT ablation and antiarrhythmic therapy are associated with complication risks. Currently, it is unclear if patients with ATP episodes should be treated like patients who received ICD shocks. For this reason, it is important to know which clinical relevance ATP-treated VT has in clinical practice.

The aim of this study was to evaluate the clinical course and prognostic impact of ATP-terminated VTs on mortality in ICD patients.

Methods

Patient characteristics

A total of 1398 patients, who underwent an ICD implantation from 1992 to May 2008 for primary or secondary prevention of sudden cardiac death, were consecutively enrolled in the prospective single-centre ICD-registry Ludwigshafen that has been previously described in detail. Informed consent was obtained from all patients. The implanted devices were manufactured by Biotronik, Guidant, ELA Medical, Medtronic, and St. Jude Medical. After ICD implantation, all patients visited the defibrillator outpatient clinic every 3 months as well as in case of any adverse event. Evaluation in ICD clinic consisted of interrogation of the ICD-registry Ludwigshafen that has been previously described in detail. A total of 1398 patients, who underwent an ICD implantation from 1992 to May 2008 for primary or secondary prevention of sudden cardiac death, were consecutively enrolled in the prospective single-centre ICD-registry Ludwigshafen that has been previously described in detail. Informed consent was obtained from all patients. The implanted devices were manufactured by Biotronik, Guidant, ELA Medical, Medtronic, and St. Jude Medical. After ICD implantation, all patients visited the defibrillator outpatient clinic every 3 months as well as in case of any adverse event. Evaluation in ICD clinic consisted of interrogation of the ICD-registry Ludwigshafen that has been previously described in detail. A total of 1398 patients, who underwent an ICD implantation from 1992 to May 2008 for primary or secondary prevention of sudden cardiac death, were consecutively enrolled in the prospective single-centre ICD-registry Ludwigshafen that has been previously described in detail. Informed consent was obtained from all patients. The implanted devices were manufactured by Biotronik, Guidant, ELA Medical, Medtronic, and St. Jude Medical. After ICD implantation, all patients visited the defibrillator outpatient clinic every 3 months as well as in case of any adverse event. Evaluation in ICD clinic consisted of interrogation of the ICD-registry Ludwigshafen that has been previously described in detail. A total of 1398 patients, who underwent an ICD implantation from 1992 to May 2008 for primary or secondary prevention of sudden cardiac death, were consecutively enrolled in the prospective single-centre ICD-registry Ludwigshafen that has been previously described in detail. Informed consent was obtained from all patients. The implanted devices were manufactured by Biotronik, Guidant, ELA Medical, Medtronic, and St. Jude Medical. After ICD implantation, all patients visited the defibrillator outpatient clinic every 3 months as well as in case of any adverse event. Evaluation in ICD clinic consisted of interrogation of the ICD-registry Ludwigshafen that has been previously described in detail. A total of 1398 patients, who underwent an ICD implantation from 1992 to May 2008 for primary or secondary prevention of sudden cardiac death, were consecutively enrolled in the prospective single-centre ICD-registry Ludwigshafen that has been previously described in detail. Informed consent was obtained from all patients. The implanted devices were manufactured by Biotronik, Guidant, ELA Medical, Medtronic, and St. Jude Medical. After ICD implantation, all patients visited the defibrillator outpatient clinic every 3 months as well as in case of any adverse event. Evaluation in ICD clinic consisted of interrogation of the ICD-registry Ludwigshafen that has been previously described in detail. A total of 1398 patients, who underwent an ICD implantation from 1992 to May 2008 for primary or secondary prevention of sudden cardiac death, were consecutively enrolled in the prospective single-centre ICD-registry Ludwigshafen that has been previously described in detail. Informed consent was obtained from all patients. The implanted devices were manufactured by Biotronik, Guidant, ELA Medical, Medtronic, and St. Jude Medical. After ICD implantation, all patients visited the defibrillator outpatient clinic every 3 months as well as in case of any adverse event. Evaluation in ICD clinic consisted of interrogation of the ICD-registry Ludwigshafen that has been previously described in detail.

