Comparable risk of recurrent ventricular tachyarrhythmias in implantable cardioverter-defibrillator recipients treated with single beta-blocker or combined amiodarone

Tobias Schupp1 | Michael Behnes1 | Seung-hyun Kim1 | Julian Müller1 | Kathrin Weidner1 | Linda Reiser1 | Aydin Huseynov1 | Armin Bollow1 | Martin Borggrefe1 | Gabriel Taton1 | Thomas Reichelt1 | Dominik Ellguth1 | Niko Engelke1 | Muharrem Akin2 | Dirk Große Meininghaus3 | Thomas Bertsch4 | Ibrahim Akin1

1First Department of Medicine, Faculty of Medicine Mannheim, University Medical Centre Mannheim (UMM), University of Heidelberg, DZHK (German Center for Cardiovascular Research) Partner Site Heidelberg/Mannheim, Mannheim, Germany
2Department of Cardiology and Angiology, Hannover Medical School, Hannover, Germany
3Department of Cardiology, Carl-Thiem-Klinikum Cottbus, Cottbus, Germany
4Institute of Clinical Chemistry, Laboratory Medicine and Transfusion Medicine, General Hospital Nuremberg, Paracelsus Medical University, Nuremberg, Germany

Correspondence
Michael Behnes, First Department of Medicine, University Medical Center Mannheim (UMM), Theodor-Kutzer-Ufer 1-3, Mannheim 68167, Germany.
Email: michael.behnes@umm.de.

Abstract
This study sought to assess the prognostic impact of treatment with single beta-blocker (BB) compared to combined therapy with BB plus amiodarone (BB-AMIO) on recurrences of ventricular tachyarrhythmias in implantable cardioverter-defibrillator (ICD) recipients. A large retrospective registry was used including consecutive ICD recipients with index episodes of ventricular tachyarrhythmias from 2002 to 2016. Patients treated with BB were compared to patients treated with BB-AMIO. Kaplan-Meier and Cox regression analyses were applied for the evaluation of the primary end-point defined as first recurrences of ventricular tachyarrhythmias at five years. Secondary end-points comprised first appropriate ICD therapies, first cardiac rehospitalization and all-cause mortality at five years. Among 512 ICD recipients, 81% were treated with BB and 19% with BB-AMIO. BB and BB-AMIO were associated with comparable risk of first recurrences of ventricular tachyarrhythmias (46% vs. 43%; log rank P = 0.941; HR = 1.013; 95% CI 0.725-1.415; P = 0.941) and appropriate ICD therapies (35% vs. 37%; log rank P = 0.389; HR = 0.852; 95% CI 0.591-1.228; P = 0.390). BB was associated with decreased long-term all-cause mortality within an univariable analysis only (20% vs. 28%; log rank p = 0.023). In conclusion, BB and BB-AMIO were associated with comparable risks regarding recurrences of ventricular tachyarrhythmias at five years.

Keywords
amiodarone, atrial fibrillation, beta-blocker, heart failure, ICD, ventricular fibrillation, ventricular tachycardia
1 | INTRODUCTION

Strategies to decrease the risk of appropriate implantable cardioverter-defibrillator (ICD) therapies consist of an optimal pharmacotherapy and ICD programming, as well as ventricular tachycardia (VT) ablation. After exclusion of secondary causes of recurrent ICD shocks (such as electrolyte disorders, significant coronary artery disease), beta-blockers (BB), amiodarone (AMIO) or sotalol may be effective to improve freedom from appropriate ICD therapies, quality of life and overall survival.4,5,12,13 Prior studies focused on short-term impact of intravenous AMIO therapy and demonstrated decreased rates of life-threatening arrhythmias and ICD shocks.14 In contrast, long-term administration of oral AMIO therapy has only been studied among pre-selected subgroups and therefore needs to be further investigated according to the current medical and scientific status.5

