

**Evaluation of arrhythmia detection and discrimination efficacy of modern
cardioverter defibrillators**

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PUBLICATIONS RELATED TO THE THESIS

Full papers

- I. Gausz FD, Lena KNM, Gedeon PE, Miklos M, Benak A, Bencsik G, Makai A, Kranyak D, Gagyí RB, Pap R, Saghy L, Szili-Torok T, Vamos M. Arrhythmia Detection in Atrioventricular, Single-Lead, Floating Atrial Dipole ICD Systems Compared with Conventional Single- and Dual-Chamber Defibrillators. *J Cardiovasc Dev Dis.* 2024 Dec 1;11(12):386. doi: 10.3390/jcdd11120386. PMID: 39728276; PMCID: PMC11677019. **(2025 – Impact factor: 2.3, Q1)**
- II. Gausz FD, Fodor D, Turani M, Miklos M, Benak A, Kranyak D, Makai A, Bencsik G, Bogyi P, Pap R, et al. Head-to-Head Comparison of Single- Versus Dual-Chamber ICD Discriminators for Tachyarrhythmia Detection: A Single-Manufacturer, Remote Monitoring-Based Bicentric Study. *Journal of Clinical Medicine.* 2025; 14(16):5859. <https://doi.org/10.3390/jcm14165859> **(2025 - Impact factor: 2.9, Q1)**
- III. Gausz, Flóra Diána; Bári, Zsolt; Vámos, Máté How does the ICD recognize the type of arrhythmia? Tachyarrhythmia discrimination in modern transvenous cardioverter defibrillators *Cardiologia Hungarica*
DOI: 10.26430/CHUNGARICA.2025.55.4.308 **(2025 – Q4)**

Congress abstracts

- I. F Gausz, D Fodor, M Miklos, A Benak, D Kranyak, A Makai, G Bencsik, R Pap, L Saghy, A Nemes, T Szili-Torok, M Vamos, Single- versus dual-chamber ICD discriminators for tachyarrhythmia detection: a remote monitoring based, single center study, *EP Europace*, Volume 27, Issue Supplement_1, May 2025, euaf085.583, <https://doi.org/10.1093/europace/euaf085.583> (EHRA Congress 2025, Vienna)
- II. Gausz FD, Fodor D, Turani M, Miklos M, Benak A, Kranyak D, Makai A, Bencsik G, Bogyi P, Pap R, et al., Head-to-head comparison of single- versus dual-chamber ICD discriminators for tachyarrhythmia detection: a remote monitoring based, bicentric study (ESC Congress 2025, Madrid)
- III. Gausz, Flóra Diána ; Fodor, Dániel ; Miklós, Márton ; Benák, Attila ; Krányák, Dóra ; Makai, Attila ; Bencsik, Gábor ; Pap, Róbert ; Sággy, László ; Nemes, Attila et al. Egy- és kétüregi ICD diszkriminátorok hatékonyságának vizsgálata távollátásba

bevont betegeken = Single- versus dual-chamber ICD discriminators for tachyarrhythmia detection: A remote monitoring based, single-center study
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- IV. Gausz, Flóra Diána ; Lena, Kom Nangob Manuela ; Gedeon, Paul Emmanuel ; Miklós, Márton ; Benák, Attila ; Bencsik, Gábor ; Makai, Attila ; Pap, Róbert ; Sággy, László ; Szili-Török, Tamás et al. Atrioventrikuláris, egyelektrodás, lebegő pitvari dipólussal rendelkező defibrillátorok ritmuszavar felismerési képességeinek összehasonlítása hagyományos egy- és kétüregű ICD rendszerekkel = Arrhythmia detection in atrioventricular, single-lead, floating atrial dipole ICD systems compared to conventional single- and dual chamber defibrillators
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- V. Gausz Flóra Diána, Fodor Dániel, Turáni Mirjam, Miklós Márton, Benák Attila, Krányák Dóra, Makai Attila, Bencsik Gábor, Bógyi Péter, Pap Róbert, Sággy László, Nemes Attila, Szili-Török Tamás, Duray Gábor Zoltán, Vámos Máté, Egy- és kétüregű ICD diszkriminátorok ritmuszavar detekciós hatékonyságának vizsgálata: távellátásba bevont betegeken alapuló, egy gyártó készülékeire kiterjedő, kétcentrumos vizsgálat = Head -to-Head Comparison of Single- Versus Du-al-Chamber ICD Discriminators for Tachyarrhythmia Detection: A Single-Manufacturer, Remote Monitoring-Based Bicentric Study (XV. Aritmia és Pacemaker Kongresszus, Hajdúszoboszló)

ABBREVIATIONS

A	atrial electrogram
ACEI	angiotensin-converting-enzyme inhibitor
AFib	atrial fibrillation
aHR	adjusted hazard ratio
AHRE	atrial high-rate episode
ANOVA	one-way analysis of variance
ARB	angiotensin II receptor blocker
ARNI	angiotensin receptor-neprilysin inhibitor
Ars	atrial refractory sensed event
ARVC	arrhythmogenic right ventricular cardiomyopathy
As	atrial sensed event
AT	atrial tachycardia
ATP	antitachycardia pacing
AV	atrioventricular
CCB	calcium channel blocker
CI	confidence interval
CIED	cardiac implantable electronic device
CMP	cardiomyopathy
CRT	cardiac resynchronization therapy
CRT-D	cardiac resynchronization therapy with defibrillator
DC	dual-chamber
DDD ICD	dual-chamber ICD
DOAC	direct oral anticoagulant
DX	Diagnostic eXtension
eGFR	estimated glomerular filtration rate
ECG	electrocardiogram
ECV	electrical cardioversion
EGM	electrogram
FF	far-field electrogram
HCM	hypertrophic cardiomyopathy
HF	heart failure
HM	Home Monitoring
HR	hazard ratio
ICD	implantable cardioverter defibrillator
IRB	Institutional Review Board
LBBB	left bundle branch block
LVEF	left ventricular ejection fraction
N/A	not applicable

NYHA	New York Heart Association
MRA	mineralocorticoid receptor antagonist
pMSw	pacing mode switch
PSVT	paroxysmal supraventricular tachycardia
Q1	first quartile
Q3	third quartile
RA	right atrium
RAAS	renin-angiotensin-aldosterone system
RBBB	right bundle branch block
SC	single-chamber
SD	standard deviation
SGLT2	sodium–glucose cotransporter-2
SJM	Saint Jude Medical
SinT	sinus tachycardia
SMART	specific, morphology-based arrhythmia recognition technology
SSS	sick sinus syndrome
SVT	supraventricular tachycardia
TIA	transient ischemic attack
V	ventricular electrogram
VDD ICD	single-lead ICD device with a floating atrial dipole
VF	ventricular fibrillation
Vs	ventricular sensed event
VT	ventricular tachycardia
VT1	lower-rate ventricular tachycardia
VT2	higher-rate ventricular tachycardia;
VVI ICD	single-chamber ICD

1. INTRODUCTION

In the treatment of malignant tachyarrhythmias the role of implantable cardioverter defibrillators (ICDs) is inevitable [1]. Via adequate arrhythmia detection, ICDs are capable to recognize malignant ventricular arrhythmias and cease them by delivering therapy (in forms of antitachycardia pacing (ATP) and/or shock) [1-3]. However, the identification of tachyarrhythmias is complex process with the risk of misdetection, which may result in inappropriate therapy delivery [2, 4, 5]. Beside oversensing of cardiac and non-cardiac signals, the main reason of inappropriate therapy delivery is the misidentification of high-frequency supraventricular arrhythmias [4-6]. To prevent inappropriate therapy delivery, modern cardioverter defibrillators apply discrimination algorithms to differentiate between tachyarrhythmias of supraventricular and ventricular origin: if the detected tachyarrhythmia is classified as supraventricular tachycardia (SVT), therapy delivery will be withheld [2, 7]. With the application of modern discrimination algorithms, the risk of inappropriate therapy delivery significantly decreased in the last decade (from 16-18% to 4-6%) [5, 8-10]. Beside tachyarrhythmia discrimination, proper detection of supraventricular arrhythmias has other clinical importance. Modern ICDs are capable to detect and record atrial tachyarrhythmias in form atrial high-rate episodes (AHREs) [11-13]. With AHRE interpretation subclinical atrial fibrillation (or atrial flutter) can be identified allowing for early optimization of medical treatment (e.g. oral anticoagulation) and consideration of rhythm control strategies (e.g. catheter ablation) [11, 12]. Building upon the previous context, the present thesis focuses on two primary topics. First, we aimed to evaluate the atrial arrhythmia detection efficacy of VDD ICD devices, which are distinguished by their special integrated atrial sensing dipole. Our goal was to assess the advantage of this sensing dipole in AHRE detection and its role in tachyarrhythmia discrimination. Second, we analysed the tachyarrhythmia discrimination capabilities of the most widely used device manufacturer in Hungary by conducting a direct, head-to-head comparison between single-chamber and dual-chamber discrimination algorithms. Notably, the clinical relevance of this thesis is grounded in the recognition that selecting the appropriate device type and programming approach can be challenging for the physicians, as the underlying scientific evidence is often unclear given a wide variety of ICD models and manufacturer-specific programming options.

1.1. The clinical importance of implantable cardioverter defibrillators

Implantable cardioverter defibrillators have been developed to protect against sudden cardiac death and cease malignant tachyarrhythmias by therapy delivery [1, 3]. The standard indications for ICD implantation are summarized in the recent guidelines published by ESC in 2022 [1]. The most important indications are as follows: to provide secondary prevention, ICD implantation is recommended in patients with documented ventricular fibrillation or haemodynamically instable ventricular tachycardia (in the absence of reversible causes) if the expectation of good quality survival is more than 1 year (Class I indication). In symptomatic heart failure patients (NYHA II-III) with reduced left ventricular ejection fraction (if $LVEF \leq 35\%$ despite ≥ 3 months of optimal medical therapy) an ICD is recommended with a Class I indication in ischemic, and with a Class IIa indication in non-ischemic etiology [1, 14]. Notably, if the patient meets the further criteria of cardiac resynchronisation therapy a CRT-D device should be implanted [1, 14].

1.2. Modern ICD configurations

Based on the number of the implanted leads we distinguish single-chamber (SC) and dual-chamber (DC) ICD devices [3]. VVI ICDs are designed with a right ventricular lead and able to pace and sense in the ventricle. DDD devices utilize both atrial and ventricular leads, enabling pacing and sensing in the atrium and in the ventricle. In addition to conventional VVI and DDD configurations, modern VDD ICD systems are also available [2, 3, 15, 16]. VDD ICD (also known as DX ICD) was developed by Biotronik (Berlin, Germany). This special device has a ventricular lead equipped with an integrated floating atrial dipole. Although its pacing function is limited to the ventricle, sensing is not only available in the ventricle, but also in the atrium provided by the floating atrial dipole. “DX” stands for “Diagnostic eXtension” reflecting the extended atrial sensing capabilities of these devices [15, 16]. Since atrial sensing is available with a single lead implantation in case of VDD devices, the procedural time and infection risk is decreased compared to conventional DDD ICDs [13, 17, 18]. When a conventional ICD system is supplemented with a left ventricular lead (implanted in the sinus coronarius) aiming cardiac resynchronisation, the device is referred to as a CRT with defibrillator (CRT-D)(Figure 1) [3]. Additionally, CRT can be performed using DX systems by incorporating a left ventricular lead alongside the specialized VDD lead (CRT-DX system) [13].

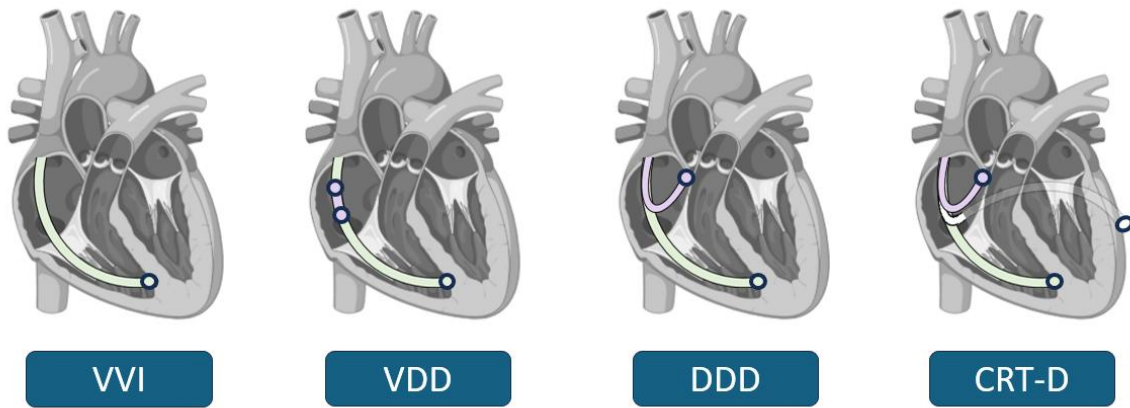


Figure 1. Modern ICD configurations.

1.3. Detection of atrial arrhythmias

Proper atrial sensing improves the detection of supraventricular arrhythmias. If the atrial frequency exceeds the preset detection limit (e.g. in case of atrial fibrillation or atrial flutter), the episode will be recorded as an atrial high-rate episode [3, 13, 19]. With AHRE detection, subclinical supraventricular arrhythmias can be identified. As atrial fibrillation is a widespread condition accompanied by increased risk of stroke risk and mortality, its early detection has an undoubtable clinical importance [20]. With early and appropriate detection, optimal medical therapy can be initiated including oral anticoagulant therapy. Furthermore, early steps towards rhythm control therapy (e.g. catheter ablation) can be initiated [20-23].

Beside DDD ICDs, VDD systems are also able to provide atrial sensing by the integrated atrial sensing dipole. The sensing dipole evaluates amplified and filtered atrial signals leading to proper and reliable atrial sensing in the long run [13, 19, 24, 25]. Previous studies evaluated the atrial arrhythmia detection capacity of VDD devices compared to VVI and DDD ICD devices. THINGS trial was a prospective, observational and multicenter study comparing 140 patients with VDD-ICDs and 236 patients with conventional VVI devices. THINGS registry revealed superiority of VDD systems in comparison with VVI ICDs regarding detection of subclinical atrial fibrillation as the ability to detect atrial arrhythmias was almost 4 times higher in this group (2-year incidence of atrial tachycardia/atrial fibrillation was 11.4% vs. 3.6%; aHR 3.85; 95% CI 1.58-9.41; $p=0.003$) [12]. The prospective, cohort-controlled and multicenter SENSE trial evaluated a total of 150 patients with VDD devices and compare them to patients with conventional VVI and DDD devices. SENSE trial showed evidence regarding superiority of DX systems compared to VVI ICDs in AHRE detection (within a 12 months follow-up

period)(13% vs. 5.3%; $p=0.026$) and revealed non-inferiority of VDD devices in comparison with DDD ICDs (13% vs. 13%; $p=1.00$). In multivariate analysis the use of the DX system was independently associated with AHRE detection (aHR 2.40; 95% CI 1.05-5.48; $p=0.038$) [11]. The study by Hindricks et al. analysed the utility of VDD systems ($n=1841$, patients from the MATRIX registry) in combination with daily automatic remote monitoring transmissions. The results revealed a 99.7% detection accuracy for $AHRE \geq 1$ hour in patients with DX systems in combination with daily remote monitoring [24]. Despite the promising results of previous studies, the first prospective, multicenter, randomized-controlled trial assessing the subclinical atrial fibrillation detection capacity of VDD ICDs ($n=90$) compared to VVI ICD devices ($n=88$) showed only a borderline superiority of DX systems (atrial arrhythmias detected by device, ECG or ECG monitoring HR 2.36; 95% CI 0.73–7.58; $p=0.15$; atrial arrhythmias detected by device HR 8.39; 95% CI 1.06–66.24; $p=0.04$) [26].

1.4. Tachycardia discrimination

The two main configurations of tachycardia discrimination algorithms are SC and DC configurations. SC discrimination algorithms analyse exclusively ventricular signals, whereas DC discriminators evaluate both atrial and ventricular activity, enabling comparison of atrial and ventricular frequency and assessment of atrioventricular (AV) synchrony [2, 3, 7, 27-29]. By their nature, DC algorithms are applicable only to dual-chamber devices (VDD and DDD ICDs). Conversely, SC discrimination is programmable both in SC (VVI ICD) and DC devices (VDD and DDD ICDs)(Figure 2) [2, 5]. The most recent expert consensus statement on ICD programming (published by HRS/EHRA/APHRS/SOLAECE) recommends the programming of SC vs. DC discrimination algorithms determined by the number of the implanted leads [30, 31]. Notably, the consensus statement emphasizes that the capability to extend discrimination with DC algorithms alone should not be considered an indication for implanting an additional atrial lead, in the absence of other clinical indications for atrial sensing or pacing [31]. This is based on the assumption that, despite the additional information and enhanced discrimination capabilities provided by the atrial lead, the implantation of an extra lead lengthens the implantation procedure and also increases the risk of short-term and long-term complications [13, 32, 33].

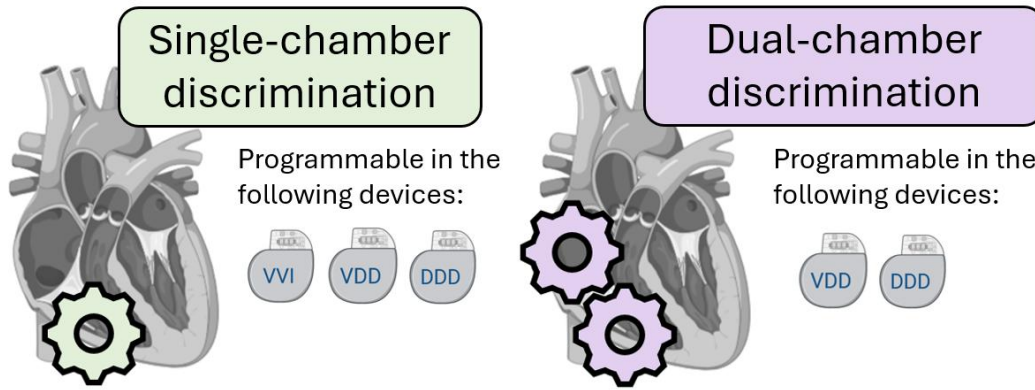


Figure 2. Programmable discrimination configurations in different device types.