Implantable cardioverter-defibrillator programming

The protocol for the programming of the ICD was dependent on the indication of the ICD and the year of ICD implantation. From 1992 to 2005, all patients received two zones of therapy programmed independently of the ICD indication: (i) a ventricular fibrillation (VF) zone which was defined as an episode of tachycardia with at least 12 beats at a rate of 200 beats/min or more; in this zone up to six shocks could be delivered per episode; (ii) a VT zone with an episode of tachycardia with at least 12 beats at a rate between 167 and 200 beats/min. Three ATP bursts were followed by up to five shocks if the tachycardia did not terminate previously. In secondary prophylactic patients with slower sustained VT, an additional VT zone <167 min⁻¹ with only ATP therapy could be programmed. In 2005, clinical routine changed for primary prophylactic ICD patients. Patients with primary prophylactic ICD indication received only a VF therapy zone, and a monitor zone was programmed for detection of VTs between 167 and 200 beats/min. If sustained VT was detected in the monitor zone during follow-up, a VT therapy zone was activated, too. During the follow-up, VT zones, number of beats to detect VT, or ATP therapy was only changed if there was a clinical reason.

Discriminators were programmed to differentiate between supraventricular and VT. Anti-bradycardiac pacing was programmed at 40 beats/ min in patients with single-chamber device and at 60 beats/min in patients with dual-chamber or cardiac resynchronization therapy devices. Fast VT was defined as VT which fell into the VF zone and was treated like VF. Slow VTs were defined as VTs falling into the VT zone. Slow VTs were terminated by shock after ATP therapy failed. In nearly all patients, ATP therapy was only programmed for the VT zones as ATP during charging in the VF zone was not available in most patients who received their devices before 2008.

Electrogram classification

All electrograms showing episodes that triggered ICD therapy were classified according to pre-determined diagnostic criteria for cardiac rhythms. To discriminate ventricular from supraventricular rhythms, onset characteristics, electrogaphs recorded before detection of the arrhythmia and after delivery of the shock, and plots of RR intervals were analysed. Routine ICD controls were performed by one physician. Antitachycardia pacing or shock episodes, which could not be classified as appropriate or inappropriate by the first investigator and those episodes which led to medical measures such as hospitalization or ablation, were adjudicated by at least two physicians. If agreement about classification of ATP or shock episodes could not be obtained, a third physician was involved. All physicians had long-term experience in ICD therapy and cardiac electrophysiology. Antitachycardia pacing or shock episodes were considered to be appropriate if the triggering rhythm was determined to be VF or VT. In the present study, only appropriate shocks or ATP was evaluated. The term ‘ATP therapy’ in this analysis refers to ATP only therapy that was triggered for a single rhythm event, regardless of the total number of ATP therapies that were required to satisfy the criteria for termination of tachycardia by the ICD. If a tachycardia episode triggered ICD shocks as well as ATP, this episode was classified as an ICD shock episode. An ATP therapy was viewed as successful, when the post-therapy rhythm was not a ventricular tachyarrhythmia.

Statistical analysis

The patient population is described by absolute numbers and percentages. The distribution of continuous variables is characterized by means and standard deviation, or medians with upper/lower quartile. Categorical variables were compared by using the Pearson χ² or Fisher’s exact test, as appropriate. As described before by Moss et al., Kaplan–Meier survival curves were calculated before and after appropriate ICD therapy for VT or VF. When patients developed their first device therapy for VT or VF, they were censored from the before-therapy group and moved to their respective post-therapy group. The time origin for the before-therapy curve was the day of ICD implantation, whereas that for the post-therapy curve was the day of first ICD therapy. This method differences between the groups were analysed by using the log-rank test. The relationship between ICD shocks, ATP therapy, and death from any cause was examined with the use of Cox proportional-hazards models, with adjustment for 11 prognostic or clinically relevant factors which were different in the baseline characteristics between the different groups.
groups: age, gender, ejection fraction (EF), diabetes, primary prophylactic indication, β-blocker, digoxin, sotalol, aldosterone antagonist, interim first ATP therapy, and interim first appropriate shock. In addition, the association of first ATP therapy with death was further evaluated in different subgroups by Cox proportional-hazards models, with adjustment for the above-mentioned factors. The occurrence of first ATP therapy or first ICD shocks was treated as two separate time-dependent covariates, allowing the risk to change after the occurrence of ATP therapy or shock. If patients suffered from both ATP and ICD shock at the same episode, this episode was regarded as an ICD shock episode. If patients suffered from more than one episode during follow-up, they were stratified according to the type of the first episode.