The “European Myocardial Infarct Amiodarone Trial” (EMIAT) included over 1.400 patients with acute myocardial infarction (AMI) and heart failure (HF) defined as left ventricular ejection fraction (LVEF) ≤40%. After a median follow-up of 21 months, AMIO reduced the risk of arrhythmic death by 35%.5 However, patients were not stratified for the use of BB and less than 50% had a concomitant BB therapy. This combined pharmacotherapy was recently investigated demonstrating that BB that BB therapy was superior compared to BB-AMIO regarding all-cause mortality in consecutive patients with ventricular tachyarrhythmias with and without an ICD. In contrast, arrhythmic end-points were not assessed.15 Therefore, this study evaluates the prognostic impact of a BB- versus BB-AMIO therapy on the primary endpoint of first recurrence of ventricular tachyarrhythmias, as well as secondary end-points (ie appropriate ICD therapies, first cardiac rehospitalization and all-cause mortality) in consecutive ICD recipients at 5 years.

2 | METHODS

2.1 | Data collection and documentation

The present all-comers study retrospectively included all consecutive patients with index episodes of ventricular tachyarrhythmias on index hospital admission, who were discharged from our institution with an ICD between 2002 and 2016, as previously published.16 The study was conducted in accordance with the Basic & Clinical Pharmacology & Toxicology policy for experimental and clinical studies.17

ICD recipients routinely presented every three to six months for device check and unscheduled in case of noticed device interrogations at our clinic. Device settings and programming was performed according to current international guidelines by specialized cardiologist in electrophysiology during routine clinical care.18

2.2 | Inclusion and exclusion criteria

For the present study, all patients surviving index hospitalization after presenting with ventricular tachyarrhythmias between 2002 and 2016 were included as previously being described.15 All patients were analysed according to the presence of BB or BB-AMIO at discharge from index hospitalization. The BB group comprised patients with a sole BB therapy, and the BB-AMIO group comprised patients with a combined therapy of BB and AMIO. All kinds of BB were allowed, and individual dosages at discharge were documented. All other medical therapies apart from BB or BB-AMIO were allowed. Indication to treat patients with BB and AMIO was based on European guidelines on heart failure and ventricular tachyarrhythmias.2,18

Despite the retrospective study design, risk stratification was performed as follows: All patients were included and analysed according to the presence of BB or BB-AMIO therapy at discharge from index hospitalization, as being prescribed by the intention of the physicians during clinical care (“intention-to-treat”). Results were re-evaluated in patients without any evidence of discontinuing AMIO therapy, which reflects an “as-treated” status. All patients without an activated ICD or beta-blocker treatment, as well as patients who did not survive index hospitalization, were excluded from the present analysis. To guarantee sufficient documentation of recurrent ventricular tachyarrhythmias, patients not presenting for at least one ICD check at follow-up were excluded from the present study.

2.3 | Primary and secondary end-points

Follow-up period was set at 5 years for all outcome. The primary prognostic end-point was the first recurrence of ventricular tachyarrhythmias (VT or VF) as documented within ICD protocols. Secondary end-points were overall recurrences at follow-up, recurrences per patient, associated appropriate or inappropriate device therapies (first, overall, per patient), first rehospitalization and all-cause mortality at follow-up.
Further stratification was performed into subgroups of primary or secondary prevention and appropriate or inappropriate device therapies.

2.4 | Statistical methods

Quantitative data are presented as mean ± standard error of mean (SEM), median and interquartile range (IQR), and ranges depending on the distribution of the data and were compared using Student’s t test for normally distributed data or the Mann-Whitney U test for non-parametric data. Deviations from a Gaussian distribution were tested by the Kolmogorov-Smirnov test. Spearman’s rank correlation for non-parametric data was used to test univariate correlations. Qualitative data are presented as absolute and relative frequencies and compared using the Chi-square test or Fisher’s exact test, as appropriate.