Even though the core principles of tachycardia discrimination are similar in most of the ICD devices, each manufacturer has individual algorithms with manufacturer-specific features [2, 7, 27-29]. Since the studies forming the basis of this dissertation primarily involved Biotronik devices, a more detailed presentation of the discrimination algorithms employed by this manufacturer will be presented. Single-chamber discrimination of modern Biotronik ICDs involves stability, sudden onset and morphology-based discrimination (MorphMatch algorithm)(Figure 3) [2, 7, 34]. Stability analyses consecutive ventricular beats assessing the regularity of the tachyarrhythmia via comparing RR-intervals. If the evaluated rhythm is regular, it indicates ventricular tachycardia (VT), while irregular RR-intervals suggest atrial fibrillation [2, 7]. Sudden onset estimates the onset of the detected tachyarrhythmia: VT typically starts suddenly in contrast with sinus tachycardia, which usually has a gradual onset [2, 7]. MorphMatch algorithm evaluates far-field electrograms of tachyarrhythmias. Far-field electrograms are suitable for morphology assessment and MorphMatch algorithm compares the detected morphology to a previously recorded template, which is continuously updated during tachyarrhythmia-free periods. If the morphology comparison reveals significant differences, the arrhythmia will be classified as VT. In contrast, similar morphology indicates SVT [2, 7, 34].

The DC discrimination configuration of Biotronik is known as SMART algorithm. This multilevel discrimination system integrates different discrimination algorithms accompanied by frequency analysis of both atrial and ventricular rates [2, 7]. If ventricular frequency exceeds atrial frequency, the diagnosis of ventricular tachycardia is established. In every other scenario (e.g. atrial rate is higher or equals with ventricular frequency) SMART algorithm applies further discrimination methods [7]. The possible applied algorithms include stability, sudden onset and algorithms that evaluate AV synchrony (AV trend and AV regularity). A so-called multiplicity algorithm is also available, which is useful in the identification of atrial flutter as it can identify

atrial arrhythmias with a fixed ratio of A:V frequency (e.g. atrial flutter with 2:1 AV ratio). The main elements of the SMART algorithm is summarized in Figure 3 [7, 34].

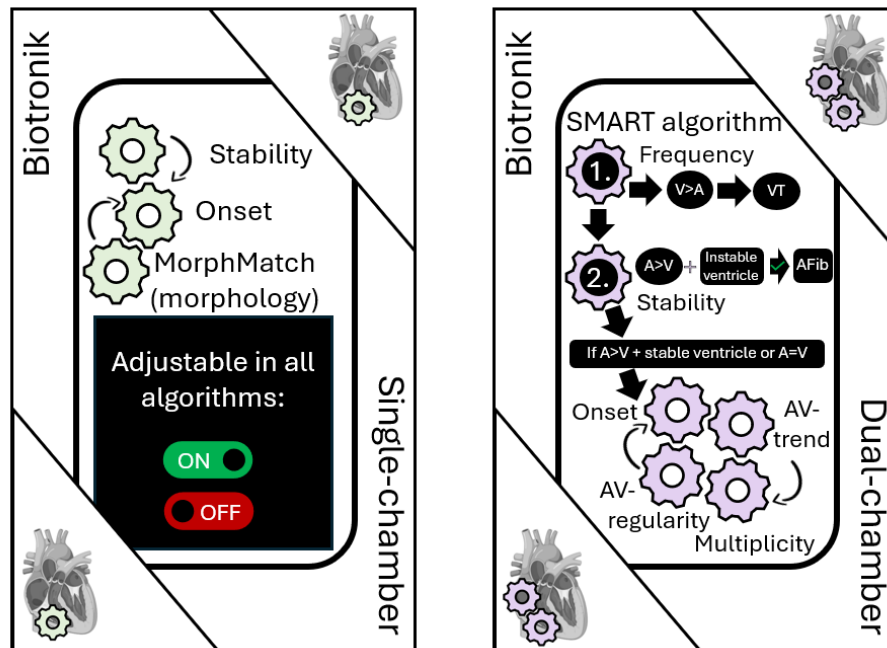


Figure 3. Summary of tachyarrhythmia discrimination algorithms available in Biotronik devices.

The comparative efficacy of SC vs. DC discrimination remains a subject of ongoing debate, due to the limited and controversial data in the literature, which challenges the assumed superiority of DC algorithms [13, 35-37]. Discrimination algorithms are under constant development and expert opinion suggests, that modern morphology-based SC discrimination algorithms may achieve similar efficacy as DC configurations [6, 8, 38]. However, it is important to note that many previous studies (even the latest meta-analysis) regarding tachyarrhythmia discrimination involved outdated ICDs with old-fashioned discrimination algorithms. Moreover, the available studies usually included devices from different manufacturers [35].

A recent study by Biffi et al. compared SC and DC discrimination (DC group involved exclusively VDD ICDs) and revealed no significant difference in efficacy of malignant tachyarrhythmia detection. However, the SC group consisted of devices from different manufacturers [8]. As switching between a specific manufacturer's SC and DC discrimination is possible in DC ICDs during the follow-up, the importance of studies focused on a single manufacturer should be highlighted. The aforementioned reprogramming may be considered

when the original discrimination settings failed appropriate arrhythmia detection and resulted in inappropriate therapy delivery [2].

1.5. The evaluated device spectrum of our work

Modern implantable cardioverter defibrillators encompass a broad range of devices that share common features but also include manufacturer-specific characteristics. In our work, we primarily concentrated on modern Biotronik devices, as Biotronik is traditionally the most frequently applied manufacturer in Hungary and the sole manufacturer of VDD systems.

2. OBJECTIVES

2.1. We aimed to evaluate the arrhythmia detection and discrimination efficacy of VDD ICDs. To assess the clinical advantages of the floating atrial dipole integrated in these systems, we performed a comparison with conventional single- (VVI) and dual-chamber (DDD) defibrillators focusing on the performance in new-onset atrial arrhythmia detection and on the efficacy in malignant tachyarrhythmia detection.

2.2. Our second goal was to evaluate the efficacy of single- versus dual-chamber discrimination algorithms in malignant tachyarrhythmias by performing a direct, head-to-head comparison using remote monitoring-based data.

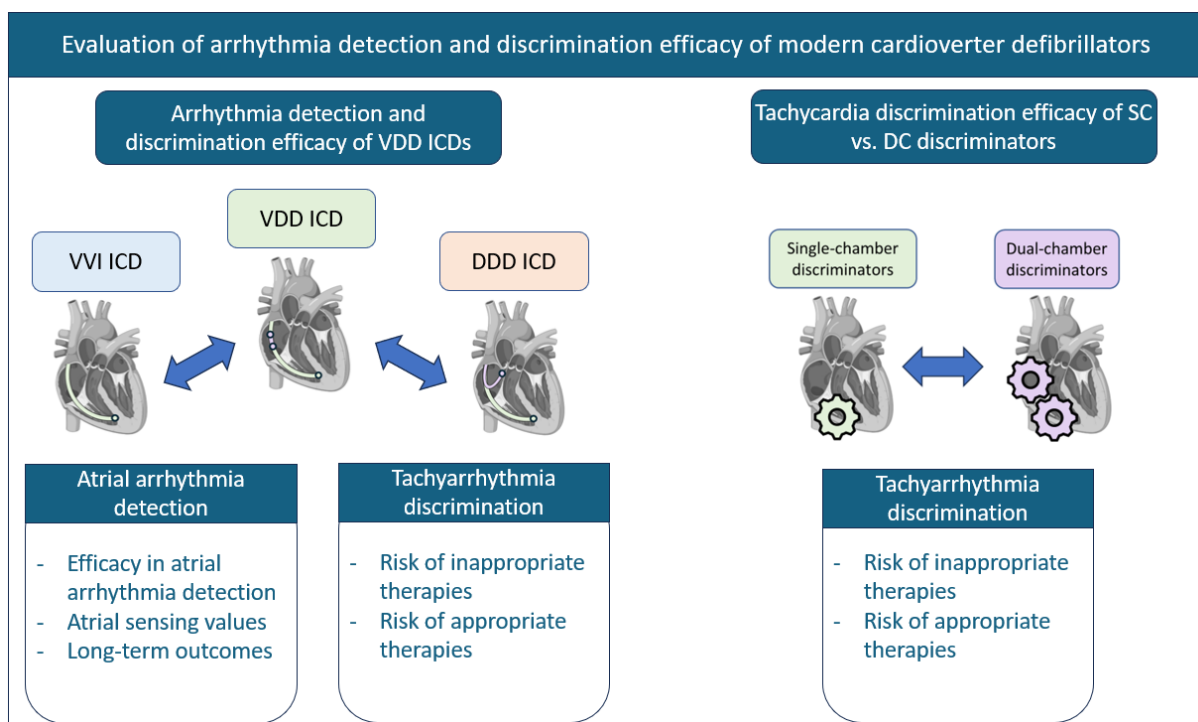


Figure 4. Aims of our work.

3. METHODS

3.1. Arrhythmia detection and discrimination efficacy of VDD ICDs

3.1.1. Patient population and baseline characteristics

We retrospectively collected data from consecutive patients undergoing ICD implantation between 2009 and 2023. The devices were implanted with standard indications in the Cardiology Center of the University of Szeged. ICDs from all manufacturers were included and CRT devices were excluded from the analysis. We gathered baseline clinical characteristics like age, gender, ICD indication (i.e., primary or secondary), ischemic etiology, previously diagnosed atrial fibrillation, hypertension, dyslipidaemia, diabetes mellitus previous stroke/transient ischemic attack (TIA), left ventricular ejection fraction (LVEF) and NYHA classification. Data regarding ICD implantation were also collected including bradypacing indication and manufacturer of the implanted device. We analysed baseline ECG and laboratory parameters: QRS width, heart rate, creatinine and hemoglobin values. Moreover, the rate of remote monitoring was also assessed. Baseline medical therapy was also collected. The study was approved by the Institutional Review Board (IRB) of the University of Szeged (No. 4870) and it conforms to the ethical guidelines of the Declaration of Helsinki.

3.1.2. Endpoints of interests

We created 3 groups according to the implanted device type: VVI, VDD and DDD ICD groups. The primary outcome was the incidence of the first device detected atrial arrhythmia: regarding this outcome we included patients with paroxysmal or persistent atrial fibrillation (patients with permanent atrial fibrillation were excluded) and collected episodes of new-onset atrial fibrillation (or atrial flutter). Our secondary endpoints were atrial (at 6 months after implantation and at the end of follow-up) and ventricular sensing parameters (at 6 months after implantation), atrial and ventricular pacing percentages (at 6 months after implantation), incidence of appropriate and inappropriate ICD therapy (ATP and/or shock), incidence of hospitalization due to arrhythmic or heart failure events and all-cause mortality. Detailed reasons of arrhythmia-related hospitalizations were evaluated involving acute admissions due to arrhythmic events, device-related problems and hospital admissions aiming rhythm control of atrial fibrillation or flutter (i.e., electrical cardioversion (ECV), catheter ablation of atrial fibrillation/flutter). Complication rates were also assessed (short-term and long-term complications). Assessed complications included pneumothorax, bleeding, thrombosis, lead- or device-related complications, repeated surgery, and CIED-related infections.

3.1.3. Evaluation of intracardiac electrograms

The minimum detection limit of AHREs was 1 minute. AHRE interpretation and the assessment of the appropriateness of the delivered ICD therapies were performed by expert physicians. In cases of uncertainty, clinical field engineers of the different device manufacturers were also involved.

3.2. Tachycardia discrimination efficacy of SC vs. DC discriminators

3.2.1. Patient population and baseline characteristics

Data were collected from two tertiary referral centers (Cardiology Center, University of Szeged, Szeged, Hungary; Department of Cardiology, Central Hospital of Northern Pest–Military Hospital, Budapest, Hungary). We retrospectively analysed all consecutive patients who underwent an ICD implantation from a single manufacturer (Biotronik) and were remotely followed up via the Home Monitoring[®] (HM) system. The patients were registered in the HM system between 2009 and 2024.

Baseline clinical characteristics included age at ICD implantation, time from ICD implantation to HM registration, gender, ICD indication (i.e., primary or secondary), chronic coronary syndromes, structural heart diseases, hypertension, previously diagnosed atrial fibrillation or atrial flutter, diabetes mellitus, prior stroke/TIA and LVEF. We also gathered the implanted device types (VVI, VDD, DDD, CRT-D), the applied discrimination algorithms (i.e., SC or DC) and indications for antibradycardia pacing. Baseline ECG and laboratory parameters were also assessed: QRS morphology, heart rate, creatinine, estimated glomerular filtration rate (eGFR) and hemoglobin values. Baseline medical therapy was also evaluated, and ICD sensing parameters (at HM registration) and pacing percentages (at one month after HM registration) were collected. Additionally, we gathered the baseline detection limits of the different VT zones. The study was approved by the Institutional Review Board (IRB) of the University of Szeged (No. 5514) and it conforms to the ethical guidelines of the Declaration of Helsinki.

3.2.2. Endpoints of interests

Based on the applied discrimination algorithm patients were divided into two groups: SC and DC discrimination group. If the discrimination algorithm was reprogrammed during follow-up – such as a switch between SC and DC configurations – patient data were analysed only until the original settings remained unchanged. The primary outcome was the time to first

inappropriate therapy (resulted in ATP and/or shock delivery) completed with separate analysis of first inappropriate therapies that resulted in ATP delivery alone and therapies that resulted in ATP + shock delivery. Our secondary endpoints were the time to first appropriate ICD therapy and all-cause mortality. We also performed a sensitivity analysis including only a subgroup of SC patients with active morphology discrimination to assess the risk of inappropriate therapy compared to the DC group. A subgroup analysis was also conducted within the DC group, comparing the incidence of inappropriate therapies between patients with VDD vs. DDD devices.

3.2.3. Evaluation of intracardiac electrograms

To assess the appropriateness of the delivered ICD therapies, we reviewed the intracardiac electrograms (EGMs) recorded by the HM system. EGMs were adjudicated by an expert physician and a clinical field engineer, while uncertain cases were further evaluated by a senior electrophysiologist.

3.3. Statistical analysis

Statistical analysis was performed by using SPSS Statistics (version 27 and 29, IBM, Armonk, NY, USA). Continuous variables are expressed as “mean±standard deviation (SD)” or “median (first quartile (Q1)-third quartile (Q3))” forms and categorical variables as numbers (percentages). Given three groups in the evaluation of VDD ICD efficacy (compared to VVI and DDD ICDs), for the comparison of continuous variables we performed one-way analysis of variance (ANOVA). Notably, in case of non-normal distribution Kruskal-Wallis test was used. Comparing two groups, for the evaluation of continuous variables, we conducted independent samples t-test (or Mann-Whitney U test if the distribution of variables was non-normal). Categorical variables were assessed by Chi-squared test.

We applied time-to-event analysis in both main objectives to evaluate the following parameters accordingly: incidence of the first device-detected atrial arrhythmia, risk of appropriate/inappropriate therapies, all-cause mortality, risk of hospitalization due to arrhythmic causes and risk of hospitalization due to heart failure causes. Time-to-event analysis was performed calculating hazard ratios (HR) along with 95% confidence intervals (CI). Statistical significance was determined as a p-value ≤ 0.05 . In most of the cases, time-to-event analysis was completed with a multivariate model. All predictor variables, which were

considered potentially impactful regarding the evaluated parameter underwent a univariate analysis. (The included variables are listed in Supplementary Table 1.). After this, all predictor variables that demonstrated a statistically meaningful association ($p \leq 0.1$) in the univariate analysis were incorporated into the multivariate model. Evaluating the performance of VDD ICD, device type was included in the multivariate models regardless of the significance in the univariate analysis. Similarly, in the head-to-head comparison of SC vs. DC discriminators, the discrimination algorithm was involved in all of the multivariate models independently of its significance in the univariate analysis (and device type was included in the multivariate model of the predefined subgroup analysis accordingly).

4. RESULTS

4.1. Arrhythmia detection and discrimination efficacy of VDD ICDs

4.1.1. Baseline clinical characteristics and medical therapy

256 patients were included with a mean follow-up time of 3.7 years. The mean age was 64 years, 75% were male, and two third of the patients (61%) had ischemic etiology. The distribution of the implanted device types was as follows: 93 VVI, 94 VDD and 69 DDD ICD systems. 28% of the devices were implanted with a primary prophylactic indication (Supplementary Table 2).

Majority of baseline clinical characteristics were similar across the VVI, VDD and DDD ICD groups (Table 1). The prevalence of dyslipidaemia was lower in the DDD group, but the mean LVEF was increased compared to the other groups. Bradycardia indication was more prevalent in DDD group, accompanied by decreased heart rate and broader QRS complexes. As Biotronik is the sole manufacturer of VDD ICD 98% of the VDD ICDs were implanted with a generator from this manufacturer. In the remaining two cases a St. Jude Medical (SJM)/Abbott (Chicago, USA) or a Sorin (New York, USA) generator was connected to the implanted VDD leads. In the VVI and DDD groups Biotronik, Boston Scientific (Marlborough, USA), Medtronic (Minneapolis, USA) and SJM generators were applied. Remote monitoring system was most frequently applied in the VDD group. Notably, the baseline characteristics for the different subgroup comparisons (VVI vs. VDD, VVI vs. DDD, VDD vs. DDD) are presented in Supplementary Table 3.

Table 1. Baseline clinical characteristics

	VVI (N=93)	VDD (N=94)	DDD (N=69)	p-value
Age (mean±SD)	64±12	63±12	64±14	0.307
Male, n (%)	65 (70%)	76 (81%)	50 (73%)	0.203
Primary prophylaxis, n (%)	19 (20%)	29 (31%)	24 (35%)	0.101
Ischemic etiology, n (%) ^a	57 (61%)	58 (62%)	40 (59%)	0.926
Previously diagnosed atrial fibrillation, n (%) ^a	27 (29%)	35 (37%)	25 (37%)	0.430
Hypertension, n (%) ^a	86 (93%)	91 (97%)	60 (88%)	0.107
Dyslipidaemia, n (%) ^a	79 (85%)	85 (90%)	48 (71%)	0.003
Diabetes mellitus, n (%) ^b	29 (31%)	33 (35%)	22 (33%)	0.850
Stroke/TIA, n (%) ^b	11 (12%)	8 (9%)	9 (14%)	0.571
Bradypacing indication, n (%) ^b	1 (1%)	3 (3%)	36 (55%)	<0.001
<i>No bradypacing indication</i>	92 (99%)	91 (97%)	30 (45.5%)	
<i>Sick sinus syndrome</i>	0 (0%)	0 (0%)	3 (4.5%)	
<i>Second-degree AV block</i>	1 (1%)	0 (0%)	11 (16.7%)	
<i>Third-degree AV block</i>	0 (0%)	2 (2%)	21 (31.8%)	
<i>Atrial fibrillation with bradycardia</i>	0 (0%)	1 (1%)	1 (1.5%)	
Manufacturer, n (%)				<0.001

<i>Biotronik</i>	2 (2%)	92 (98%)	20 (29%)	
<i>Boston Scientific</i>	10 (11%)	0 (0%)	9 (13%)	
<i>Medtronic</i>	45 (48%)	0 (0%)	37 (54%)	
<i>SJM/Abbott</i>	36 (39%)	1 (1%)	3 (4%)	
<i>Sorin</i>	0 (0%)	1 (1%)	0 (0%)	
NYHA, n (%) ^c				0.707
<i>No</i>	30 (34%)	34 (40%)	21 (33%)	
<i>NYHA I</i>	22 (25%)	20 (24%)	17 (27%)	
<i>NYHA II</i>	25 (28%)	18 (21%)	11 (18%)	
<i>NYHA III</i>	12 (14%)	12 (14%)	13 (21%)	
<i>NYHA IV</i>	0 (0%)	1 (1%)	1 (2%)	
LVEF (mean±SD) ^d	38.5±13.5	37.5±13.9	47.5±16.3	<0.001
QRS width (mean±SD) ^e	116.9±21.2	119±21.6	136.9±29.2	0.001
HR (mean±SD) ^f	70.7±15.4	73.1±14.8	66.9±18.6	0.038
Creatinine (mean±SD) ^g	91.1±31.6	99.6±52.9	94.9±27.9	0.598
Hemoglobin (mean±SD) ^h	130.7±20.6	136±16.8	126.2±20.7	0.019
Remote monitoring, n (%)	6 (7%)	48 (51%)	13 (19%)	<0.001

a) Available for 255 patients. b) Available for 253 patients. c) Available for 237 patients. d) Available for 249 patients. e) Available for 175 patients. f) Available for 229 patients. g) Available for 198 patients. h) Available for 196 patients.