In a second subgroup analysis, the association of ATP therapy with all-cause mortality was examined after excluding patients with appropriate ICD shocks. Kaplan–Meier survival curves were calculated before and after appropriate ICD therapy as already mentioned above. Differences were calculated using the log-rank test. The impact of first ATP only therapy on death was evaluated by Cox proportional-hazards models, with adjustment for the above-mentioned factors. All P-values were two-tailed. A P-value of < 0.05 was considered to be statistically significant. To reduce the chance of Type 1 error, Bonferroni correction was applied by dividing the α by the number of performed tests 0.05/3. Hence, a significance level of 0.016 was used to indicate the statistical significance for these analyses. The tests were performed using SPSS.

The authors had full access to the data and take complete responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

### Results

#### Patient characteristics and antitachycardia pacing therapy

During the median follow-up time of 6 years, 749 (54%) patients experienced 17 827 episodes of VT or VF which were terminated by ATP only in 74% and by shock in 26% of patients. A total of 0.6% of ATP therapies accelerated to VF and were successfully terminated by ICD shock. The median time from ICD implantation to first VT/VF episode was 411 (115–1124) days and the time from first VT/VF episode to the end of follow-up 45 (20–83) months. In patients with VT/VF, first episode was terminated by ATP in 43% (n = 321) and in 57% by ICD shock. All first ATP-terminated episodes were VT episodes. None of those episodes were episodes which were terminated by ATP during charging in the VF zone. Baseline clinical data of the patients stratified according to the first therapy are summarized in Table 1. Patient characteristics at baseline were similar in all groups with regard to age, EF, and organic heart disease. Group differences were observed in gender, diabetes, implanted ICD device, and ICD indication. Patients with ATP or ICD shock had less often β-blocker therapy and more often sotalol than patients without ICD therapy (Table 2). The median time between first ATP therapy and death was ~3.7 years. One per cent of patients suffered from syncope during ATP-terminated VT and in 6% of patients ATP

### Table 1 Clinical characteristics of patients at ICD implantation

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>First ATP (n = 321)</th>
<th>First shock (n = 428)</th>
<th>No therapy (n = 649)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>65 (59–70)</td>
<td>64 (56–71)</td>
<td>65 (57–71)</td>
<td>ns</td>
</tr>
<tr>
<td>Female sex</td>
<td>11%</td>
<td>19%</td>
<td>22%</td>
<td>0.002</td>
</tr>
<tr>
<td>Ejection fraction &lt; 40%</td>
<td>83%</td>
<td>81%</td>
<td>77%</td>
<td>ns</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>63%</td>
<td>60%</td>
<td>59%</td>
<td>ns</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>29%</td>
<td>27%</td>
<td>26%</td>
<td>ns</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>28%</td>
<td>34%</td>
<td>32%</td>
<td>ns</td>
</tr>
<tr>
<td>Diabetes</td>
<td>24%</td>
<td>25%</td>
<td>30%</td>
<td>0.012</td>
</tr>
<tr>
<td>Prior stroke</td>
<td>9%</td>
<td>11%</td>
<td>11%</td>
<td>ns</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>26%</td>
<td>29%</td>
<td>29%</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Indications for ICD implantation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary prevention</td>
<td>74%</td>
<td>75%</td>
<td>61%</td>
<td>0.0001</td>
</tr>
<tr>
<td><strong>Implanted ICD systems</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single-chamber device</td>
<td>40%</td>
<td>48%</td>
<td>40%</td>
<td>0.009</td>
</tr>
<tr>
<td>Dual-chamber device</td>
<td>38%</td>
<td>37%</td>
<td>35%</td>
<td>ns</td>
</tr>
<tr>
<td>Biventricular device</td>
<td>22%</td>
<td>15%</td>
<td>25%</td>
<td>0.008</td>
</tr>
<tr>
<td>Total number of ATP episodes</td>
<td>7715</td>
<td>5482</td>
<td>n.a.</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total number of shock episodes</td>
<td>799</td>
<td>3831</td>
<td>n.a.</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Time from implantation to first therapy (days)</td>
<td>451 (143–1079)</td>
<td>384 (94–1193)</td>
<td>n.a.</td>
<td>ns</td>
</tr>
<tr>
<td>Time from first therapy to end of follow-up (days)</td>
<td>1566 (752–2620)</td>
<td>1143 (501–2452)</td>
<td>n.a.</td>
<td>0.06</td>
</tr>
<tr>
<td>Total follow-up (days)</td>
<td>2539 (1566–3588)</td>
<td>2217 (1161–3304)</td>
<td>2052 (952–2841)</td>
<td>0.0004</td>
</tr>
</tbody>
</table>