Firstly, univariable Kaplan-Meier method was applied to evaluate prognostic differences within the entire cohort, in subgroups of primary versus secondary prevention, in subgroups of patients with and without atrial fibrillation (AF) and LVEF ≥ 35% or <35%, each stratified according to BB and BB-AMIO therapy. Secondly, multivariable Cox regression models were developed using the “forward selection” option, where only statistically significant variables (P < .05) were included and analysed simultaneously. Pre-defined variables being used for multivariable Cox-regressions included age, chronic kidney disease (CKD), diabetes mellitus, AF, coronary artery disease (CAD), LVEF < 35% and BB versus BB-AMIO therapy. Cox regression analyses were applied for the end-points of first recurrence of ventricular tachyarrhythmias and first appropriate ICD therapy. Patients without complete follow-up were censored (accepted lost to follow-up rate < 10%). The result of a statistical test was considered significant for P < .05. Release 9.4 (SAS Institute Inc, Cary, NC, USA) and SPSS (Version 25, IBM, Armonk, New York) were used for statistics.

3 | RESULTS

3.1 | Study cohort

From a total of 874 consecutive ICD recipients with index ventricular tachyarrhythmias, 362 patients were excluded because of in-hospital death (n = 32), not presenting for at least one ICD check-up (n = 250) or not being treated with BB (n = 80). Finally, a total of 512 ICD recipients were included in this study and treated with BB or combined BB-AMIO (Figure 1; Flow chart). Significantly more patients were treated with BB compared to BB-AMIO (81% vs. 19%; P = .001; Table 1).

Target dosages were already reached at discharge, including metoprolol as the most frequently administered type of BB (mean dosage 77-80 mg per day) followed by carvedilol (mean dosage 20-21 mg per day) and bisoprolol (mean dosage 5-6 mg per day). AMIO was taken at mean dosages of 200 mg per day following the individual in-hospital loading regimen (Table S1; study drugs).

Patients were median aged at 66 years, and most patients were males (Table 1). Most patients had index episodes of VT compared to VF (72% - 73% vs. 27% - 28%; P = .959). There was no significant difference for the distribution of cardiovascular risk factors between patients with BB and BB-AMIO (P ≥ .055). Higher rates of AF, mainly attributed to higher rates of paroxysmal AF, were seen in patients treated with BB-AMIO (P = .001). No differences of the rates of chronic kidney disease, cardiopulmonary resuscitation (CPR) and acute myocardial infarction was observed in both groups (P = .120). Medication at discharge, including angiotensin-converting enzyme (ACE) inhibitors, aldosterone antagonists and digitalis, was equally distributed, except for a slightly higher rate of angiotensin receptor blocker (ARB) therapy in
BB patients (P = .024). Moreover, LVEF < 35% was most common in patients with BB-AMIO therapy (P = .001).

Table 2 outlines ICD-related data of the study population. Most patients had an activated transvenous ICD (88% vs. 92%), whereas a minor part of patients had a transvenous CRT-D or subcutaneous ICD (1%-11%). ICD were commonly implanted for secondary compared to primary prevention (57%-61% vs. 39%-43%; P = .447).

### 3.2 Primary and secondary end-points

At five years of follow-up, the primary end-point of first recurrence of ventricular tachyarrhythmias occurred in 46% of the patients with BB and in 43% of patients with BB-AMIO. The BB- and the BB-AMIO therapies were associated with comparable risk of recurrence of ventricular tachyarrhythmias (46% vs. 43%; log rank P = .941; HR = 1.013; 95% CI 0.725-1.415; P = .941; Figure 2, left panel; Table 2).

Most patients presented with recurrent sustained VT in both groups (34% vs. 25%; P = .095), whereas higher rates of non-sustained VT were observed in the BB cohort (BB vs. BB-AMIO 14% vs. 3%; P = .004; Table 2). No differences were observed in patients with BB and BB-AMIO regarding the primary end-point of first recurrences after stratification by ICD for primary (42% vs. 39%; P = .858) and secondary prevention (49% vs. 45%; P = .774; Figure 2, middle and right panel; Table 2).