Baseline medical therapy is described in Table 2. Beta-blockers and mineralocorticoid receptor antagonists were more frequently used in the VVI and VDD groups, while more digitalis glycosides were applied in the VVI group. The baseline medical therapy for the different subgroup comparisons (VVI vs. VDD, VVI vs. DDD, VDD vs. DDD) are presented in Supplementary Table 4.

Table 2. Baseline medical therapy

	VVI (N=93)	VDD (N=94)	DDD (N=69)	p-value
Antiplatelet therapy, n (%) ^a	62 (67%)	55 (59%)	41 (64%)	0.502
Anticoagulation, n (%) ^b	33 (36%)	46 (49%)	26 (40%)	0.167
Beta-blockers, n (%) ^a	90 (97%)	90 (96%)	53 (83%)	0.001
ACEI/ARB/ARNI, n (%) ^a	81 (87%)	84 (89%)	50 (78%)	0.125
Diuretics, n (%) ^a	50 (54%)	49 (52%)	28 (44%)	0.436
Calcium channel blockers, n (%) ^a	17 (18%)	20 (21%)	19 (30%)	0.230
Mineralocorticoid receptor antagonists, n (%) ^a	48 (52%)	52 (55%)	17 (27%)	0.001
Statins, n (%) ^a	67 (72%)	66 (70%)	44 (69%)	0.903
Amiodarone, n (%) ^a	17 (18%)	21 (22%)	10 (16%)	0.555
Digitalis glycosides, n (%) ^a	13 (14%)	3 (3%)	3 (5%)	0.012
SGLT2 inhibitor, n (%) ^a	2 (2%)	5 (5%)	3 (5%)	0.512

a) Available for 251 patients. b) Available for 252 patients.

4.1.2. Clinical outcomes

4.1.2.1. Device-detected atrial arrhythmias

The incidence of new-onset device detected atrial arrhythmias was significantly higher in the VDD group compared to the VVI group (HR 6.506; 95% CI 2.176–19.446; p=0.001; adjusted

hazard ratio (aHR) 7.087; 95% CI 2.371–21.183; $p<0.001$)(Table 3, Figure 5A, Supplementary Table 5). After adjustment for clinically and statistically relevant confounders, the efficacy of atrial arrhythmia detection in VDD ICDs was non-inferior to conventional DDD devices (aHR 1.781; 95% CI 0.737–4.301; $p=0.200$)(Table 3, Figure 5B, Supplementary Table 6). The distribution of the detected atrial arrhythmias (e.g. paroxysmal or persistent atrial fibrillation, regular atrial arrhythmias) did not differ among the groups ($p=0.609$)(Supplementary Table 7).

Table 3. Long-term clinical outcomes

	VVI vs. VDD	95% CI	p-value
Time to first device detected atrial arrhythmia ^a	HR (univariate) 6.506 HR (multivariate) ^b 7.087	2.176-19.446 2.371-21.183	0.001 <0.001
Time to first appropriate therapy	HR (univariate) 0.874 HR (multivariate) ^c 0.983	0.574-1.332 0.641-1.508	0.523 0.937
Time to first inappropriate therapy	HR (univariate) 0.782 HR (multivariate) ^c 0.742	0.338-1.811 0.313-1.757	0.566 0.497
Time to first hospitalization due to arrhythmic cause	HR (univariate) 1.463 HR (multivariate) ^c 1.706	0.899-2.379 1.043-2.792	0.125 0.033
Time to first HF hospitalization	HR (univariate) 0.949 HR (multivariate) ^d 1.628	0.449-2.006 0.619-4.279	0.891 0.323
All-cause mortality	HR (univariate) 0.914	0.543-1.537	0.734
	VDD vs. DDD		
Time to first device detected atrial arrhythmia ^a	HR (univariate) 2.011 HR (multivariate) ^e 1.781	1.110-3.642 0.737-4.301	0.021 0.200
Time to first appropriate therapy	HR (univariate) 0.611 HR (multivariate) ^f 0.651	0.359-1.040 0.371-1.142	0.069 0.135
Time to first inappropriate therapy	HR (univariate) 0.710 HR (multivariate) ^g 0.618	0.249-2.024 0.203-1.878	0.522 0.396
Time to first hospitalization due to arrhythmic cause	HR (univariate) 0.638 HR (multivariate) ^h 0.700	0.366-1.113 0.365-1.341	0.114 0.282
Time to first HF hospitalization	HR (univariate) 0.586 HR (multivariate) ⁱ 0.949	0.219-1.570 0.301-2.991	0.287 0.928
All-cause mortality	HR (univariate) 0.812	0.442-1.490	0.501
	VVI vs. VDD vs. DDD		
All-cause mortality	HR (univariate) 0.906 HR (multivariate) ^j 0.960	0.696-1.179 0.711-1.295	0.463 0.787

a) In the time-to-event analysis of device detected atrial tachyarrhythmia, patients with permanent atrial fibrillation were excluded. b) Available for 147 patients. c) Available for 187 patients. d) Available for 129 patients. e) Available for 87 patients. f) Available for 157 patients. g) Available for 155 patients. h) Available for 130 patients. i) Available for 126 patients. j) Available for 221 patients.

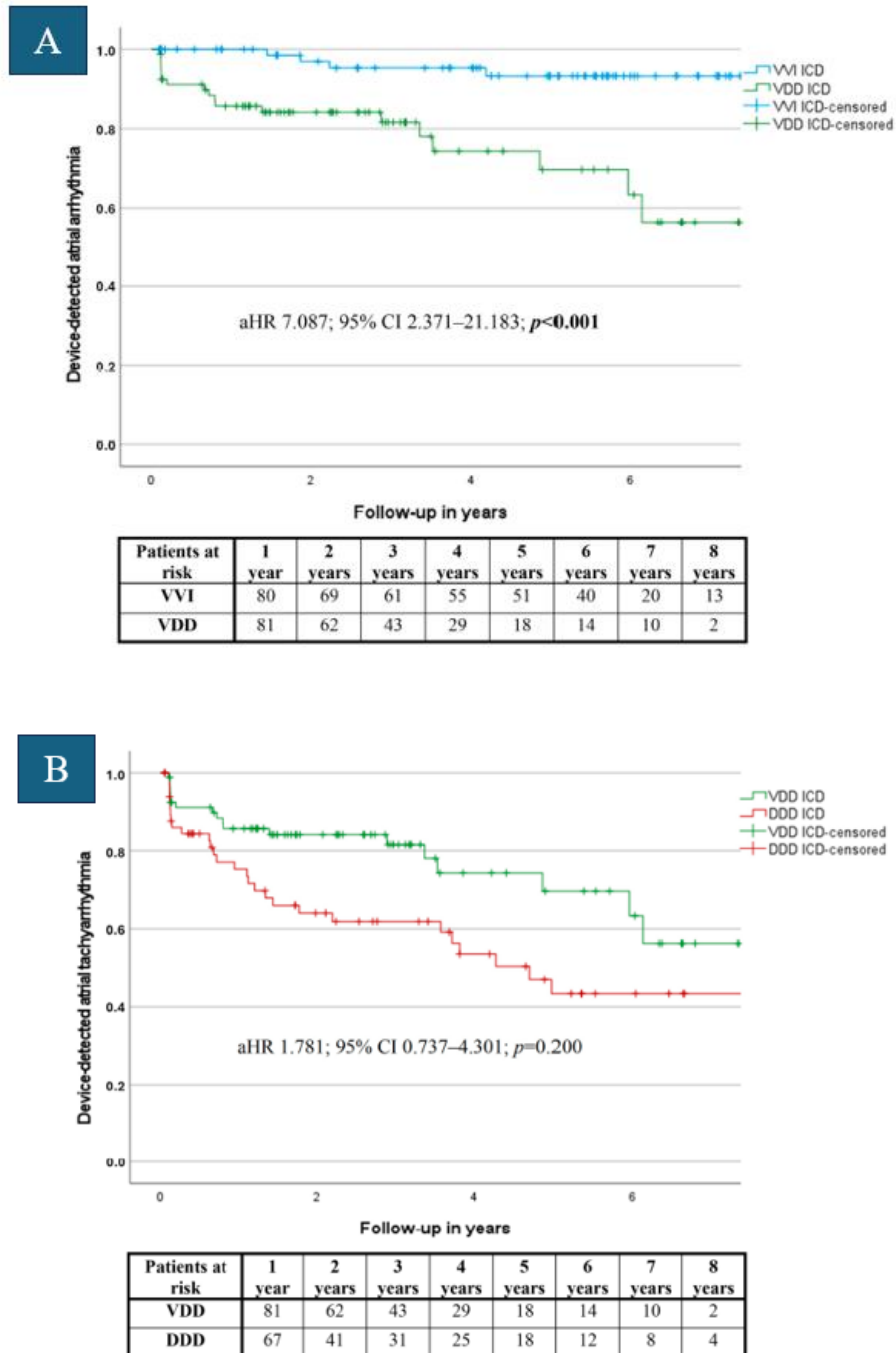


Figure 5. (A) Time to first device-detected atrial arrhythmia – VVI vs. VDD. **(B)** Time to first device detected atrial arrhythmia – VDD vs. DDD.

4.1.2.2. Sensing and pacing parameters

Atrial sensing was higher in the VDD ICDs compared to DDD devices at both evaluated occasions: 6 months after implantation (5.3 ± 3.7 vs. 3.1 ± 2.1 mV; $p < 0.001$) and at the end of the follow-up (4.2 ± 3.2 vs. 2.7 ± 1.8 mV; $p = 0.009$) (Table 4, Figure 6). Ventricular sensing at 6

months was similar in the three groups (VVI 12.8 ± 4.8 vs. VDD 14.0 ± 6.0 vs. DDD 13.2 ± 5.7 mV; $p=0.313$)(Table 4, Supplementary Figure 1). In the DDD group, mean atrial pacing percentage was 23% at 6 months. Ventricular pacing percentage was highest in DDD group (VVI 2.2 ± 7.0 vs. VDD 2.8 ± 14.4 vs. DDD $33.6 \pm 41.9\%$; $p<0.001$)(Table 4).

Table 4. Sensing/pacing parameters, and complication rates in the 3 ICD groups

	VVI (N=93)	VDD (N=94)	DDD (N=69)	p-value
Atrial sensing at 6 months (mean \pm SD) ^a	N/A	5.32 ± 3.72	3.14 ± 2.09	<0.001
Atrial sensing at the end of the follow-up (mean \pm SD) ^b	N/A	4.15 ± 3.19	2.67 ± 1.81	0.009
Ventricular sensing at 6 months (mean \pm SD) ^c	12.76 ± 4.83	13.98 ± 6.00	13.17 ± 5.71	0.313
AP (mean \pm SD) ^d	N/A	N/A	22.58 ± 33.67	-
VP (mean \pm SD) ^e	2.16 ± 6.95	2.83 ± 14.40	33.61 ± 41.91	<0.001
Complications, n (%)	7 (8%)	12 (13%)	14 (20%)	0.056

a) Available for 127 patients. b) Available for 144 patients. c) Available for 239 patients. d) Available for 55 patients. e) Available for 246 patients.

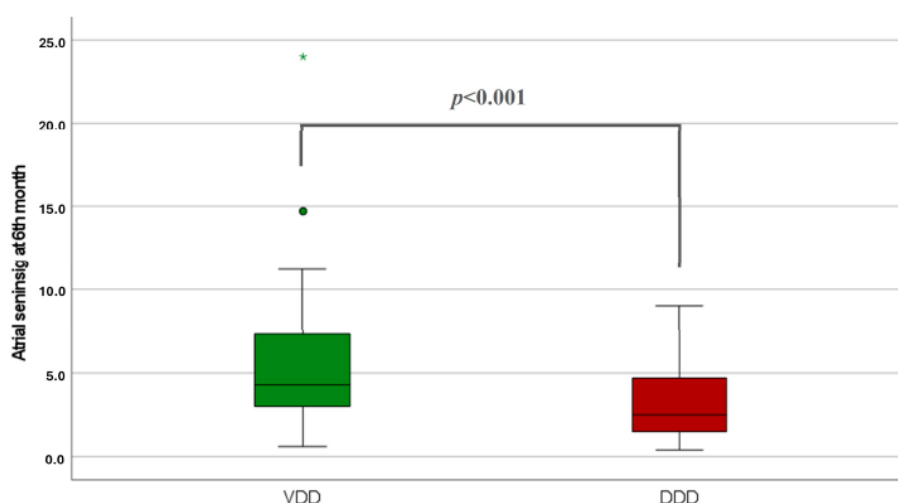


Figure 6. Atrial sensing in VDD vs. DDD ICDs at 6th month.

4.1.2.3. Complications

Numerically, complications were more frequently observed in the DDD group (20%), while the rates were 13% in the VDD group and 8% in the VVI group ($p=0.056$)(Table 4). In the VDD and DDD groups, most complications were associated with infection (VDD: 5 cases, DDD: 6 cases) or lead-related problems (VDD: 5 cases, DDD: 5 cases). We also performed a subgroup analysis, which detected a significant difference between the complication rates of VVI and DDD devices ($p=0.017$), but not between the VVI and VDD (0.236) or VDD and DDD groups (0.195)(Table 5). The detailed distribution of complications is described in Table 6.

Table 5. Subgroup analysis of complication rates

	VVI (N=93)	VDD (N=94)	p-value
Complications, n (%)	7 (8%)	12 (13%)	0.236
	VVI (N=93)	DDD (N=69)	p-value
Complications, n (%)	7 (8%)	14 (20%)	0.017
	VDD (N=94)	DDD (N=69)	p-value
Complications, n (%)	12 (13%)	14 (20%)	0.195

Table 6. Distribution of complications between all groups

	VVI (N=93)	VDD (N=94)	DDD (N=69)
Superficial infection (n,%)	2 (2%)	5 (5%)	3 (4%)
Pocket infection (n,%)	1 (1%)	0 (0%)	2 (3%)
Systemic infection (n,%)	2 (2%)	0 (0%)	1 (1%)
Hematoma (n,%)	1 (1%)	2 (2%)	2 (3%)
Deep venous thrombosis (n,%)	0 (0%)	0 (0%)	1 (1%)
Lead-related complication (n,%)	1 (1%)	5 (5%)	5 (7%)

4.1.2.4. Tachyarrhythmia discrimination

The risk of appropriate (aHR 0.983; 95% CI 0.641–1.508; p=0.937) and inappropriate ICD therapies (aHR 0.742; 95% CI 0.313–1.757; p=0.497) were similar between VVI and VDD devices (Table 3, Supplementary Table 8 and 10, Supplementary Figure 2A and 2C). Furthermore, the comparison of VDD and DDD ICDs revealed no difference in the risk appropriate (aHR 0.651; 95% CI 0.371–1.142; p=0.135) and inappropriate ICD therapy delivery (aHR 0.618; 95% CI 0.203–1.878; p=0.396)(Table 3, Supplementary Table 9 and 11, Supplementary Figure 2B and 2D).

4.1.2.5. Arrhythmia and heart failure-related hospitalization

The risk of hospitalization due to arrhythmic causes was elevated in VDD group compared to patients with VVI devices (aHR 1.706; 95%CI 1.043–2.792; p=0.033)(Table 3, Supplementary Table 12, Supplementary Figure 3A). Notably, arrhythmia-caused hospitalization was similar in VDD and DDD groups (aHR 0.700; 95% CI 0.365–1.341; p=0.282)(Table 3, Supplementary Table 13, Supplementary Figure 3B). The detailed reasons of arrhythmia-related admission are summarized in Table 7. The most common cause for arrhythmia-related hospitalization was admission due to ventricular tachycardia or electric storm in all groups. However, admissions that aimed the management of supraventricular arrhythmias (including elective admissions for rhythm control therapy of atrial fibrillation (or atrial flutter)) were more frequently observed in the VDD and the DDD ICD groups (VVI 10%, VDD 23% and DDD 24%).

The risk of heart failure-related hospitalization was similar both in VVI vs. VDD (aHR 1.628; 95% CI 0.619–4.279; $p=0.323$) and VDD vs. DDD (aHR 0.949; 95% CI 0.301–2.991; $p=0.928$) comparisons (Table 3, Supplementary Table 14 and 15, Supplementary Figure 4A and B).

Table 7. Arrhythmia-related hospitalization events in the different groups

	VVI (N=93)	VDD (N=94)	DDD (N=69)
Total number of first arrhythmia-related hospitalization events	32	35	21
Admission due to ventricular tachycardia or electric storm, n (%)	27 (84%)	23 (66%)	10 (48%)
Admission due to management of supraventricular tachycardia (including elective admission due to ECV or catheter ablation), n (%)	3 (10%)	8 (23%)	5 (24%)
Admission due to other causes (electrode malfunction, BIV-up-grade, syncope, etc.), n (%)	2 (6%)	4 (11%)	6 (28%)

4.1.2.6. All-cause mortality

All-cause mortality did not differ among the three groups (aHR 0.960; 95% CI 0.711–1.295; $p=0.787$) (Table 3, Supplementary Table 16, Figure 7).