ATP, antitachycardia pacing; ICD, implantable cardioverter-defibrillator; n.a., not applicable; ns, non-significant.

| Patients are stratified according to first therapy after implantation. Significant differences observed: 1between ATP vs. shock (P = 0.002) and ATP vs. no therapy (P = 0.0003); 2between ATP vs. no therapy (P = 0.001) and shock vs. no therapy (P = 0.005); 3between ATP vs. no therapy (P = 0.0001) and shock vs. no therapy (P < 0.0001); 4between shock vs. no therapy (P = 0.009); 5between ATP vs. shock (P = 0.008) and shock vs. no therapy (P = 0.0002); 6between ATP vs. no therapy (P < 0.0001) and shock vs. no therapy (P = 0.0004).
occurred in tandem with worsening heart failure. Patients of the first ATP group had a five times lower incidence of appropriate shocks during follow-up than patients with first ICD shock (Table 1).

### Outcome after first antitachycardia pacing therapy

About two-thirds of patients \((n = 168)\) with first ATP episode experienced further VT or VF episodes (Figure 1). The second ICD therapy after the first ATP therapy was an ICD shock in 76 patients and again an ATP therapy in 140 patients. The first ICD shock after the ATP episode was triggered by VF in 35 patients and by VT in 98 patients and occurred at average 572 days after the first ATP episode. Until the end of the follow-up, a total of 133 (41%) patients with first ATP episode received an ICD shock. One hundred and eighty-eight (13%) patients of all 1398 ICD patients had only ATP episodes without ICD shocks during follow-up. The baseline characteristics between patients with only ATP and patients with first ATP followed by shock were not different.

During the median follow-up of 6 years, 484 (35%) patients died. In 363 patients, the mode of death was known. The main cause of death was end-stage heart failure (70%) followed by non-cardiac death (23%). Kaplan–Meier survival curves showed an increased mortality in patients with first shock compared with patients with first ATP (log rank \(P = 0.001\), Figure 2). In a subgroup of patients where all patients with appropriate shocks during follow-up were excluded, patients with ATP only episodes had a worse prognosis than patients without any therapy (log rank \(P = 0.0007\), Figure 3). In a multivariate analysis adjusted for potential confounders (age, gender, EF, diabetes, primary prophylactic indication, \(\beta\)-blocker, digoxin, sotalol, aldosterone antagonist, and interim appropriate shock), the occurrence of first ATP therapy was independently associated with an increased all-cause mortality [hazard ratio (HR) 2.60, 95% confidence interval (CI) 2.02–3.35, Figure 4]. This was consistent in all subgroups

### Table 2 Discharge medication after ICD implantation

<table>
<thead>
<tr>
<th></th>
<th>First ATP ((n = 321)) (%)</th>
<th>First shock ((n = 428)) (%)</th>
<th>No therapy ((n = 649)) (%)</th>
<th>(P)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitor</td>
<td>92</td>
<td>90</td>
<td>89</td>
<td>ns</td>
</tr>
<tr>
<td>(\beta)-Blocker</td>
<td>73</td>
<td>67</td>
<td>80</td>
<td>0.009(^1)</td>
</tr>
<tr>
<td>Diuretics</td>
<td>68</td>
<td>70</td>
<td>68</td>
<td>ns</td>
</tr>
<tr>
<td>Digoxin</td>
<td>38</td>
<td>48</td>
<td>37</td>
<td>0.008(^2)</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>30</td>
<td>25</td>
<td>34</td>
<td>0.0007(^3)</td>
</tr>
<tr>
<td>Class I AA</td>
<td>1.0</td>
<td>1.4</td>
<td>1.7</td>
<td>ns</td>
</tr>
<tr>
<td>Sotalol</td>
<td>8</td>
<td>7</td>
<td>2.8</td>
<td>0.003(^4)</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>9</td>
<td>11</td>
<td>12</td>
<td>ns</td>
</tr>
</tbody>
</table>

AA, antiarrhythmic agent; ACE, angiotensin converting enzyme; ATP, antitachycardia pacing; ns, non-significant.