Moreover, a comparable risk of appropriate ICD therapies was observed in the presence of BB and BB-AMIO therapy (35% vs. 37%; log rank P = .389; HR = 0.852; 95% CI 0.573-1.267; P = .430; Table 3). Inappropriate device therapies were not affected by BB or BB-AMIO (13% vs. 10%; P = .632; Figure 3, right panel; Table 2).

Comparable risk of rehospitalization was observed in BB and BB-AMIO patients (32% vs. 29%; P = .605). The most common reason for rehospitalization was recurrent VT in both groups (Table 2). Finally, improved long-term survival was seen in patients with BB compared to BB-AMIO (28% vs. 20%; log rank P = .023; HR = 0.605; 95% CI 0.390-0.936; P = .024; Figure 4).

### 3.3 Multivariable Cox regression models

After multivariable adjustment, BB- and BB-AMIO therapy were associated with comparable risk of recurrences of ventricular tachyarrhythmias (HR = 1.025; 95% CI 0.712-1.476; P = .895) and appropriate ICD therapies (HR = 0.852; 95% CI 0.573-1.267; P = .430; Table 3). In contrast, especially the absence of coronary artery disease was associated with increased risk of recurrences and appropriate ICD therapies. Furthermore, advanced age, CKD and LVEF < 35% were
### TABLE 2  ICD-related data, primary and secondary end-points

| Characteristic                        | BB (n = 414; 81%) | BB-AMIO (n = 98; 19%) | P value |
|---------------------------------------|-------------------|-----------------------|---------|
| **Type of ICD, n (%)**                |                   |                       |         |
| ICD                                   | 379 (92)          | 86 (88)               | .144    |
| CRT-D                                 | 25 (6)            | 11 (11)               |         |
| s-ICD                                 | 19 (2)            | 1 (1)                 |         |
| **Implant indication, n (%)**         |                   |                       |         |
| Primary prevention                    | 178 (43)          | 38 (39)               | .447    |
| Secondary prevention                  | 236 (57)          | 60 (61)               |         |
| **ICD programming, bpm, median (IQR)**|                 |                       |         |
| VT detection threshold                | 171 (167-176)     | 167 (164-171)         | .001    |
| VF detection threshold                | 214 (214-222)     | 214 (214-222)         | .551    |
| **Primary end-point**                 |                   |                       |         |
| First recurrence ventricular tachyarrhythmias, n (%) | | | |
| Overall                               | 191 (46)          | 42 (43)               | .558    |
| Non-sustained VT                      | 56 (14)           | 3 (3)                 | .004    |
| Sustained VT                          | 105 (25)          | 33 (34)               | .095    |
| VF                                    | 30 (7)            | 6 (6)                 | .696    |
| Electrical storm                      | 28 (7)            | 10 (10)               | .243    |
| **Secondary end-points**              |                   |                       |         |
| Overall recurrences at follow-up, n (%)|                 |                       |         |
| Non-sustained VT                      | 85 (21)           | 16 (16)               | .347    |
| Sustained VT                          | 132 (32)          | 38 (39)               | .193    |
| VF                                    | 44 (11)           | 8 (8)                 | .468    |
| Electrical storm                      | 28 (7)            | 10 (10)               | .243    |
| VT cycle length, ms, mean ± SEM       | 310 ± 5           | 349 ± 14              | .002    |
| **Recurrences per patient, mean ± SEM** |                   |                       |         |
| Non-sustained VT                      | 6.1 ± 2.0         | 2.4 ± 0.8             | .386    |
| Sustained VT                          | 4.7 ± 0.9         | 9.3 ± 4.0             | .088    |
| VF                                    | 1.1 ± 0.8         | 0.2 ± 0.1             | .604    |
| Electrical storm                      | 0.1 ± 0.0         | 0.1 ± 0.0             | .199    |
| **First device therapies, n (%)**     |                   |                       |         |
| Overall appropriate device therapy    | 145 (35)          | 36 (37)               | .750    |
| Appropriate shock                     | 58 (14)           | 14 (14)               | .944    |
| Appropriate ATP only                  | 87 (21)           | 22 (22)               | .755    |
| **Overall device therapies at follow-up, n (%)** | | | |
| Overall appropriate device therapy    | 145 (35)          | 36 (37)               | .750    |
| Appropriate shock                     | 81 (20)           | 23 (24)               | .361    |
| Appropriate ATP only                  | 110 (27)          | 30 (31)               | .386    |
| Inappropriate device therapy          | 56 (14)           | 10 (10)               | .395    |
| **Device therapies per patient, mean ± SEM** | | | |
| Appropriate shock                     | 0.7 ± 0.1         | 1.1 ± 0.4             | .266    |
| Appropriate ATP only                  | 3.6 ± 0.7         | 7.9 ± 3.9             | .074    |
| Inappropriate device therapy          | 0.4 ± 0.1         | 0.2 ± 0.1             | .457    |
| **First rehospitalization, n (%)**    |                   |                       |         |
| Overall                               | 120 (29)          | 31 (32)               | .605    |