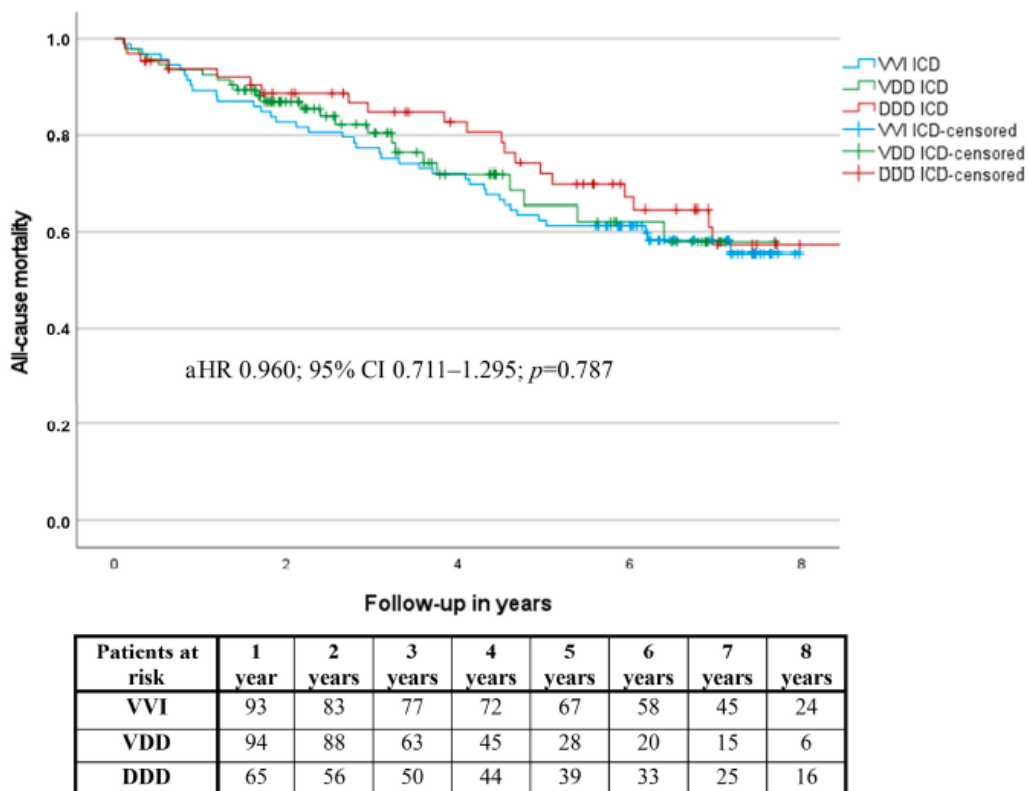


Figure 7. All-cause mortality in all groups

4.2. Tachycardia discrimination efficacy of SC vs. DC discriminators

4.2.1. Baseline clinical characteristics and medical therapy

We included 557 patients with a median follow-up time of 2.4 (1.1–3.6) years. The distribution of the implanted device types was as follows: 76 VVI, 226 VDD, 76 DDD ICD and 179 CRT-D systems (Table 8). The applied device models are listed in Supplementary Table 17. 124 ICDs were programmed to utilize SC discrimination and 433 were assigned to the DC discrimination group. Within the SC group, 47 ICDs (39%) applied active morphology discrimination (i.e. MorphMatch algorithm). The distribution of discrimination algorithms across the ICD types is presented in Figure 8.

Table 8. Baseline clinical characteristics

	Overall (N=557)	Single-chamber (N=124)	Dual-chamber (N=433)	p-value
Age at implantation, years (median [Q1-Q3])	65 (55-72)	67 (59-75)	64 (54-71)	0.002
Time from ICD implantation to Home Monitoring registration, days (median [Q1-Q3])	5 (1-225)	129 (3-682)	4 (1-62)	<0.001
Male, n (%)	431 (77 %)	94 (76 %)	337 (78 %)	0.635
Primary prophylaxis, n (%) ^a	321 (58 %)	57 (46 %)	264 (61 %)	0.002
Chronic coronary syndromes, n (%) ^b	270 (49 %)	61 (49 %)	209 (49 %)	0.979
Structural heart disease, n (%) ^c	460 (83%)	99 (80%)	361 (84%)	0.282
Ischemic cardiomyopathy	266 (48 %)	61 (49 %)	205 (48 %)	
Dilatative cardiomyopathy	165 (30 %)	32 (26 %)	133 (31 %)	
Hypertrophic cardiomyopathy	23 (4 %)	6 (5 %)	17 (4 %)	
Arrhythmogenic right ventricular cardiomyopathy	6 (1 %)	0 (0 %)	6 (1 %)	
Other	94 (17 %)	25 (20 %)	69 (16 %)	
Previously diagnosed atrial fibrillation/atrial flutter, n (%) ^c	213 (39 %)	71 (58 %)	142 (33 %)	<0.001
Paroxysmal	117 (55%)	21 (29.5%)	96 (67.5%)	
Persistent	23 (11%)	2 (3%)	21 (15%)	
Permanent	73 (34%)	48 (67.5%)	25 (17.5%)	
Hypertension, n (%) ^a	436 (79 %)	110 (89 %)	326 (76 %)	0.002
Diabetes mellitus, n (%) ^a	166 (30 %)	39 (32 %)	127 (30 %)	0.670
Stroke/TIA, n (%) ^c	39 (7 %)	13 (11 %)	26 (6 %)	0.083
Bradypacing indication, n (%) ^d	98 (18%)	20 (16%)	78 (18%)	0.623
No bradypacing indication	454 (82 %)	103 (84 %)	351 (82 %)	
Sick sinus syndrome	44 (8 %)	2 (2 %)	42 (10 %)	
AV block	34 (6 %)	3 (2 %)	31 (7 %)	
Atrial fibrillation with slow ventricular response	20 (4 %)	15 (12 %)	5 (1 %)	
QRS, n (%) ^c				0.545
Narrow QRS	255 (48 %)	57 (50 %)	198 (47 %)	
LBBB	115 (21 %)	20 (17 %)	95 (22 %)	
RBBB	43 (8 %)	10 (9 %)	33 (8 %)	
Paced rhythm / Other	124 (23 %)	27 (24 %)	97 (23 %)	
LVEF % (median [Q1-Q3]) ^f	30 (25-40)	35 (25-48)	30 (23-38)	0.002
Heart rate, bpm (median [Q1-Q3]) ^g	70 (61-81)	73 (62-84)	70 (60-81)	0.273
Creatinine, umol/l (median [Q1-Q3]) ^h	98 (82-120)	99 (80-119)	98 (82-121)	0.615
eGFR, ml/min/1.73 m ² (median [Q1-Q3]) ⁱ	63 (50-81)	60 (48-80)	64 (50-81)	0.473
Hemoglobin, mmol/l (median [Q1-Q3]) ^j	137 (125-148)	135 (121-148)	137 (125-148)	0.449

Implanted device type, n (%)				
VVI	76 (14 %)	76 (61 %)	0 (0 %)	<0.001
VDD	226 (40 %)	23 (19 %)	203 (47 %)	
DDD	76 (14 %)	1 (<1 %)	75 (17 %)	
CRT-D	179 (32 %)	24 (19 %)	155 (36 %)	

a) Available for 555 patients, b) Available for 550 patients, c) Available for 554 patients, d) Available for 552 patients, e) Available for 537 patients, f) Available for 541 patients, g) Available for 539 patients, h) Available for 519 patients, i) Available for 500 patients, j) Available for 517 patients.

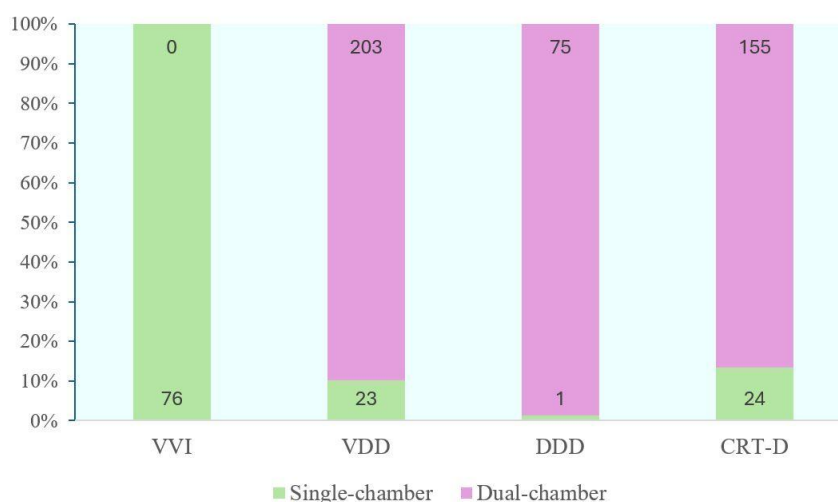


Figure 8. Single-chamber and dual-chamber discrimination algorithms by ICD device type.

The baseline clinical characteristics are presented in Table 8. The median age of the patients was 65 (55-72) years. 77% of the patients were male, 49% had chronic coronary syndromes and 39% were previously diagnosed with atrial fibrillation (or flutter). ICDs were implanted with a primary prophylactic indication in 58% of cases.

The median age was higher in the SC group ($p=0.002$) and the prevalence of atrial fibrillation or flutter (58% vs. 33%, $p<0.001$) and hypertension were increased in this group. The history of diabetes mellitus and prior stroke/TIA did not differ among the groups. Primary prophylactic indication was more common in the DC group (61% vs. 46%). The prevalence of bradypacing indication was similar between the groups, however the distribution of underlying conduction disorders varied: atrioventricular (AV) block was more common in the SC group, whereas sick sinus syndrome was more frequently observed in the DC group. Baseline median left ventricular ejection fraction (35% vs. 30%, $p=0.002$) was higher in the SC group. Baseline ECG parameters and laboratory values showed no differences among the SC and DC groups.

Detailed information regarding baseline medical therapy is provided in Table 9. Overall, baseline medical therapy was similar between the groups, with the exception that diuretics and mineralocorticoid receptor antagonists (MRA) were more frequently used in the DC group.

Table 9. Baseline medical therapy

	Overall population (N=557)	Single-chamber (N=124)	Dual-chamber (N=433)	p-value
Antiplatelets, n (%) ^a	266 (48%)	51 (41 %)	215 (50 %)	0.082
Anticoagulation, n (%) ^a	311 (56%)	77 (62 %)	234 (54 %)	0.129
Beta-blocker, n (%) ^a	534 (96%)	120 (97 %)	414 (96 %)	0.795
RAAS inhibitor, n (%) ^b	493 (89%)	108 (88 %)	385 (90 %)	0.586
Diuretics, n (%) ^a	375 (68%)	74 (60 %)	301 (70 %)	0.030
MRA, n (%) ^a	395 (71%)	75 (61 %)	320 (74 %)	0.003
Digitalis, n (%) ^a	35 (6%)	11 (9 %)	24 (6 %)	0.185
CCB, n (%) ^a	54 (10%)	17 (14 %)	37 (9 %)	0.091
Amiodaron, n (%) ^a	144 (26%)	28 (23 %)	116 (27 %)	0.325
Statin, n (%) ^a	364 (66%)	80 (65 %)	284 (66 %)	0.752
SGLT2-inhibitor, n (%) ^b	87 (16%)	20 (16 %)	67 (16 %)	0.890

a) Available for 554 patients, b) Available for 553 patients.

4.2.2. Sensing/Pacing parameters and VT zone settings

Atrial sensing values were similar among SC and DC discrimination groups at time of HM registration (5.7 [3.4–6.8] mV vs. 4.1 [2.4–6.3] mV; $p=0.166$)(Table 10, Figure 9A). Baseline ventricular sensing values (14.6 [9.4–19.5] mV vs. 16.9 [12.0–20.0] mV; $p = 0.016$)(Table 10, Figure 9B) and ventricular pacing percentages were higher in the DC group in comparison with the SC group (0 [0–21]% vs. 1 [0–96]%; $p=0.002$)(Table 10).

The baseline lower detection limit for the VT1 zone was comparable between the SC and DC groups (340 [330–375] ms vs. 340 [330–360] ms). The lower limit for the VT2 zone was slightly higher in the DC group (320 [290–340] ms vs. 300 [290–320] ms). For the VF zone, the lower detection limit was similar between groups, at 260 [253–280] ms in the SC group and 260 [250–280] ms in the DC group.

Table 10. Baseline sensing/pacing parameters

	Single-chamber (N=124)	Dual-chamber (N=433)	p-value
Atrial sensing at HM registration, mV (median [Q1-Q3]) ^a	5.7 (3.4-6.8)	4.1 (2.4-6.3)	0.166
Ventricular sensing at HM registration, mV (median [Q1-Q3]) ^b	14.6 (9.4-19.5)	16.9 (12.0-20.0)	0.016
Atrial pacing at 1 st month after HM registration, % (median [Q1-Q3]) ^c	N/A	3.0 (0.0-42.0)	
Ventricular pacing at 1 st month after HM registration, % (median [Q1-Q3]) ^d	0 (0-21)	1 (0-96)	0.002

a) Available for 428 patients, b) Available for 515 patients, c) Available for 224 patients, d) Available for 544 patients.

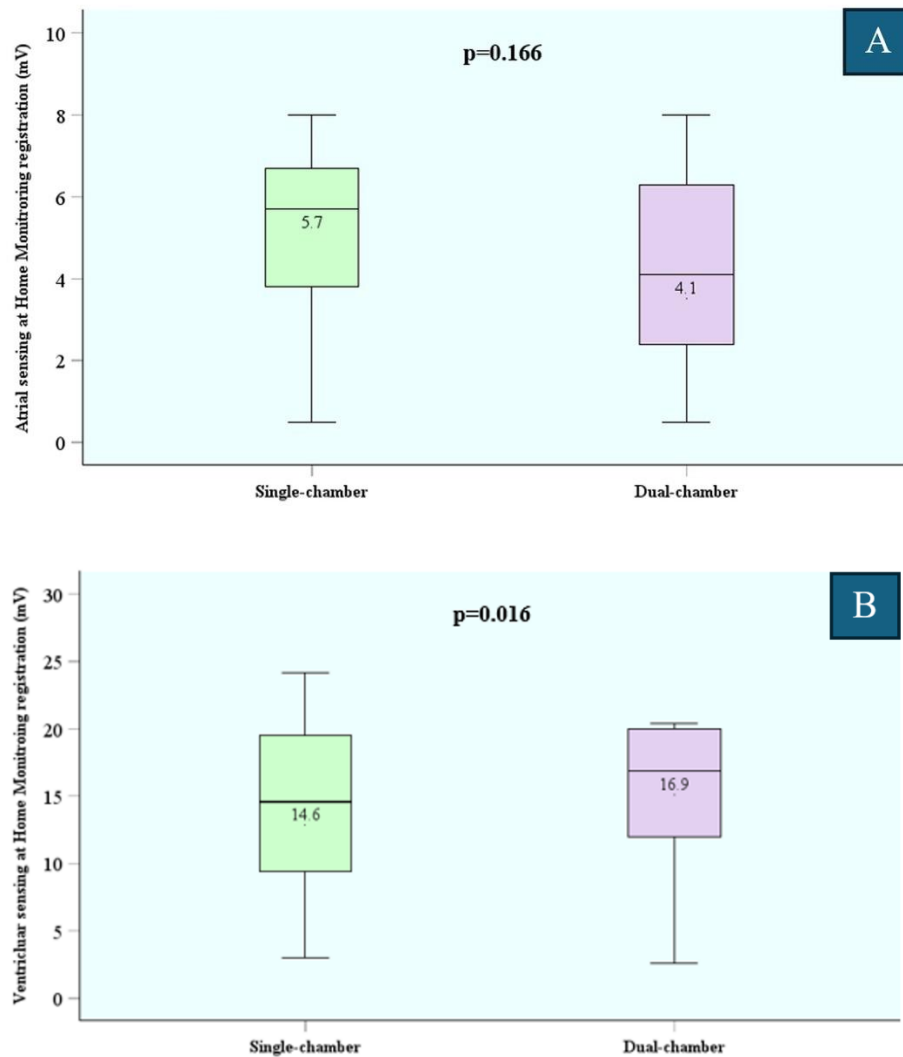


Figure 9. (A) Baseline atrial sensing parameters in single-chamber and dual-chamber discrimination groups. **(B)** Baseline ventricular sensing parameters in single-chamber and dual-chamber discrimination groups.

4.2.3. Clinical outcomes

4.2.3.1. Inappropriate therapies

The incidence of inappropriate therapies was 3.2% (0.01% per patient-year) in the SC and 4.4% (0.01% per patient-year) in the DC discrimination group. We revealed also no difference in the risk of inappropriate therapies between the SC and DC discrimination groups on the time-to-event analysis (HR 1.165; 95% CI 0.393–3.448; $p=0.783$; adjusted HR 1.152; 95% CI 0.387–3.433; $p=0.799$) (Table 11, Figure 10, Supplementary Table 18). Furthermore, the comparison of inappropriate therapies resulted in ATP delivery alone (HR 1.264; 95% CI 0.365–4.377; $p=0.712$) (Table 11) and inappropriate therapies resulted in ATP + shock delivery (HR 0.871;

95% CI 0.091–8.372; $p=0.905$)(Table 11) showed no difference between the SC and DC discrimination groups.

Table 11. Clinical outcomes

	Single-chamber (N=124)	Dual-chamber (N=433)	p-value
Inappropriate therapy, n (%)	4 (3.2%)	19 (4.4%)	0.566
<i>resulted in ATP therapy alone</i>	3 (75%)	16 (84%)	0.659
<i>resulted in ATP + shock therapy</i>	1 (25%)	3 (16%)	
Appropriate therapy, n (%)	19 (15.3%)	56 (12.9%)	0.492
	Single-chamber vs. Dual-chamber	95% CI	p-value
Inappropriate therapy	HR (univariate) 1.165	0.393-3.448	0.783
<i>resulted in ATP therapy alone</i>	HR (multivariate) ^a 1.152	0.387-3.433	0.799
<i>resulted in ATP + shock therapy</i>	HR (univariate) 1.264	0.365-4.377	0.712
	HR (univariate) 0.871	0.091-8.372	0.905
Appropriate therapy	HR (univariate) 0.724	0.428-1.224	0.228
	HR (multivariate) ^b 0.699	0.389-1.257	0.232
All-cause mortality	HR (univariate) 0.930	0.598-1.448	0.749
	HR (multivariate) ^c 0.714	0.426-1.197	0.201
	Single-chamber MorphMatch ON vs. Dual-chamber		
Inappropriate therapy	HR (univariate) 1.809	0.241-13.577	0.564
	HR (multivariate) ^d 1.571	0.208-11.851	0.661
	Dual-chamber VDD vs. Dual-chamber DDD		
Inappropriate therapy	HR (univariate) 0.586	0.230-1.490	0.262
	HR (multivariate) ^e 0.597	0.226-1.579	0.299

a) Available for 553 patients, b) Available for 509 patients, c) Available for 467 patients, d) Available for 476 patients, e) Available for 423 patients.