Patients are stratified according to first therapy after implantation. Significant differences observed: \(^1\)between ATP vs. no therapy \((P = 0.01)\) and shock vs. no therapy \((P < 0.0001)\); \(^2\)between ATP vs. shock \((P = 0.008)\) and shock vs. no therapy \((P = 0.0003)\); \(^3\)between shock vs. no therapy \((P = 0.0007)\); \(^4\)between ATP vs. no therapy \((P = 0.0004)\) and shock vs. no therapy \((P = 0.003)\).

![Figure 1](https://academic.oup.com/eurheartj/article-abstract/17/7/1068/2398727/177716862387727) Type of ICD therapies following first ATP therapy.
(Figure 5). When excluding all patients with appropriate ICD shocks during follow-up, ATP only therapy remained associated with a worse prognosis (HR 1.92, 95% CI 1.38–2.67, Figure 6).

Discussion

Major findings

About three-fourths of ventricular arrhythmias are terminated by ATP. One-third of patients with first ATP-terminated episode will experience an ICD shock afterwards. The occurrence of ATP-terminated episode is independently associated with an increased mortality rate even among patients without appropriate ICD shocks.

Impact of antitachycardia pacing on mortality

It is well known that ICD shocks are associated with a worse outcome.\(^1\)–\(^6\) This association could also be observed in the present study where patients had a four-fold increase in risk of death after receiving an appropriate shock. Patients with first ATP had a better prognosis than patients with first shock. The better prognosis of patients receiving ATP than shock could be due to the arrhythmias which engender a shock namely VF and faster VT or VTs that are recalcitrant to ATP. This hypothesis is supported by a study of Moss et al.,\(^3\) which showed that patients with slower ventricular arrhythmias had a better outcome. Interestingly, in the present study, ATP therapy was also associated with a worse prognosis. This might be partly attributed to the observation that one-third of patients who experience an ATP episode will have further appropriate ICD shocks. But even when excluding patients with ICD shocks, ATP therapy remains associated with a worse prognosis. These findings suggest that the occurrence of appropriate ATP therapy represents a marker for the progression of the underlying heart disease as it is hypothesized for the occurrence of appropriate ICD shock therapy.\(^14\) This is underlined by a recently published study of Bencardino et al.,\(^8\) where sustained ventricular arrhythmias per se had a negative impact on prognosis rather than the modality of ICD therapy. On the other hand, in the MADIT-RIT study, it was suggested that ATP itself might be harmful.\(^5\) The reduction of inappropriate ATP with the improved programming led to a markedly decreased mortality rate. It was postulated that the marked decrease in ATP with the improved programming would also be associated with fewer episodes of atrial fibrillation induced by ATP, which would also result in reduced mortality.\(^15\) A recent subanalysis of the MADIT-RIT study showed that the delivery of appropriate shock, inappropriate shock, and inappropriate ATP but not the delivery of appropriate ATP was associated with an increased mortality.\(^16\) Antitachycardia pacing therapy was also not associated with increased risk of death in earlier studies such as MADIT II,\(^17\) PainFREE Rx,\(^18\) or EMPRIC.\(^19\) These results are in contrast to our results and might be due to patient selection and shorter follow-up duration. MADIT II and
MADIT-RIT included only patients for primary prophylactic ICD patients whereas in our study population 75% of patients had a secondary prophylactic ICD indication. The follow-up duration in MADIT II, MADIT-RIT, PainFree, and EMPIRIC was markedly shorter (<2 years) compared with the follow-up in the present study, where the median time between first ATP therapy and death

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**Figure 4** Cox proportional-hazards models on all-cause mortality. The results are adjusted for age, gender, EF, diabetes, primary prophylactic indication, β-blocker, digoxin, sotalol, aldosterone antagonist, interim first ATP therapy, and interim first appropriate ICD shock therapy. ATP, antitachycardia pacing; CI, confidence interval; HR, hazard ratio.