(Continues)
 Abbreviations: ATP, anti-tachycardia pacing; HF, heart failure; SEM, standard error of mean; VF, ventricular fibrillation; VT, ventricular tachycardia. Bold type indicates \( P < .05 \).

**TABLE 2** (Continued)

| Characteristic                        | \( \text{BB (n = 414; 81\%)} \) | \( \text{BB-AMIO (n = 98; 19\%)} \) | \( P \) value |
|---------------------------------------|-------------------------------|-----------------------------------|---------------|
| VT                                    | 41 (10)                       | 11 (11)                           | .697          |
| VF                                    | 8 (2)                         | 1 (1)                             | .537          |
| Acute myocardial infarction           | 6 (2)                         | 2 (2)                             | .671          |
| Acute heart failure                   | 26 (6)                        | 8 (8)                             | .501          |
| Inappropriate device therapy          | 20 (5)                        | 4 (4)                             | .752          |
| Other                                 | 19 (5)                        | 5 (5)                             | .752          |
| All-cause mortality, at 5 years, \( n (\%) \) | 79 (20)                      | 27 (28)                           | .063          |

**FIGURE 2**  Freedom from first recurrence of ventricular tachyarrhythmias comparing BB versus BB-AMIO therapy within the entire cohort (left panel) and stratified by ICDs for primary (middle panel) and secondary prevention (right panel)

**FIGURE 3**  Freedom from appropriate (left panel) and inappropriate ICD therapies (right panel) comparing BB versus BB-AMIO therapy
associated with an increased risk of appropriate ICD therapies. Finally, no mortality differences were observed between BB and BB-AMIO in the multivariable Cox regression analysis.

### 3.4 Stratification by AF and LVEF

Furthermore, similar outcome were observed for patients with (54% vs. 39%; *P* = .146) and without AF (43% vs. 48%; *P* = .435; Figure 5A), as well as patients with LVEF ≥ 35% (42% vs. 34%; *P* = .756) and LVEF < 35% (49% vs. 46%; *P* = .944; Figure 5B).

### 3.5 Patients without discontinuation of AMIO therapy

At five years, 21% of patients (n=21) discontinued treatment with AMIO. Most documented reason was a significant QT prolongation (n = 4), followed by freedom from recurrent ventricular tachyarrhythmias (n = 3; Table S2). Even after exclusion of patients with discontinuation of AMIO therapy, BB and BB-AMIO still had comparable risk of recurrent ventricular tachyarrhythmias (46% vs. 38%; *P* = .587; HR = 1.114; 95% CI 0.754-1.647; *P* = .587).

### 4 DISCUSSION

The present study evaluates the prognostic impact of BB compared to combined BB-AMIO therapy regarding the risk of recurrent ventricular tachyarrhythmias and ICD therapies in ICD recipients surviving index episodes of ventricular tachyarrhythmias. This data suggests comparable risk of recurrences of ventricular tachyarrhythmias in patients with BB- or BB-AMIO therapy at five years. Furthermore, similar risk of appropriate ICD therapies and rehospitalization was observed for both cohorts. Finally, the BB therapy was univariably associated with improved survival compared to the BB-AMIO therapy was shown within the univariable analysis only.