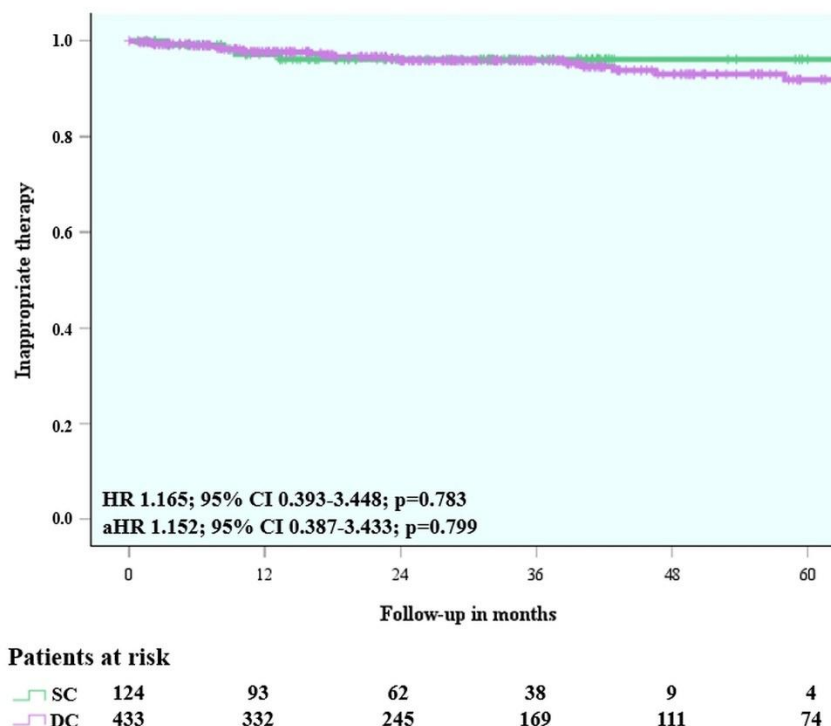


Figure 10. Time to first inappropriate therapy – single-chamber vs. dual-chamber.

Moreover, we detected no difference in the risk of inappropriate therapies in the predefined sensitivity analysis comparing the SC algorithm with activated morphology discrimination to the DC algorithm (HR 1.809; 95% CI 0.241–13.577; $p=0.564$; adjusted HR 1.571; 95% CI 0.208–11.851; $p=0.661$)(Table 11, Figure 11, Supplementary Table 19). The reasons of inappropriate therapy delivery are described in Table 12. All delivered inappropriate therapies were associated with high-frequency supraventricular arrhythmias. In the DC group, the most common underlying mechanisms were atrial undersensing and misclassification by sudden onset discriminator (as part of SMART algorithm). In the SC group, 75% of inappropriate therapies occurred without the application of morphology discrimination. In the predefined subgroup analysis, no difference was observed in the risk of inappropriate therapies between patients with VDD devices and those with DDD devices, both utilizing DC discrimination (HR 0.586; 95% CI 0.230–1.490; $p=0.262$; adjusted HR 0.597; 95% CI 0.226–1.579; $p=0.299$)(Table 11, Supplementary Table 20, Supplementary Figure 5).

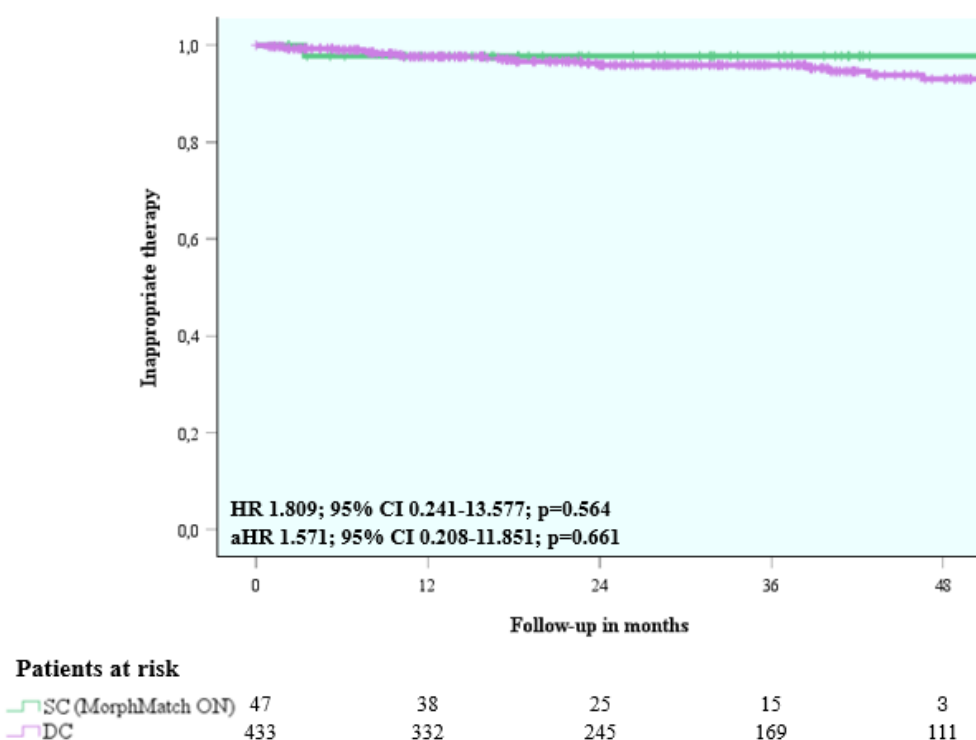


Figure 11. Time to first inappropriate therapy – single-chamber (MorphMatch ON) vs. dual-chamber

Table 12. Specific causes of inappropriate therapy delivery by the programmed discrimination algorithms

	Single-chamber (N=124)	Dual-chamber (N=433)
Underlying arrhythmia, n		
<i>Atrial fibrillation or atrial flutter</i>	3	5
<i>Sinus tachycardia or PSVT</i>	1	14
Underlying mechanism, n		
<i>Atrial undersensing</i>	-	10
<i>Atrial blanking causing misdetection of atrial rate by the SMART algorithm</i>	-	2
<i>1:1 SVT, but the SMART algorithm identifies VT due to sudden onset</i>	-	6
<i>Sinus tachycardia, but SC discrimination identifies VT due to sudden onset (MorphMatch algorithm was not available)</i>	1	-
<i>Atrial fibrillation, but both stability and sudden onset identified VT (MorphMatch algorithm was not available)</i>	2	-
<i>Other</i>	1	1

4.2.3.2. Appropriate therapies

The rate of appropriate therapies was also comparable between the SC and DC discrimination groups (15.3% (0.07% per patient-year) vs. 12.9% (0.04% per patient-year))(HR 0.724; 95% CI 0.428–1.224; p=0.228; adjusted HR 0.699; 95% CI 0.389–1.257; p=0.232)(Table 11, Supplementary Table 21, Supplementary Figure 6).

4.2.3.3. All-cause mortality

All-cause mortality also did not differ among the SC and DC discriminator groups (21.6% (0.09% per patient-year) vs. 26.6% (0.09% per patient-year))(HR 0.930; 95% CI 0.598–1.448; p=0.749; adjusted HR 0.714; 95% CI 0.426–1.197; p=0.201)(Table 11, Supplementary Table 22, Supplementary Figure 7).

5. DISCUSSION

The aim of this thesis was to evaluate the efficacy of tachyarrhythmia detection and discrimination capacity of modern ICDs. Our work focused on two primary objectives. First, we aimed to assess the performance of VDD ICDs in tachyarrhythmia detection and discrimination, with an emphasis in their role in atrial tachyarrhythmia detection. Second, we sought to compare the efficacy of single-chamber vs. dual-chamber discrimination algorithms in malignant tachyarrhythmia detection by performing a head-to-head comparison of devices from a single-manufacturer, remotely followed-up via the Home Monitoring system.

5.1. Arrhythmia detection and discrimination efficacy of VDD ICDs

5.1.1. Main findings

We conducted a retrospective, single-center study to evaluate arrhythmia detection and discrimination capacity of VDD ICD (DX) systems, comparing these devices with conventional VVI and DDD ICDs. Our results demonstrated the superiority of VDD systems in the detection of novel atrial arrhythmias compared to VVI ICDs. Additionally, DX systems were non-inferior compared to DDD devices concerning this outcome. Evaluation of atrial sensing values indicated that VDD ICDs provided higher atrial sensing amplitude compared to DDD devices. As expected, the risk of complications was highest in the DDD ICD group. Regarding long-term clinical outcomes, arrhythmia-related hospitalizations were more frequently observed in the VDD group than in the VVI group, including elective admissions aiming rhythm control therapy of atrial fibrillation (e.g. ECV or catheter ablation). The risk of heart failure-related hospitalization and all-cause mortality did not differ among the three groups.

5.1.2. Atrial arrhythmia detection

Beyond the detection and treatment of malignant arrhythmias, modern ICDs play a significant role in the detection of supraventricular arrhythmias [2, 20]. As VVI ICDs access ventricular signals, supraventricular arrhythmias are only recorded if the ventricular frequency of the conducted supraventricular arrhythmia exceeds the present ventricular tachyarrhythmia limit. Consequently, only episodes with relatively high ventricular frequency are registered [3]. In contrast, DDD ICDs with an additional atrial lead can detect episodes with high atrial frequency (AHREs) [11, 24]. This allows differentiation among various atrial arrhythmias, facilitating early therapy optimization and timely consideration of invasive interventions such as catheter ablation, especially in atrial fibrillation or atrial flutter [11, 20, 24]. Moreover, with the constant

monitoring of atrial frequency even the burden of atrial fibrillation can be closely assessed [24]. However, the implantation of an extra atrial lead lengthens the procedural duration and may increase the risk of complications [13, 18, 19, 39]. To mitigate the possible disadvantages of an extra lead implantation, VDD ICD leads were developed, integrating a specialized atrial sensing dipole into a single ventricular lead to ensure reliable atrial sensing [13].

To compare the efficacy of VDD ICDs to conventional ICD configurations in a real word cohort, we retrospectively analysed data of ICD recipients from our tertiary cardiology center. Based on our results, VDD ICDs proved to be more effective in detection of novel atrial arrhythmia compared to VVI devices and demonstrated non-inferiority to DDD ICDs. Our results are in line with the finding of SENSE and THINGS trial. SENSE and THINGS trials were the first prospective, multicenter studies assessing the feasibility of VDD devices, revealing superiority to VVI ICDs in atrial arrhythmia detection [11, 12]. SENSE trial also confirmed non-inferiority in AHRE detection to conventional DDD devices [11]. The results of these trials were also involved in a recent metanalysis revealing similar results [19]. The study of Hindricks et al. evaluated AHRE detection of VDD systems supplemented by remote monitoring, and showed reliable atrial arrhythmia detection, which can be suitable for guideline defined subclinical atrial fibrillation assessment [24]. The aforementioned studies described reliable atrial sensing in the long run, however, to the best of our knowledge, our study was the first to demonstrate superior atrial sensing in VDD ICDs compared to DDD ICDs [11, 12, 24]. Furthermore, given the ability of DX systems to precisely detect novel atrial fibrillation episodes, a recent, nationwide, prospective Hungarian survey revealed an elevated risk of stroke as most important influencing factor to select a VDD ICD implantation instead of a conventional VVI or DDD ICD systems [40].

Despite the previous findings, the first prospective, multicenter, randomized-controlled trial (Dx-AF study) only described a borderline superiority regarding atrial arrhythmia detection in DX systems compared to conventional VVI devices. Although the Dx-AF trial recorded no significant difference in the efficacy of atrial fibrillation (or flutter) detection compering VDD and VVI systems (evaluating arrhythmia detection by device, ECG or ECG monitoring), analysing exclusively the device-detected episodes, a borderline significance was described favouring VDD systems [26]. However, it should be emphasized, that the minimal AHRE duration limit varied among the aforementioned studies. While the Dx-AF trial has a stricter minimum AHRE detection limit of 6 minutes, SENSE and THINGS studies accepted shorter intervals [11, 12, 26]. Similarly, the minimal duration of AHRE was also shorter in our study,

defining a minimal AHRE detection limit of 1 minute. Notably, since the publication of the ASSERT study, the traditional threshold for AHRE detection has been set at 6 minutes. However, shorter atrial arrhythmia episodes should not be underestimated, as Steinberg et al. demonstrated that episodes of shorter duration can also be associated with thromboembolic events [41, 42].

5.1.3. Clinical importance of device-detected atrial fibrillation – clinical aspects of anticoagulation

Atrial fibrillation is a prevalent condition with an increased risk of thromboembolism, accompanied by increased mortality and a greater likelihood of developing dementia, heart failure and impaired quality of life [20]. Early and appropriate anticoagulation therapy offers a significant benefit in reducing the risk of thromboembolic events, and it should be initiated as promptly as possible in patients with elevated stroke risk [20]. The detection of AHREs enables identification of subclinical atrial fibrillation (and flutter), facilitating early initiation of oral anticoagulation [20].

First the ASSERT study evaluated the relationship between asymptomatic, device-detected atrial fibrillation and thromboembolic risk. The results revealed a higher risk of ischemic stroke or systemic embolism in patients with device-detected atrial fibrillation compared to those without such episodes (HR 2.49; 95% CI 1.28-4.85; $p=0.007$) [41]. The feasibility of oral anticoagulant therapy initiated by device-detected AHRE episodes have been recently investigated: the NOAH-AFNET and ARTESiA trials evaluated whether the use of direct oral anticoagulants could reduce the risk of stroke or systemic embolism in patients with AHREs compared to the control group (placebo or aspirin) [21, 23]. Although, the ARTESiA study demonstrated a reduction in stroke and systemic embolism with apixaban, the NOAH-AFNET trial (applying edoxaban) did not find a difference in the primary composite endpoint of cardiovascular death, stroke, or embolic events, including systemic embolism, myocardial infarction, and pulmonary embolism in comparison with the control group. The combined results of these trials were also assessed in a meta-analysis, which revealed a consistent reduction in stroke and systemic embolism (35%) with edoxaban or apixaban compared to control/aspirin, however the risk of major bleeding events consistently increased [21-23, 43]. The latest ESC guidelines on atrial fibrillation management recommends that direct oral anticoagulant (DOAC) therapy may be considered in subgroups of patients with asymptomatic device-detected subclinical atrial fibrillation who have high estimated stroke risk and absence of major bleeding risk factors [20]. In light of these findings, shared decision-making and close

follow-up are emphasized for this patient population, with careful assessment and periodic re-evaluation of thromboembolic risk factors.

5.1.4. Long-term clinical outcomes

No difference was observed in heart-failure related hospitalizations and all-cause mortality among the three groups. Notably, the risk of arrhythmia-related hospitalization was significantly higher in the VDD group in comparison with the VVI group, with rates comparable between the VDD and DDD groups. Although arrhythmia related-hospitalization encompassed a broad spectrum of arrhythmic events in our analysis, the higher proportion of elective admission aiming rhythm control therapy of atrial arrhythmias should be highlighted in the VDD and DDD groups. As VDD devices were more efficient in atrial arrhythmia detection (compared to conventional VVI devices), the number of referrals for procedures like ECV or ablation was correspondingly higher, underscoring the clinical relevance of accurate AHRE detection in managing atrial arrhythmias.

5.1.5. Tachyarrhythmia discrimination – VDD vs. conventional ICD configurations

Our results revealed no difference in the risk of inappropriate therapies comparing VDD ICDs to VVI and DDD devices. The risk of appropriate ICD therapies was also comparable among the groups. The unique feature of VDD systems is that they enable the programming of SC or DC discrimination algorithms using only a single lead [2, 13]. While the superiority of SC versus DC discrimination remains a topic of debate with controversial and limited results, the ability to switch between these algorithms should not be underestimated, as certain scenarios – such as programming after inappropriate therapy delivery in certain cases – can be addressed through this flexibility [2, 13]. Notably, the second objective of the present thesis evaluates the efficacy of SC vs. DC discrimination in Biotronik devices. Moreover, the current guidelines do not recommend the implantation of an additional atrial lead solely to improve tachycardia discrimination, because of the elevated risk of infectious, perioperative and long-term complications of dual-lead implantations [30]. The efficacy of DC discrimination programming in VDD devices has been recently evaluated by Biffi et al. by comparing patients with conventional VVI devices (and consequently with SC discrimination algorithms)(n=343) and patients with VDD devices (programmed to DC algorithms)(n=183). In a propensity score-matched comparison, there was no difference in the risk of inappropriate therapies between SC and DC discrimination algorithms (1-year incidence 1.8% vs. 3.5%; p=0.105) [8]. For note, in our second objective – assessing tachyarrhythmia discrimination efficacy of SC vs. DC

discriminators – we performed a subgroup analysis comparing VDD and DDD ICDs with DC programming, which also revealed no significant difference in the risk of inappropriate therapies.

5.2. Tachycardia discrimination efficacy of SC vs. DC discriminators

5.2.1. Main findings

In our retrospective, bicentric study, we performed a head-to-head comparison of SC and DC discrimination algorithms to evaluate their efficacy in malignant tachyarrhythmia detection. We analysed remote monitoring data involving devices exclusively from a single manufacturer (i.e. Biotronik). Our findings revealed no significant difference in the performance of SC vs. DC discrimination algorithms, with comparable risk of both inappropriate and appropriate therapies. Additionally, we also conducted a sensitivity analysis focusing solely on patients with active morphology discrimination within the SC group and compared them with the DC discrimination group. The sensitivity analysis demonstrated no difference in the risk of inappropriate therapy between the groups. Based on our findings, SC discrimination algorithms can be a viable alternative even in patients with DC devices.

5.2.2. Tachyarrhythmia discrimination – SC vs. DC discriminators

Although the fundamental components of tachyarrhythmia discrimination are similar across the different manufacturers, notable differences exist between their tachycardia discrimination algorithms with manufacturer-specific features [2, 3, 5, 7]. While modern Biotronik devices apply morphology-based differentiation only in SC discrimination (and not in SMART algorithm), other manufacturers (e.g. Medtronic (Minneapolis, USA), Abbott (Chicago, USA), Boston Scientific (Marlborough, USA)) incorporate morphology-based discrimination within their DC algorithms [7, 27-29]. Given these manufacturer-specific differences, the role of single manufacturer studies should be highlighted, as reprogramming of tachyarrhythmia discrimination settings is possible during the follow-up and even switching between SC and DC algorithms is feasible [13]. Furthermore, it is essential for clinicians to have scientific evidence to guide their choice among the available programming options.

Most prior studies, which involved Biotronik ICDs and assessed the efficacy of SC vs. DC algorithms involved devices from other manufacturers as well [35, 44, 45]. Furthermore, many of these studies used older device models with outdated discrimination algorithms. The latest meta-analysis regarding tachyarrhythmia discrimination was conducted nearly 20 years ago and

its findings revealed similar risk of inappropriate therapies between SC and DC devices ($p=0.31$) in a per-patient based analysis. However, per-episode based analysis demonstrated a benefit for DC discrimination algorithms ($p<0.001$) [35].

Tachyarrhythmia discrimination algorithms are under constant development and expert opinion suggests that modern SC discrimination algorithms with morphology-based differentiation could be equally effective as DC discriminators [6, 38, 46]. Moreover, the recently published and previously mentioned study by Biffi et al. demonstrated no difference in tachyarrhythmia discrimination between SC and DC discriminators (HR 0.81; 95% CI 0.38-1.72; $p=0.586$). In this study the DC discrimination group consisted only of VDD ICDs (Biotronik), but the SC group included devices from Medtronic, Boston Scientific and Abbott, with active morphology discrimination in most of the cases [8]. The morphology-based differentiation algorithm of Biotronik devices (MorphMatch algorithm) was developed in the 2010s. For note, the recent expert consensus statement on ICD programming recommends the programming of MorphMatch without stability and sudden onset in SC, and SMART algorithm in DC Biotronik devices [30].