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**Figure 5** Cox proportional-hazards models on all-cause mortality in different subgroups. The results are adjusted for age, gender, EF, diabetes, primary prophylactic indication, β-blocker, digoxin, sotalol, aldosterone antagonist, and interim first appropriate ICD shock therapy. ATP, antitachycardia pacing; CI, confidence interval; CRT, cardiac resynchronization therapy; HR, hazard ratio.
was about 4 years. A longer follow-up might have revealed an adverse association of ATP therapy on prognosis.

**Antitachycardia pacing therapy and clinical consequences**

Antitachycardia pacing-terminated episodes are often detected during routine ICD controls even in asymptomatic patients. In the present study, most of the ATP episodes were asymptomatic. There is no evidence that ATP has adverse cardiac effects. Antitachycardia pacing termination of VT or FVT, unlike shocks, does not cause biomarker release or reduce ventricular pump function. On the other hand, it is a marker for an increased mortality and for recurrent episodes. Among patients with first ATP therapy, two-thirds will have recurrent ventricular tachyarrhythmias, every third patient will develop subsequent VT/VF episodes with ICD shocks and among those patients two-thirds will have a conversion towards faster ventricular arrhythmias such as FVT or VF. Similarly as in patients suffering from ICD shocks, a general clinical assessment of the ICD patient after the occurrence of first ATPs is needed. This should include an evaluation of the underlying heart disease with identification of potential triggering factors such as myocardial ischaemia, progressive heart failure, or electrolyte derangements. However, it is not known which represents the best strategy after occurrence of first ATP to improve the outcome. Further studies should focus on the management of patients after first ATP episode and clarify if treatment to prevent VT episodes for example by more and more proactive approach towards VT ablation, avoidance of ATP where possible by a longer detection times or identification of changes in clinical variables that lead to VT episodes might ameliorate the adverse association of ATP with mortality.

**Study limitations**

As the present study is a single-centre registry, our observations and conclusions may not be necessarily generalized. Implantable cardioverter-defibrillators were implanted over a 15-year period, on account of that, evolving and expanding guidelines for the implantation of ICDs, different device programming, different detection schemes used in the hardware or change of heart failure treatment might have created a heterogeneous population. The rate of β-blocker therapy, spironolactone or CRT treatment was very low at the beginning of the ICD registry but increased over time. We tried to control for potential confounders using multivariate statistical analysis. The adjudication of SVT vs. VT can be difficult and is unavoidably different in single-chamber vs. dual-chamber devices and thus a limitation of the study. Antitachycardia pacing or shock episodes which could not be classified as appropriate or inappropriate by the first investigator were adjudicated by at least two physicians. Inappropriate ATP therapies were not systematically registered in the present study. Potential interactions between appropriate and inappropriate ATP therapies could not be analysed.

After the results of MADIT-RIT, it is obvious that the selected VT detection algorithms were too sensitive. Nevertheless, our ICD programming standards followed the ICD programming as previously recommended and have been used in different relevant ICD studies. Antitachycardia pacing therapy was routinely programmed in all secondary prophylactic ICD patients but not in all primary prophylactic patients. All patients received at least a monitor zone and if prolonged VT was detected, ATP therapy was turned on without significant time delay. In those patients, the occurrence of the first ATP therapy might have corresponded to a recurrent episode similarly to patients with secondary prophylactic patients due to sustained VT who came with first ATP episode. Kaplan-Meier survival curves were calculated before and after appropriate ICD therapy for VT or VF as described by Moss et al. There is a bias towards higher mortality in the ICD therapy group when presenting the curves from the point of device therapy.
Implantable cardioverter-defibrillator therapies can occur during periods of acute clinical decompensation which will have an impact on mortality. On the other hand, when presenting the curves from the day of implantation there will be a bias towards higher mortality in the no-therapy group because patients could die from the day of implantation, whereas in the ATP or shock group patients could only die after experiencing first appropriate ICD therapy during follow-up.

Conclusions

Antitachycardia pacing-terminated episodes are very common in ICD patients. One-third of patients with first ATP therapy will have appropriate ICD shocks during follow-up. The occurrence of ATP therapy is a marker for worse prognosis.

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Conflict of interest: none declared.

References