Both, BB and AMIO therapy can be effective in patients with acute ventricular tachyarrhythmias and in patients with

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**TABLE 3** Multivariable Cox regression analyses

| End-point                     | HR     | 95% CI            | *P* value |
|-------------------------------|--------|-------------------|-----------|
| **Recurrences of VT/VF**      |        |                   |           |
| Age                           | 1.010  | 0.997-1.024       | .119      |
| Diabetes                      | 0.762  | 0.545-1.066       | .112      |
| Chronic kidney disease        | 1.249  | 0.944-1.653       | .120      |
| Atrial fibrillation           | 1.303  | 0.973-1.746       | .076      |
| Coronary artery disease       | 0.633  | 0.463-0.864       | **.004**  |
| LVEF < 35%                    | 1.254  | 0.942-1.668       | .120      |
| Cardiopulmonary resuscitation | 0.948  | 0.742-1.211       | .669      |
| **Appropriate ICD therapy**   |        |                   |           |
| Age                           | 1.019  | 1.004-1.035       | **.015**  |
| Diabetes                      | 0.696  | 0.472-1.028       | .069      |
| Chronic kidney disease        | 1.428  | 1.037-1.966       | **.029**  |
| Atrial fibrillation           | 1.183  | 0.850-1.648       | .320      |
| Coronary artery disease       | 0.698  | 0.500-0.973       | **.034**  |
| LVEF < 35%                    | 1.395  | 1.002-1.942       | **.049**  |
| Cardiopulmonary resuscitation | 0.698  | 0.500-0.973       | **.034**  |
| **All-cause mortality**       |        |                   |           |
| Age                           | 1.040  | 1.018-1.063       | **.001**  |
| Diabetes                      | 1.022  | 0.657-1.591       | .924      |
| Chronic kidney disease        | 2.095  | 1.371-3.203       | **.001**  |
| Atrial fibrillation           | 1.321  | 0.874-1.995       | .186      |
| Coronary artery disease       | 1.076  | 0.656-1.765       | .771      |
| LVEF < 35%                    | 1.946  | 1.236-3.066       | **.004**  |
| Cardiopulmonary resuscitation | 1.278  | 0.935-1.747       | .124      |
| **BB vs. BB-AMIO**            | 1.025  | 0.712-1.476       | .895      |

Abbreviations: CI, confidence interval; HR, hazard ratio; LVEF, left ventricular ejection fraction.

Bold type indicates statistical significance.

Level of significance *P* < .05.
recurrent episodes of ventricular tachyarrhythmias leading to multiple ICD shocks. A recently published study investigated the impact of BB and AMIO in patients with electrical storm (ES). 60 patients with ES were randomized for treatment with metoprolol or propranolol combined with intravenous AMIO for 48 hours. Propranolol plus AMIO was superior compared to metoprolol plus AMIO in decreasing the risk of ventricular arrhythmias and ICD shocks.14 Regarding the long-term administration of AMIO, three clinical milestone studies including over 1,800 patients (AVID, CASH, CIDS study)6,7,19,20 proved ICD implantation to be superior compared to AMIO while reducing all-cause mortality by 28%.19 Interestingly, important pre-selection was present in all of the three trials: Within the CASH study, only patients with VF were enrolled and patients with index episodes of sustained VT were excluded.20 In contrast, the AVID and CIDS studies included patients with systolic heart failure only (mean LVEF: 32%-34%).6,7 Thus, it is well known that sudden cardiac death and ventricular tachyarrhythmias occur frequently in patients without impaired LVEF.2 Moreover, medication with BB differed significantly between important randomized trials (EMIAT: 45%; SCD-HeFT: 69%).5,13 A meta-analysis of the AVID, CIDS and CASH trials demonstrated an increased BB supply in patients with ICD compared to AMIO (42% vs. 19%). However, none of the studies evaluated the impact of AMIO in patients with concomitant BB therapy. Therefore, the inclusion of patients with BB only represents the major strength of the present study.