5.2.3. Common reasons of inappropriate therapy delivery in our study

In our cohort, all inappropriate therapy delivery were associated with supraventricular arrhythmias. Most inadequate therapies occurred because of supraventricular arrhythmias with 1:1 AV ratio (e.g. sinus tachycardia, paroxysmal supraventricular arrhythmia or atrial ectopic rhythms). The second most common underlying arrhythmia was high-frequency atrial fibrillation (and atrial flutter). Interestingly, the underlying mechanism differed among the cases.

5.2.3.1. Dual-chamber discrimination

Programming SMART detection, the primary causes of inappropriate therapy included atrial undersensing, misclassification due to sudden onset, and atrial blanking. The first step of tachyarrhythmia discrimination in SMART algorithm is frequency comparison of atrial and ventricular rates. If ventricular rate exceeds the atrial frequency, the algorithm “diagnoses” ventricular tachycardia [2, 7]. Atrial undersensing can lead to underestimation of the atrial rate, resulting in a false assessment where the ventricular rate appears higher than the atrial rate, prompting therapy delivery. Although atrial undersensing is often linked to lead malfunction or dislocation, atrial fibrillation can cause intermittent low-amplitude signals by its nature, which may lead to atrial undersensing without any lead-related issues.

In our study, we observed atrial undersensing during episodes of atrial fibrillation (Figure 12A), as well as during sinus tachycardia (Figure 12B). For note, the measured sensing values at Home Monitoring registration were sufficiently high.

Atrial blanking can similarly result in inappropriate therapy by ignoring atrial signals within the blanking period during far-field protection. If atrial signals occur within this period, they are excluded from tachyarrhythmia discrimination, leading to an underestimated atrial rate and a false diagnosis of ventricular tachycardia based on the “higher ventricular than atrial frequency” criterion (Figure 12C). In Biotronik ICDs, the far-field protection mechanism triggers an atrial blanking period around each ventricular sensed event. The blanking lasts for a fixed value of 16 ms before each ventricular sensed event and the total blanking duration is programmable (the default value is 75 ms) [7, 34].

Lastly, in cases of tachyarrhythmias with 1:1 AV ratio and equal and stable PP and RR intervals, as well as regular AV times, the SMART algorithm applies the sudden onset discriminator to differentiate between tachyarrhythmias. While sudden onset indicates ventricular tachycardia, gradual onset is rather typical for sinus tachycardia [2, 7]. However, PSVT episodes or ectopic atrial rhythms can also meet these criteria and mimic VT due to sudden onset causing inappropriate VT detection (Figure 12D).

In such scenarios as those described above, the use of SC discrimination may offer a practical alternative, as it diminishes issues related to incorrect atrial detection (such as atrial undersensing or atrial blanking) by relying exclusively on ventricular signals supported by morphology-based algorithms.

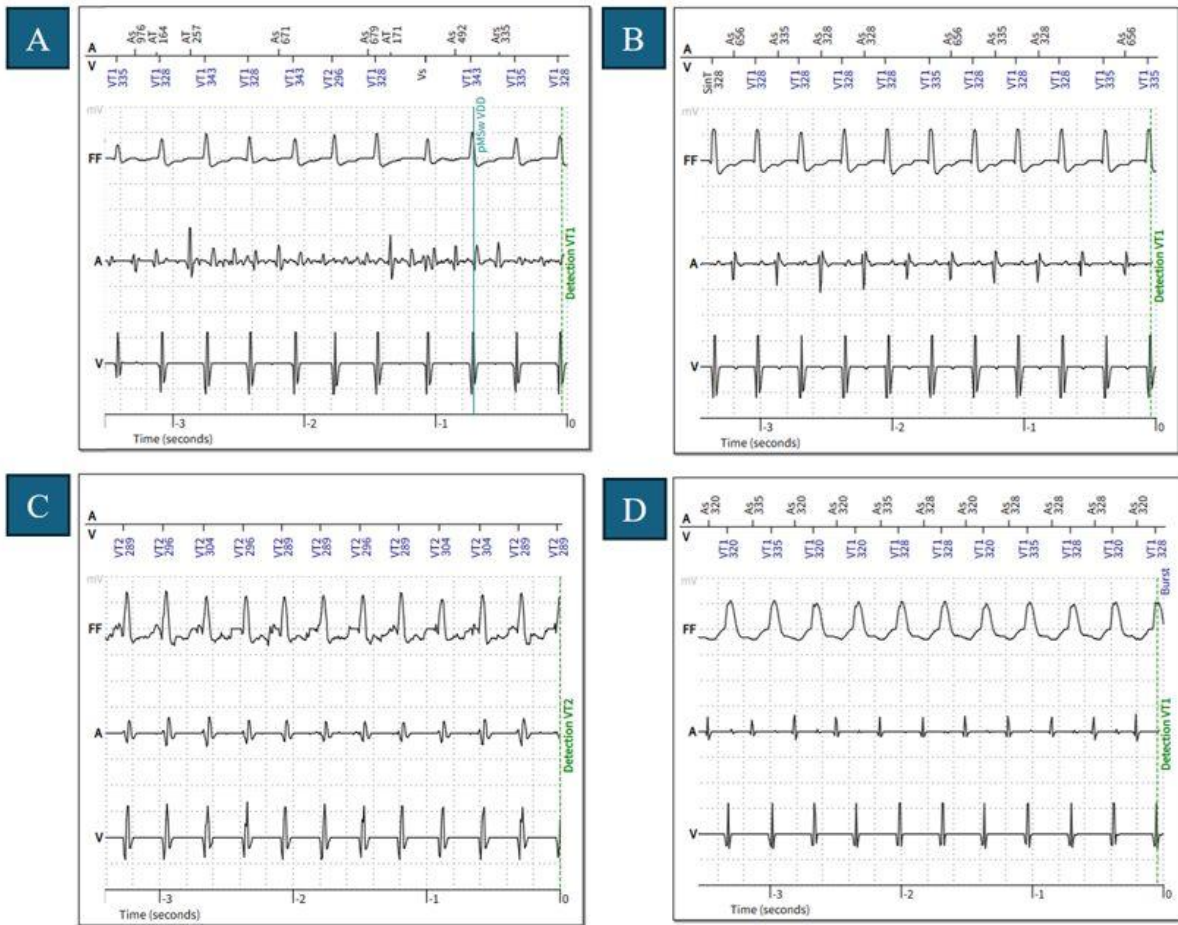


Figure 12. Main reasons leading to inappropriate detection in cases of dual-chamber discrimination: **(A)** intermittent atrial undersensing during atrial fibrillation (last measured RA sensing value: 3.2 mV; device type: Iforia 5 VR-T DX); **(B)** intermittent atrial undersensing during sinus tachycardia (last measured RA sensing value: 3.2 mV; device type: Iforia 5 VR-T DX); and **(C)** inappropriate VT detection due to blanking of the atrial signals (last measured RA sensing value: 2.8 mV; device type: Itreivia 5 VR-T DX). **(D)** 1:1 SVT with stable RR and PP intervals. The sudden onset criterium was fulfilled leading to inappropriate VT detection (last measured RA sensing value: 2.4 mV; device type: Lumax 640 DR-T). All the cases resulted in inappropriate therapy delivery.

5.2.3.2. Single-chamber discrimination

We observed that most of the inappropriate therapies in the SC group occurred when morphology-based discrimination was not programmed, and the classification of tachycardia episodes relied solely on sudden onset and/or stability criteria. However, it should be noted, that also the morphology-based discrimination can be tricked in certain scenarios. As the reference morphology template is recorded in “tachyarrhythmia-free” periods, SVTs with

aberrant conduction or frequency dependent bundle branch block can mislead the algorithm, as the wide QRS complex of the tachyarrhythmia is compared to the narrow reference QRS. Moreover, in Biotronik devices stable morphology templates cannot be obtained in complete AV block or during biventricular pacing [2, 7, 34].

5.2.3. Recommendations for discrimination programming of dual-chamber devices

Based on the available literature data supplemented with our findings, it is demonstrated that neither SC nor DC algorithms are capable of achieving 100% success in appropriate detection with the recently available discrimination methods, so an evidence-based approach that considers individual patient aspects may be the most reasonable strategy. To support this, we developed a programming recommendation for tachyarrhythmia discrimination settings in Biotronik devices, as described in Figure 13. Programming SC discrimination with active morphology analysis appears to be a preferable approach when prior DC discrimination led to inappropriate therapy due to issues such as atrial undersensing or incorrect interpretation of SVTs with the decision-tree of SMART algorithm. Additionally, SC discrimination with active morphology analysis may serve as a suitable first-line option for patients with known SVTs, such as atrial fibrillation, atrial flutter, PSVT or atrial ectopic rhythm. Conversely, DC discrimination should still be preferred in patients with rate-dependent bundle branch block or previously documented SVT with aberrant conduction. Finally, SC discrimination is not recommended for patients in whom stable morphology templates cannot be established, such as those with complete AV block or biventricular pacing.

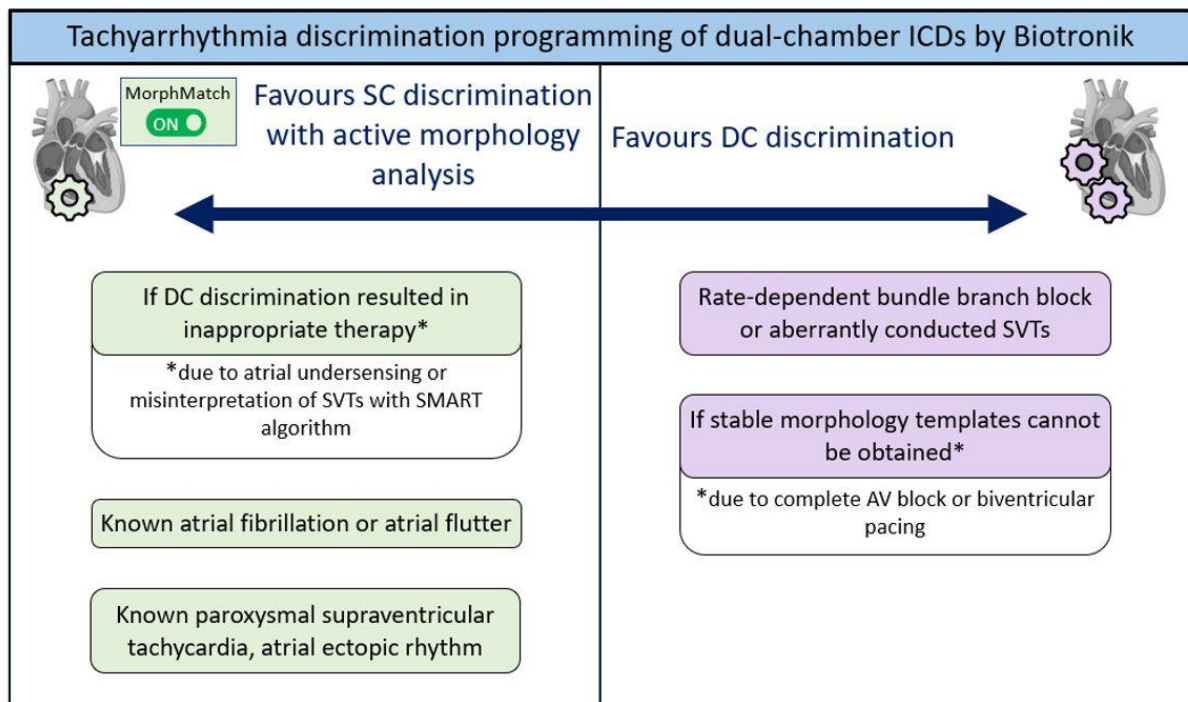


Figure 13. Recommendations for tachyarrhythmia discrimination programming of dual-chamber devices (i.e., VDD or DDD ICDs) by Biotronik.

5.3. Limitations

Our data collection was retrospective for both objectives; therefore, all potential limitations of such a design apply to these analyses.

9. CONCLUSIONS

1. VDD ICD systems demonstrated superior atrial arrhythmia detection compared to conventional VVI devices and achieved comparable efficacy to conventional DDD devices.
2. To the best of our knowledge, this study was the first to show significantly higher atrial sensing values in DX systems compared to DDD devices.
3. The tachyarrhythmia discrimination performance of VDD devices was comparable to that of traditional VVI and DDD systems.
4. Our results indicate that the primary advantage of VDD systems lies in their enhanced atrial arrhythmia detection, facilitated by the integrated sensing dipole. These devices enable reliable atrial sensing through a single-lead implantation, thereby reducing complication rates relative to DDD systems.
5. Our head-to-head comparison of SC vs. DC discrimination algorithms revealed similar efficacy in malignant tachyarrhythmia detection. To the best of our knowledge, this was the first study to perform a direct comparison of discrimination algorithms in Biotronik devices.
6. Based on our findings, SC discrimination – particularly when morphology-based algorithm is available – constitute a viable and effective alternative even for patients with dual-chamber devices.
7. Based on results, we developed a programming recommendation for tachyarrhythmia discrimination in dual-chamber Biotronik devices.

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12. SUPPLEMENTARY MATERIAL

Supplementary Table 1. Included predictors in the multivariate models

Arrhythmia detection and discrimination efficacy of VDD ICDs	
Parameters evaluated with time-to-event analysis	Predictor variables included in the multivariate models
Time to first device detected atrial arrhythmia Time to first appropriate therapy Time to first inappropriate therapy Time to first hospitalization due to arrhythmic cause Time to first HF hospitalization All-cause mortality	ICD type; Age; Male; Primer prophylaxis; Ischemic etiology; Previously diagnosed atrial fibrillation; Hypertonia; Dyslipidaemia; Diabetes mellitus; Stroke/TIA; Bradypacing indication; EF; QRS width; Heart rate; Creatinine; Hemoglobin; Remote monitoring; Antiplatelet therapy; Anticoagulation; Beta-blocker; ACEI/ARB/ARNI; Diuretics; Calcium channel blockers; Mineralocorticoid receptor antagonists; Statin; Amiodarone; Digitalis
Tachycardia discrimination efficacy of SC vs. DC discriminators – Primer analysis	
Parameters evaluated with time-to-event analysis	Predictor variables included in the multivariate models
Inappropriate therapy Appropriate therapy All-cause mortality	Discrimination algorithm; Age at implantation; Male; Secondary prophylaxis; Ischemic etiology; Previously diagnosed atrial fibrillation/atrial flutter; Hypertension; Diabetes mellitus; Stroke/TIA; Bradypacing indication; LVEF; Heart rate; Creatinine; eGFR; Hemoglobin; Antiplatelets; Anticoagulation; Beta-blocker; RAAS; Diuretics; MRA; Digitalis; CCB; Amiodaron; Statins; SGLT2-inhibitors
Tachycardia discrimination efficacy of SC vs. DC discriminators – Sensitivity analysis	
Parameters evaluated with time-to-event analysis	Predictor variables included in the multivariate models
Inappropriate therapy	Discrimination algorithm; Age at implantation; Male; Secondary prophylaxis; Ischemic etiology; Previously diagnosed atrial fibrillation/atrial flutter; Hypertension; Diabetes mellitus; Stroke/TIA; Bradypacing indication; LVEF; Heart rate; Creatinine; eGFR; Hemoglobin; Antiplatelets; Anticoagulation; Beta-blocker; RAAS; Diuretics; MRA; Digitalis; CCB; Amiodaron; Statins; SGLT2-inhibitors
Tachycardia discrimination efficacy of SC vs. DC discriminators – Subgroup analysis	
Parameters evaluated with time-to-event analysis	Predictor variables included in the multivariate models
Inappropriate therapy	ICD type (VDD or DDD); Age at implantation; Male; Secondary prophylaxis; Ischemic etiology; Previously diagnosed atrial fibrillation/atrial flutter; Hypertension; Diabetes mellitus; Stroke/TIA; Bradypacing indication; LVEF; Heart rate; Creatinine; eGFR; Hemoglobin; Antiplatelets; Anticoagulation; Beta-blocker; RAAS; Diuretics; MRA; Digitalis; CCB; Amiodaron; Statins; SGLT2-inhibitors

Supplementary Table 2. Overall baseline characteristics

	All patients (N=256)
Age (mean±SD)	64±12
Male, n (%)	191 (75%)
Primary prophylaxis, n (%)	72 (28%)
Ischemic etiology, n (%) ^a	155 (61%)
Previously diagnosed atrial fibrillation, n (%) ^a	87 (34%)
EF (mean±SD) ^b	40.5±14.9
Follow-up time (mean±SD)	3.7±2.4

a) Available for 255 patients. b) Available for 249 patients.

Supplementary Table 3. Subgroup analysis of baseline characteristics

	VVI (N=93)	VDD (N=94)	p-value
Dyslipidaemia, n (%)	79 (85%)	85 (90%)	0.254
EF (mean±SD)	38.5±13.5	37.5±13.9	0.642
QRS width (mean±SD)	116.9±21.2	119±21.6	0.909
HR (mean±SD)	70.7±15.4	73.1±14.8	0.249
Bradypacing indication, n (%)	1 (1%)	3 (3%)	0.317
Hemoglobin (mean±SD)	130.7±20.6	136±16.8	0.062
Remote monitoring, n (%)	6 (7%)	48 (51%)	<0.001
	VVI (N=93)	DDD (N=69)	p-value
Dyslipidaemia, n (%)	79 (85%)	48 (71%)	0.027
EF (mean±SD)	38.5±13.5	47.5±16.3	<0.001
QRS width (mean±SD)	116.9±21.2	136.9±29.2	<0.001
HR (mean±SD)	70.7±15.4	66.9±18.6	0.117
Bradypacing indication, n (%)	1 (1%)	36 (55%)	<0.001
Hemoglobin (mean±SD)	130.7±20.6	126.2±20.7	0.237
Remote monitoring, n (%)	6 (7%)	13 (19%)	0.014
	VDD (N=94)	DDD (N=69)	p-value
Dyslipidaemia, n (%)	85 (90%)	48 (71%)	0.001
EF (mean±SD)	37.5±13.9	47.5±16.3	0.001
QRS width (mean±SD)	119±21.6	136.9±29.2	0.001
HR (mean±SD)	73.1±14.8	66.9±18.6	0.011
Bradypacing indication, n (%)	3 (3%)	36 (55%)	<0.001
Hemoglobin (mean±SD)	136±16.8	126.2±20.7	0.008
Remote monitoring, n (%)	48 (51%)	13 (19%)	<0.001

Supplementary Table 4. Subgroup analysis of baseline medical therapy

	VVI (N=93)	VDD (N=94)	p-value
Beta-blocker, n (%)	90 (97%)	90 (96%)	0.711
Mineralocorticoid receptor antagonists, n (%)	48 (52%)	52 (55%)	0.611
Digitalis, n (%)	13 (14%)	3 (3%)	0.008
	VVI (N=93)	DDD (N=69)	p-value
Beta-blocker, n (%)	90 (97%)	53 (83%)	0.003
Mineralocorticoid receptor antagonists, n (%)	48 (52%)	17 (27%)	0.002
Digitalis, n (%)	13 (14%)	3 (5%)	0.059
	VDD (N=94)	DDD (N=69)	p-value
Beta-blocker, n (%)	90 (96%)	53 (83%)	0.006
Mineralocorticoid receptor antagonists, n (%)	52 (55%)	17 (27%)	<0.001
Digitalis, n (%)	3 (3%)	3 (5%)	0.629

Supplementary Table 5. Multivariate analysis of time to first detected atrial arrhythmia **VVI** vs **VDD**

Risk factor	unadjusted HR (95% CI)	p-value	adjusted HR (95% CI)	p-value
ICD type	6.506 (2.176-19.446)	0.001	7.087 (2.371-21.183)	<0.001
Age	1.004 (0.969-1.040)	0.837		
Male	0.540 (0.226-1.291)	0.166		
Primer prophylaxis	6.989 (0.940-51.970)	0.058	9.746 (1.301-73.014)	0.027
Ischemic etiology	1.561 (0.609-4.002)	0.354		
Previously diagnosed atrial fibrillation	1.916 (0.743-4.942)	0.179		
Hypertonia	2.280 (0.303-17.126)	0.423		
Dyslipidaemia	4.127 (0.554-30.776)	0.167		
Diabetes mellitus	1.456 (0.609-3.478)	0.398		
Stroke/TIA	0.043 (0.000-28.860)	0.343		
Bradypacing indication	7.895 (0.994-62.697)	0.051	18.471 (1.973-172.887)	0.011
EF	0.981 (0.947-1.015)	0.270		
QRS width	1.009 (0.986-1.033)	0.442		
Heart rate	1.033 (1.001-1.066)	0.042	1.038 (1.004-1.074)	0.028
Creatinine	1.003 (0.996-1.009)	0.473		
Hemoglobin	1.003 (0.978-1.029)	0.809		
Remote monitoring	2.628 (1.133-6.093)	0.024	0.907 (0.347-2.368)	0.841
Antiplatelet therapy	1.013 (0.412-2.489)	0.977		
Anticoagulation	1.609 (0.686-3.770)	0.274		
Beta-blocker	0.682 (0.092-5.075)	0.709		
ACEI/ARB/ARNI	0.550 (0.186-1.627)	0.280		
Diuretics	1.564 (0.668-3.661)	0.303		
Calcium channel blockers	0.884 (0.299-2.616)	0.824		
Mineralocorticoid receptor antagonists	1.020 (0.441-2.358)	0.963		
Statin	1.057 (0.412-2.709)	0.909		
Amiodarone	1.285 (0.474-3.483)	0.623		
Digitalis	0.045 (0.000-116.944)	0.440		

Supplementary Table 6. Multivariate analysis of time to first detected atrial arrhythmia VDD vs DDD

Risk factor	unadjusted HR (95% CI)	p-value	adjusted HR (95% CI)	p-value
ICD type	2.011 (1.110-3.642)	0.021	1.781 (0.737-4.301)	0.200
Age	1.038 (1.012-1.066)	0.004	0.992 (0.959-1.026)	0.645
Male	0.731 (0.384-1.390)	0.339		
Primer prophylaxis	1.951 (0.941-4.044)	0.072	1.001 (0.379-2.643)	0.998
Ischemic etiology	1.522 (0.816-2.838)	0.187		
Previously diagnosed atrial fibrillation	3.822 (2.085-7.005)	<0.001	4.300 (1.687-10.959)	0.002
Hypertonia	3.185 (0.765-13.260)	0.111		
Dyslipidaemia	1.334 (0.617-2.881)	0.464		
Diabetes mellitus	1.344 (0.735-2.458)	0.337		
Stroke/TIA	0.451 (0.109-1.867)	0.272		
Bradypacing indication	2.195 (1.207-3.992)	0.010	0.749 (0.216-2.601)	0.649
EF	0.999 (0.981-1.018)	0.950		
QRS width	1.013 (0.999-1.026)	0.065	0.998 (0.979-1.017)	0.833
Heart rate	1.019 (0.998-1.041)	0.075	1.008 (0.974-1.043)	0.668
Creatinine	1.002 (0.997-1.007)	0.470		
Hemoglobin	0.995 (0.977-1.013)	0.582		
Remote monitoring	0.388 (0.200-0.751)	0.005	0.323 (0.123-0.852)	0.022
Antiplatelet therapy	1.139 (0.609-2.131)	0.684		
Anticoagulation	2.723 (1.506-4.924)	0.001	0.746 (0.295-1.883)	0.535
Beta-blocker	1.685 (0.520-5.456)	0.384		
ACEI/ARB/ARNI	1.043 (0.482-2.255)	0.915		
Diuretics	1.731 (0.953-3.147)	0.072	4.105 (1.610-10.462)	0.003
Calcium channel blockers	1.043 (0.527-2.066)	0.903		
Mineralocorticoid receptor antagonists	0.752 (0.403-1.405)	0.371		
Statin	1.245 (0.638-2.431)	0.520		
Amiodarone	1.901 (0.930-3.886)	0.078	1.178 (0.403-3.447)	0.765
Digitalis	3.043 (0.731-12.672)	0.126		

Supplementary Table 7. Detailed distribution of device detected atrial arrhythmias

	VVI (N=93)	VDD (N=94)	DDD (N=69)	p-value
Total number of first device detected atrial arrhythmias	4	18	28	0.609
<i>Paroxysmal atrial fibrillation, n (%)</i>	4 (100%)	15 (83%)	23 (82%)	
<i>Persistent atrial fibrillation, n (%)</i>	0 (0%)	2 (11%)	1 (4%)	
<i>Regular atrial arrhythmias, n (%)</i>	0 (0%)	1 (6%)	4 (14%)	

Supplementary Table 8. Multivariate analysis of time to first appropriate therapy VVI vs VDD

Risk factor	unadjusted HR (95% CI)	p-value	adjusted HR (95% CI)	p-value
ICD type	0.874 (0.574-1.332)	0.532	0.983 (0.641-1.508)	0.937
Age	1.023 (1.004-1.043)	0.019	1.019 (0.999-1.039)	0.057
Male	1.127 (0.691-1.838)	0.631		
Primer prophylaxis	2.760 (1.533-4.972)	0.001	2.204 (1.192-4.074)	0.012
Ischemic etiology	0.893 (0.586-1.359)	0.597		
Previously diagnosed atrial fibrillation	0.920 (0.577-1.469)	0.728		
Hypertonia	1.050 (0.483-2.281)	0.902		
Dyslipidaemia	1.275 (0.678-2.398)	0.450		
Diabetes mellitus	0.812 (0.512-1.287)	0.375		
Stroke/TIA	0.942 (0.455-1.950)	0.873		
Bradypacing indication	0.634 (0.088-4.562)	0.651		
EF	1.000 (0.985-1.014)	0.949		
QRS width	1.003 (0.991-1.014)	0.655		
Heart rate	0.993 (0.978-1.009)	0.376		
Creatinine	1.003 (0.998-1.008)	0.194		
Hemoglobin	1.000 (0.987-1.014)	0.950		
Remote monitoring	0.895 (0.565-1.419)	0.637		
Antiplatelet therapy	0.882 (0.577-1.349)	0.563		
Anticoagulation	0.827 (0.540-1.266)	0.381		
Beta-blocker	0.255 (0.103-0.636)	0.003	0.256 (0.101-0.648)	0.004
ACEI/ARB/ARNI	1.140 (0.572-2.271)	0.710		
Diuretics	1.172 (0.775-1.772)	0.452		
Calcium channel blockers	1.736 (1.088-2.770)	0.021	1.352 (0.837-2.184)	0.218
Mineralocorticoid receptor antagonists	0.975 (0.646-1.473)	0.906		
Statin	0.719 (0.464-1.114)	0.139		
Amiodarone	1.691 (1.051-2.721)	0.030	1.521 (0.926-2.498)	0.098
Digitalis	0.618 (0.270-1.416)	0.255		

Supplementary Table 9. Multivariate analysis of time to first appropriate therapy VDD vs DDD

Risk factor	unadjusted HR (95% CI)	p-value	adjusted HR (95% CI)	p-value
ICD type	0.611 (0.359-1.040)	0.069	0.651 (0.371-1.142)	0.135
Age	1.012 (0.991-1.033)	0.240		
Male	1.088 (0.597-1.983)	0.784		
Primer prophylaxis	3.488 (1.714-7.097)	<0.001	3.341 (1.564-7.138)	0.002
Ischemic etiology	1.330 (0.782-2.262)	0.293		
Previously diagnosed atrial fibrillation	0.954 (0.548-1.663)	0.869		
Hypertonia	1.353 (0.489-3.745)	0.560		
Dyslipidaemia	1.645 (0.779-3.473)	0.192		
Diabetes mellitus	0.785 (0.446-1.382)	0.401		
Stroke/TIA	0.641 (0.232-1.771)	0.391		
Bradypacing indication	0.523 (0.265-1.035)	0.063	0.721 (0.315-1.650)	0.439
EF	0.992 (0.976-1.008)	0.336		
QRS width	0.999 (0.987-1.011)	0.883		
Heart rate	0.993 (0.974-1.011)	0.438		
Creatinine	1.002 (0.996-1.008)	0.560		
Hemoglobin	1.002 (0.986-1.018)	0.822		
Remote monitoring	1.420 (0.850-2.371)	0.181		
Antiplatelet therapy	0.898 (0.529-1.526)	0.691		
Anticoagulation	1.269 (0.752-2.141)	0.371		
Beta-blocker	1.301 (0.470-3.603)	0.612		
ACEI/ARB/ARNI	0.971 (0.476-1.983)	0.936		
Diuretics	1.146 (0.681-1.927)	0.608		
Calcium channel blockers	1.483 (0.840-2.617)	0.174		
Mineralocorticoid receptor antagonists	0.962 (0.562-1.647)	0.888		
Statin	0.912 (0.521-1.594)	0.745		
Amiodarone	2.480 (1.374-4.479)	0.003	1.949 (1.073-3.540)	0.028
Digitalis	0.046 (0.000-11.224)	0.272		

Supplementary Table 10. Multivariate analysis of time to first inappropriate therapy VVI vs VDD

Risk factor	unadjusted HR (95% CI)	p-value	adjusted HR (95% CI)	p-value
ICD type	0.782 (0.338-1.811)	0.566	0.742 (0.313-1.757)	0.497
Age	0.994 (0.960-1.029)	0.729		
Male	0.613 (0.262-1.434)	0.259		
Primer prophylaxis	0.938 (0.372-2.365)	0.892		
Ischemic etiology	0.527 (0.236-1.178)	0.119		
Previously diagnosed atrial fibrillation	1.111 (0.459-2.689)	0.816		
Hypertonia	0.588 (0.173-1.996)	0.395		
Dyslipidaemia	0.332 (0.142-0.777)	0.011	0.533 (0.213-1.332)	0.178
Diabetes mellitus	0.592 (0.221-1.586)	0.297		
Stroke/TIA	0.043 (0.000-24.731)	0.332		
Bradypacing indication	0.048 (0.000-132902.528)	0.689		
EF	0.984 (0.952-1.016)	0.322		
QRS width	1.006 (0.982-1.031)	0.637		
Heart rate	1.007 (0.980-1.034)	0.628		
Creatinine	1.002 (0.996-1.009)	0.482		
Hemoglobin	1.011 (0.984-1.039)	0.430		
Remote monitoring	0.717 (0.284-1.808)	0.480		
Antiplatelet therapy	0.365 (0.161-0.824)	0.015	0.327 (0.142-0.753)	0.009
Anticoagulation	1.519 (0.677-3.410)	0.311		
Beta-blocker	0.240 (0.056-1.026)	0.054	0.167 (0.037-0.742)	0.019
ACEI/ARB/ARNI	0.406 (0.151-1.088)	0.073	0.667 (0.214-2.078)	0.485
Diuretics	1.419 (0.630-3.197)	0.398		
Calcium channel blockers	0.525 (0.156-1.761)	0.297		
Mineralocorticoid receptor antagonists	1.131 (0.506-2.530)	0.764		
Statin	0.464 (0.207-1.036)	0.061	1.158 (0.339-3.955)	0.815
Amiodarone	0.938 (0.321-2.747)	0.908		
Digitalis	1.602 (0.477-5.377)	0.446		

Supplementary Table 11. Multivariate analysis of time to first inappropriate therapy **VDD** vs **DDD**

Risk factor	unadjusted HR (95% CI)	p-value	adjusted HR (95% CI)	p-value
ICD type	0.710 (0.249-2.024)	0.522	0.618 (0.203-1.878)	0.396
Age	0.986 (0.955-1.019)	0.399		
Male	1.396 (0.397-4.907)	0.603		
Primer prophylaxis	1.927 (0.548-6.774)	0.307		
Ischemic etiology	0.483 (0.179-1.306)	0.152		
Previously diagnosed atrial fibrillation	1.703 (0.599-4.839)	0.318		
Hypertonia	1.753 (0.229-13.404)	0.589		
Dyslipidaemia	1.090 (0.309-3.847)	0.893		
Diabetes mellitus	0.624 (0.199-1.957)	0.418		
Stroke/TIA	0.042 (0.000-58.362)	0.390		
Bradypacing indication	0.383 (0.086-1.705)	0.208		
EF	0.988 (0.956-1.022)	0.491		
QRS width	1.000 (0.974-1.025)	0.971		
Heart rate	0.974 (0.936-1.014)	0.197		
Creatinine	1.002 (0.994-1.011)	0.558		
Hemoglobin	1.030 (0.988-1.074)	0.158		
Remote monitoring	0.783 (0.284-2.159)	0.636		
Antiplatelet therapy	0.484 (0.175-1.340)	0.162		
Anticoagulation	2.314 (0.796-6.723)	0.123		
Beta-blocker	0.751 (0.168-3.366)	0.708		
ACEI/ARB/ARNI	0.843 (0.237-3.001)	0.792		
Diuretics	1.754 (0.623-4.937)	0.287		
Calcium channel blockers	1.018 (0.323-3.212)	0.976		
Mineralocorticoid receptor antagonists	2.211 (0.761-6.424)	0.145		
Statin	0.606 (0.215-1.708)	0.344		
Amiodarone	1.457 (0.404-5.249)	0.565		
Digitalis	5.246 (1.169-23.545)	0.030	5.246 (1.169-23.545)	0.030

Supplementary Table 12. Multivariate analysis of time to first hospitalization due to arrhythmic cause **VVI vs VDD**

Risk factor	unadjusted HR (95% CI)	p-value	adjusted HR (95% CI)	p-value
ICD type	1.463 (0.899-2.379)	0.125	1.706 (1.043-2.792)	0.033
Age	1.009 (0.988-1.031)	0.390		
Male	0.733 (0.430-1.248)	0.253		
Primer prophylaxis	2.804 (1.339-5.869)	0.006	3.041 (1.443-6.411)	0.003
Ischemic etiology	0.770 (0.475-1.248)	0.289		
Previously diagnosed atrial fibrillation	0.981 (0.576-1.671)	0.943		
Hypertonia	0.939 (0.376-2.348)	0.893		
Dyslipidaemia	1.410 (0.672-2.957)	0.363		
Diabetes mellitus	1.380 (0.840-2.267)	0.203		
Stroke/TIA	0.881 (0.353-2.198)	0.786		
Bradypacing indication	1.258 (0.174-9.096)	0.820		
EF	0.995 (0.977-1.013)	0.555		
QRS width	0.995 (0.981-1.009)	0.491		
Heart rate	0.991 (0.973-1.009)	0.328		
Creatinine	1.004 (0.999-1.008)	0.104		
Hemoglobin	0.996 (0.982-1.011)	0.620		
Remote monitoring	1.394 (0.848-2.289)	0.190		
Antiplatelet therapy	1.054 (0.639-1.737)	0.838		
Anticoagulation	0.760 (0.459-1.260)	0.288		
Beta-blocker	0.806 (0.197-3.300)	0.764		
ACEI/ARB/ARNI	0.415 (0.226-0.761)	0.004	0.404 (0.219-0.745)	0.004
Diuretics	0.939 (0.581-1.518)	0.797		
Calcium channel blockers	1.555 (0.905-2.672)	0.110		
Mineralocorticoid receptor antagonists	0.803 (0.495-1.302)	0.374		
Statin	0.867 (0.520-1.444)	0.583		
Amiodarone	1.618 (0.942-2.778)	0.081	1.277 (0.734-2.220)	0.387
Digitalis	0.619 (0.225-1.703)	0.353		

Supplementary Table 13. Multivariate analysis of time to first hospitalization due to arrhythmic cause **VDD vs DDD**

Risk factor	unadjusted HR (95% CI)	p-value	adjusted HR (95% CI)	p-value
ICD type	0.638 (0.366-1.113)	0.114	0.700 (0.365-1.341)	0.282
Age	1.009 (0.987-1.030)	0.429		
Male	0.960 (0.523-1.761)	0.895		
Primer prophylaxis	1.523 (0.830-2.796)	0.175		
Ischemic etiology	0.936 (0.548-1.601)	0.810		
Previously diagnosed atrial fibrillation	1.106 (0.628-1.949)	0.727		
Hypertonia	1.694 (0.527-5.439)	0.376		
Dyslipidaemia	1.117 (0.561-2.221)	0.753		
Diabetes mellitus	1.221 (0.709-2.103)	0.472		
Stroke/TIA	0.643 (0.231-1.785)	0.396		
Bradypacing indication	0.647 (0.332-1.261)	0.201		
EF	0.986 (0.969-1.004)	0.117		
QRS width	1.002 (0.990-1.014)	0.786		
Heart rate	0.983 (0.962-1.003)	0.101		
Creatinine	1.005 (1.000-1.009)	0.041	1.005 (1.000-1.009)	0.049
Hemoglobin	1.005 (0.988-1.022)	0.594		
Remote monitoring	1.466 (0.862-2.492)	0.158		
Antiplatelet therapy	1.012 (0.586-1.746)	0.967		
Anticoagulation	1.118 (0.651-1.920)	0.686		
Beta-blocker	1.464 (0.525-4.086)	0.466		
ACEI/ARB/ARNI	0.764 (0.384-1.519)	0.442		
Diuretics	1.199 (0.706-2.037)	0.501		
Calcium channel blockers	1.748 (1.001-3.051)	0.050	1.412 (0.770-2.589)	0.265
Mineralocorticoid receptor antagonists	0.710 (0.398-1.265)	0.245		
Statin	0.788 (0.451-1.379)	0.404		
Amiodarone	2.744 (1.513-4.976)	0.001	2.761 (1.461-5.218)	0.002
Digitalis	0.885 (0.215-3.640)	0.865		

Supplementary Table 14. Multivariate analysis of time to first hospitalization due to heart failure VVI vs VDD