This combined pharmacotherapy was investigated in the prospective, randomized and controlled “Optimal

FIGURE 5  (A) Freedom from first recurrence of ventricular tachyarrhythmias comparing BB versus BB-AMIO therapy in patients with AF (left panel) and without AF (right panel). (B) Freedom from first recurrence of ventricular tachyarrhythmias comparing BB versus BB-AMIO therapy in patients with LVEF ≥ 35% (left panel) and LVEF < 35% (right panel)
Pharmacological Therapy in Cardioverter Defibrillator Patients” (OPTIC) trial more than one decade ago. Here, the impact of BB-, BB-AMIO- and sotalol therapy was investigated in patients presenting with VT, VF or cardiac arrest in the absence of acute myocardial infarction. More than 400 patients with LVEF ≤ 40% were included. After one year of follow-up, therapy with BB-AMIO revealed a reduced risk of ICD shocks compared to sole BB therapy. Interestingly, the OPTIC trial was not assessed to investigate the risk of rehospitalization, all-cause death and arrhythmic death.

Furthermore, the association of AMIO on the occurrence of ventricular tachyarrhythmias was investigated by Watanabe et al. 612 patients with an ICD or CRT-D for primary or secondary prevention were included. At 11 months of follow-up, the absence of AMIO therapy was associated with an increased risk of VT/VF in patients with AF and in patients without AF and LVEF ≥ 40%. Compared to this study, BB therapy was only present in less than 75% of all patients and the follow-up period was rather short, which may explain different findings. After stratification by the presence of AF and the degree of LVEF, comparable outcome of BB- and BB-AMIO therapy were observed across all subgroups in the present study.

Focusing on the risk of inappropriate device therapies, Nagai et al retrospectively included 232 patients with an ICD and structural heart disease. They found a decreased risk of inappropriate ICD therapies in those patients with AMIO therapy at median follow-up of 29 months. In contrast, the present study did not demonstrate any difference regarding inappropriate device therapies in patients with BB or BB-AMIO with rather low rates of inappropriate device therapies in both subgroups (10% vs. 13%).

Besides pharmacological treatment with antiarrhythmic drugs, ablation of VT may improve both survival and freedom from recurrent episodes of ventricular tachyarrhythmias. In line, the “Ventricular Tachycardia Ablation Versus Escalated Antiarrhythmic Drug Therapy in Ischemic Heart Disease” (VANISH) trial compared patients with catheter ablation of VTs to those receiving more aggressive treatment with antiarrhythmics. It was demonstrated that a composite end-point of all-cause mortality, ES onset and appropriate ICD therapies occurred more often in patients with antiarrhythmic pharmacotherapy compared to patients with VT ablation therapy at 28 months. A sub-study of the VANISH trial demonstrated increased risk of ventricular tachyarrhythmias and mortality in patients with AMIO-refractory VT.

5 | STUDY LIMITATIONS

Risk stratification was performed according to pharmacological therapies focusing on discharge medication at index event only. Discontinuation of medical therapies was retrospectively documented. Moreover, decision to treat patients with BB or BB-AMIO was taken by physicians during routine clinical care. Rehospitalization was assessed at one institution only.

6 | CONCLUSIONS

In conclusion, BB- and BB-AMIO therapies were associated with comparable risk of recurrent ventricular tachyarrhythmias and appropriate ICD therapies at a follow-up of 5 years in consecutive ICD recipients surviving index episodes of ventricular tachyarrhythmias. Moreover, the BB therapy was univariably associated with improved long-term all-cause mortality, which was no longer evident after multivariable analysis.

CONFLICT OF INTEREST

The authors declare that they do not have any conflict of interest.

ORCID

Tobias Schupp https://orcid.org/0000-0001-8171-7617
Michael Behnes https://orcid.org/0000-0001-5970-0093

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**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section.

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