Risk factor	unadjusted HR (95% CI)	p-value	adjusted HR (95% CI)	p-value
ICD type	0.949 (0.449-2.006)	0.891	1.628 (0.619-4.279)	0.323
Age	0.989 (0.959-1.020)	0.477		
Male	0.670 (0.305-1.474)	0.320		
Primer prophylaxis	0.330 (0.159-0.685)	0.003	0.399 (0.136-1.170)	0.094
Ischemic etiology	0.809 (0.389-1.681)	0.570		
Previously diagnosed atrial fibrillation	2.329 (1.114-4.867)	0.025	2.160 (0.670-6.967)	0.197
Hypertonia	0.660 (0.198-2.197)	0.499		
Dyslipidaemia	1.584 (0.478-5.252)	0.452		
Diabetes mellitus	1.712 (0.816-3.590)	0.155		
Stroke/TIA	2.544 (0.959-6.745)	0.061	1.980 (0.628-6.240)	0.243
Bradypacing indication	0.048 (0.000-52297.115)	0.669		
EF	0.957 (0.925-0.990)	0.011	1.002 (0.961-1.045)	0.917
QRS width	1.005 (0.985-1.025)	0.645		
Heart rate	1.021 (1.000-1.042)	0.046	1.023 (0.997-1.051)	0.087
Creatinine	1.010 (1.003-1.017)	0.005	1.012 (1.004-1.020)	0.003
Hemoglobin	0.973 (0.954-0.993)	0.009	0.958 (0.937-0.980)	<0.001
Remote monitoring	0.697 (0.297-1.635)	0.407		
Antiplatelet therapy	0.692 (0.333-1.439)	0.324		
Anticoagulation	1.875 (0.900-3.908)	0.093	0.649 (0.239-1.764)	0.397
Beta-blocker	21.124 (0.002-267352.000)	0.527		
ACEI/ARB/ARNI	0.501 (0.191-1.314)	0.160		
Diuretics	2.801 (1.237-6.339)	0.013	1.378 (0.460-4.130)	0.567
Calcium channel blockers	0.414 (0.125-1.368)	0.414		
Mineralocorticoid receptor antagonists	3.849 (1.561-9.489)	0.003	2.827 (0.934-8.560)	0.066
Statin	0.566 (0.270-1.186)	0.132		
Amiodarone	0.719 (0.250-2.067)	0.719		
Digitalis	4.770 (2.097-10.848)	<0.001	3.521 (1.224-10.132)	0.020

Supplementary Table 15. Multivariate analysis of time to first hospitalization due to heart failure **VDD vs DDD**

Risk factor	unadjusted HR (95% CI)	p-value	adjusted HR (95% CI)	p-value
ICD type	0.586 (0.219-1.570)	0.287	0.949 (0.301-2.991)	0.928
Age	0.987 (0.957-1.019)	0.436		
Male	0.633 (0.237-1.689)	0.362		
Primer prophylaxis	0.379 (0.150-0.962)	0.041	0.413 (0.151-1.126)	0.084
Ischemic etiology	0.870 (0.343-2.206)	0.769		
Previously diagnosed atrial fibrillation	1.556 (0.596-4.060)	0.366		
Hypertonia	0.757 (0.172-3.326)	0.712		
Dyslipidaemia	0.858 (0.280-2.627)	0.789		
Diabetes mellitus	1.042 (0.391-2.781)	0.934		
Stroke/TIA	1.141 (0.262-4.971)	0.860		
Bradypacing indication	0.817 (0.268-2.487)	0.722		
EF	0.941 (0.903-0.980)	0.003	0.957 (0.922-0.993)	0.019
QRS width	0.999 (0.977-1.021)	0.895		
Heart rate	1.002 (0.972-1.033)	0.887		
Creatinine	1.010 (1.003-1.018)	0.003	1.011 (1.003-1.018)	0.005
Hemoglobin	0.984 (0.958-1.011)	0.244		
Remote monitoring	0.812 (0.314-2.101)	0.668		
Antiplatelet therapy	0.736 (0.290-1.867)	0.519		
Anticoagulation	1.010 (0.389-2.622)	0.983		
Beta-blocker	23.676 (0.024-23075.647)	0.367		
ACEI/ARB/ARNI	0.635 (0.208-1.933)	0.423		
Diuretics	1.744 (0.676-4.501)	0.250		
Calcium channel blockers	0.364 (0.084-1.584)	0.178		
Mineralocorticoid receptor antagonists	1.901 (0.746-4.840)	0.178		
Statin	0.666 (0.258-1.719)	0.401		
Amiodarone	1.079 (0.310-3.762)	0.904		
Digitalis	1.572 (0.209-11.839)	0.661		

Supplementary Table 16. Multivariate analysis of all-cause mortality **all groups**

Risk factor	unadjusted HR (95% CI)	p-value	adjusted HR (95% CI)	p-value
ICD type	0.906 (0.696-1.179)	0.463	0.960 (0.711-1.295)	0.787
Age	1.060 (1.037-1.084)	<0.001	1.060 (1.031-1.089)	<0.001
Male	0.883 (0.546-1.426)	0.611		
Primer prophylaxis	0.849 (0.534-1.349)	0.488		
Ischemic etiology	1.297 (0.830-2.028)	0.253		
Previously diagnosed atrial fibrillation	1.958 (1.268-3.023)	0.002	1.536 (0.936-2.521)	0.089
Hypertonia	4.969 (1.220-20.233)	0.025	1.177 (0.272-5.094)	0.828
Dyslipidaemia	1.645 (0.872-3.105)	0.125		
Diabetes mellitus	1.968 (1.277-3.033)	0.002	2.215 (1.361-3.607)	0.001
Stroke/TIA	1.409 (0.726-2.733)	0.311		
Bradypacing indication	1.035 (0.575-1.864)	0.908		
EF	0.975 (0.959-0.991)	0.002	0.967 (0.948-0.986)	0.001
QRS width	1.008 (0.997-1.018)	0.146		
Heart rate	1.017 (1.003-1.030)	0.013	1.005 (0.992-1.018)	0.460
Creatinine	1.002 (0.997-1.006)	0.486		
Hemoglobin	0.990 (0.977-1.004)	0.163		
Remote monitoring	0.248 (0.114-0.538)	<0.001	0.320 (0.145-0.709)	0.005
Antiplatelet therapy	0.948 (0.603-1.489)	0.816		
Anticoagulation	1.840 (1.190-2.843)	0.006	1.172 (0.637-2.158)	0.609
Beta-blocker	0.935 (0.407-2.152)	0.875		
ACEI/ARB/ARNI	1.023 (0.554-1.889)	0.942		
Diuretics	1.740 (1.111-2.725)	0.015	1.451 (0.855-2.463)	0.167
Calcium channel blockers	0.888 (0.519-1.519)	0.666		
Mineralocorticoid receptor antagonists	1.347 (0.870-2.085)	0.182		
Statin	1.114 (0.686-1.808)	0.662		
Amiodarone	1.244 (0.729-2.125)	0.423		
Digitalis	1.021 (0.470-2.220)	0.958		

Supplementary Table 17. List of implanted device models

List of implanted Biotronik device models, n (%)			
Acticor 7 VR-T DX	1 (0.2%)	Itrevia 5 HF-T QP	1 (0.2%)
Iforia 5 DR-T	11 (2%)	Itrevia 5 VR-T DX	44 (7.9%)
Iforia 5 HF-T	10 (1.8%)	Itrevia 7 DR-T	6 (1.1%)
Iforia 5 VR-T DX	37 (6.6%)	Itrevia 7 HF-T	18 (3.2%)
Inlexa 3 VR-T	54 (9.7%)	Lumax 300 HF-T	8 (1.4%)
Intica 5 DR-T	1 (0.2%)	Lumax 340 HF-T	1 (0.2%)
Intica 5 VR-T DX	51 (9.1%)	Lumax 540 HF-T	13 (2.3%)
Intica 7 DR-T	25 (4.5%)	Lumax 540 VR-T DX	13 (2.3%)
Intica 7 HF-T	26 (4.7%)	Lumax 640 DR-T	4 (0.7%)
Intica 7 HF-T QP	20 (3.6%)	Lumax 640 HF-T	1 (0.2%)
Intica Neo 5 VR-T	2 (0.4%)	Lumax 640 VR-T DX	17 (3.1%)
Intica Neo 5 VR-T DX	23 (4.1%)	Rivacor 5 VR-T	20 (3.6%)
Intica Neo 7 DR-T	8 (1.4%)	Rivacor 5 VR-T DX	38 (6.8%)
Intica Neo 7 HF-T	16 (2.9%)	Rivacor 7 DR-T	21 (3.8%)
Intica Neo 7 HF-T QP	16 (2.9%)	Rivacor 7 HF-T	13 (2.3%)
Itrevia 5 HF-T	3 (0.5%)	Rivacor 7 HF-T QP	35 (6.3%)

Supplementary Table 18. Multivariate analysis of time to first inappropriate therapy – single-chamber vs. dual-chamber

Risk factor	unadjusted HR (95% CI)	p-value	adjusted HR (95% CI)	p-value
Discrimination algorithm	1.165 (0.393-3.448)	0.783	1.152 (0.387-3.433)	0.799
Age at implantation	0.988 (0.958-1.020)	0.462		
Male	1.109 (0.411-2.989)	0.838		
Secondary prophylaxis	1.957 (0.835-4.585)	0.122		
Ischemic etiology	0.608 (0.255-1.451)	0.262		
Previously diagnosed atrial fibrillation/atrial flutter	1.303 (0.555-3.059)	0.543		
Hypertension	0.800 (0.312-2.051)	0.643		
Diabetes mellitus	0.768 (0.283-2.085)	0.605		
Stroke/TIA	0.690 (0.093-5.136)	0.717		
Bradypacing indication	0.479 (0.112-2.049)	0.321		
LVEF	0.981 (0.947-1.016)	0.285		
Heart rate	0.994 (0.970-1.019)	0.638		
Creatinine	1.002 (0.995-1.010)	0.539		
eGFR	1.006 (0.984-1.030)	0.578		
Hemoglobin	1.000 (0.976-1.025)	0.993		
Antiplatelets	0.844 (0.364-1.954)	0.692		
Anticoagulation	1.048 (0.452-2.427)	0.913		
Beta-blocker	0.621 (0.083-4.629)	0.642		
RAAS	2.235 (0.300-16.632)	0.432		
Diuretics	0.704 (0.301-1.648)	0.419		
MRA	0.620 (0.265-1.454)	0.272		
Digitalis	1.618 (0.378-6.925)	0.516		
CCB	0.945 (0.221-4.049)	0.940		
Amiodaron	0.294 (0.069-1.257)	0.099	0.294 (0.069-1.257)	0.099
Statins	0.648 (0.280-1.500)	0.311		
SGLT2-inhibitors	0.041 (0.000-30.458)	0.344		

Supplementary Table 19. Multivariate analysis of time to first inappropriate therapy – single-chamber (MorphMatch ON) vs. dual-chamber

Risk factor	unadjusted HR (95% CI)	p-value	adjusted HR (95% CI)	p-value
Discrimination algorithm	1.809 (0.241-13.577)	0.564	1.571 (0.208-11.851)	0.661
Age at implantation	0.978 (0.947-1.010)	0.171		
Male	0.883 (0.321-2.432)	0.810		
Secondary prophylaxis	1.925 (0.774-4.790)	0.159		
Ischemic etiology	0.469 (0.178-1.235)	0.125		
Previously diagnosed atrial fibrillation/atrial flutter	1.291 (0.507-3.285)	0.592		
Hypertension	0.709 (0.268-1.871)	0.487		
Diabetes mellitus	0.681 (0.225-2.054)	0.495		
Stroke/TIA	0.045 (0.000-154.999)	0.455		
Bradypacing indication	0.588 (0.136-2.548)	0.478		
LVEF	0.979 (0.943-1.017)	0.283		
Heart rate	0.995 (0.969-1.022)	0.726		
Creatinine	1.001 (0.993-1.010)	0.798		
eGFR	1.013 (0.988-1.038)	0.308		
Hemoglobin	1.005 (0.980-1.031)	0.699		
Antiplatelets	0.851 (0.345-2.096)	0.726		
Anticoagulation	1.036 (0.421-2.552)	0.938		
Beta-blocker	0.483 (0.064-3.653)	0.481		
RAAS	1.740 (0.232-13.059)	0.590		
Diuretics	0.634 (0.255-1.576)	0.326		
MRA	0.556 (0.223-1.385)	0.208		
Digitalis	1.024 (0.137-7.673)	0.982		
CCB	0.570 (0.076-4.275)	0.585		
Amiodaron	0.151 (0.020-1.133)	0.066	0.151 (0.020-1.133)	0.066
Statins	0.592 (0.241-1.459)	0.255		
SGLT2-inhibitors	0.041 (0.000-56.696)	0.387		

Supplementary Table 20. Multivariate analysis of time to first inappropriate therapy – dual-chamber discriminator VDD vs. dual-chamber discriminator DDD

Risk factor	unadjusted HR (95% CI)	p-value	adjusted HR (95% CI)	p-value
ICD type (VDD or DDD)	0.586 (0.230-1.490)	0.262	0.597 (0.226-1.579)	0.299
Age at implantation	0.976 (0.945-1.008)	0.133		
Male	0.834 (0.300-2.319)	0.729		
Secondary prophylaxis	1.918 (0.757-4.862)	0.170		
Ischemic etiology	0.389 (0.139-1.092)	0.073	0.311 (0.101-0.953)	0.041
Previously diagnosed atrial fibrillation/atrial flutter	1.187 (0.444-3.169)	0.733		
Hypertension	0.710 (0.266-1.898)	0.495		
Diabetes mellitus	0.528 (0.153-1.828)	0.314		
Stroke/TIA	0.045 (0.000-310.033)	0.493		
Bradypacing indication	0.581 (0.133-2.531)	0.470		
LVEF	0.977 (0.938-1.018)	0.264		
Heart rate	0.998 (0.972-1.024)	0.863		
Creatinine	1.001 (0.991-1.011)	0.826		
eGFR	1.017 (0.991-1.044)	0.200		
Hemoglobin	1.006 (0.980-1.033)	0.643		
Antiplatelets	0.895 (0.355-2.257)	0.814		
Anticoagulation	0.935 (0.371-2.358)	0.888		
Beta-blocker	0.457 (0.060-3.470)	0.449		
RAAS	1.480 (0.197-11.140)	0.704		
Diuretics	0.537 (0.212-1.360)	0.190		
MRA	0.458 (0.181-1.161)	0.100	0.682 (0.252-1.846)	0.452
Digitalis	1.091 (0.145-8.200)	0.932		
CCB	0.664 (0.088-4.989)	0.690		
Amiodaron	0.031 (0.000-2.684)	0.127		
Statins	0.525 (0.208-1.324)	0.172		
SGLT2-inhibitors	0.042 (0.000-97.771)	0.422		

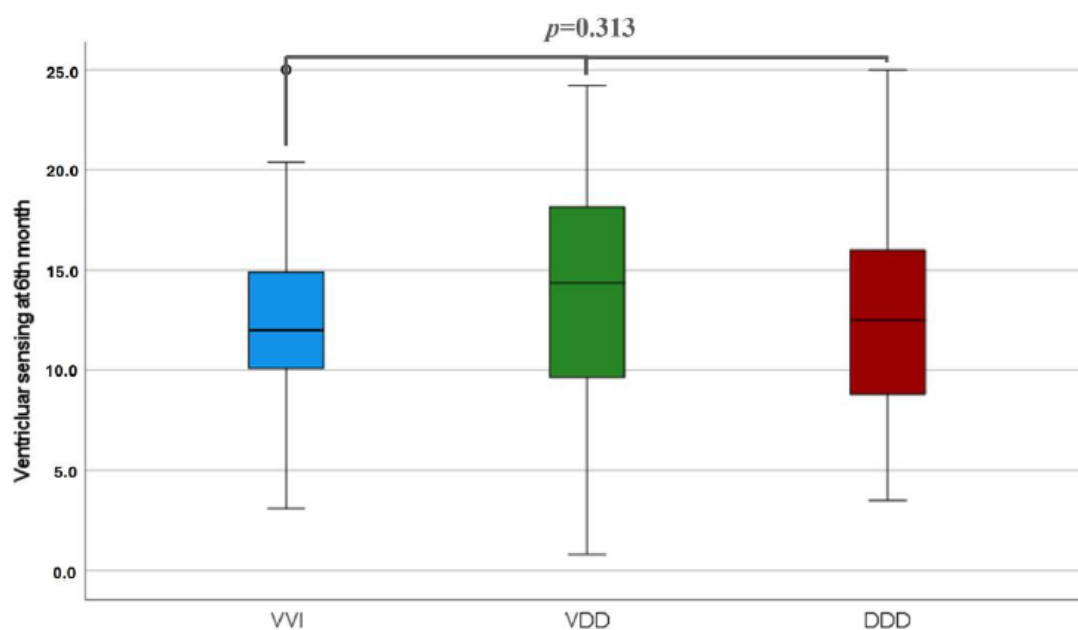
Supplementary Table 21. Multivariate analysis of time to first appropriate therapy – single-chamber vs. dual-chamber

Risk factor	unadjusted HR (95% CI)	p-value	adjusted HR (95% CI)	p-value
Discrimination algorith	0.724 (0.428-1.224)	0.228	0.699 (0.389-1.257)	0.232
Age at implantation	1.008 (0.989-1.027)	0.421		
Male	1.605 (0.865-2.975)	0.133		
Secondary prophylaxis	2.810 (1.744-4.527)	<0.001	2.641 (1.560-4.471)	<0.001
Ischemic etiology	1.976 (1.223-3.191)	0.005	2.214 (1.309-3.745)	0.003
Previously diagnosed atrial fibrillation/atrial flutter	0.955 (0.592-1.541)	0.850		
Hypertension	1.627 (0.875-3.026)	0.124		
Diabetes mellitus	1.333 (0.823-2.158)	0.243		
Stroke/TIA	1.602 (0.734-3.496)	0.236		
Bradypacing indication	0.409 (0.177-0.942)	0.036	0.348 (0.126-0.960)	0.042
LVEF	0.999 (0.983-1.016)	0.935		
Heart rate	0.992 (0.979-1.006)	0.277		
Creatinine	1.002 (0.997-1.006)	0.485		
eGFR	0.993 (0.981-1.005)	0.259		
Hemoglobin	0.989 (0.976-1.002)	0.091	0.998 (0.984-1.011)	0.738
Antiplatelets	1.627 (1.025-2.582)	0.039	1.260 (0.667-2.382)	0.476
Anticoagulation	0.941 (0.598-1.481)	0.793		
Beta-blocker	2.489 (0.346-17.924)	0.365		
RAAS	1.536 (0.620-3.808)	0.354		
Diuretics	0.848 (0.529-1.360)	0.495		
MRA	0.941 (0.576-1.538)	0.809		
Digitalis	0.420 (0.103-1.710)	0.226		
CCB	1.016 (0.466-2.215)	0.968		
Amiodaron	2.065 (1.301-3.279)	0.002	1.751 (1.053-2.911)	0.031
Statins	1.520 (0.911-2.538)	0.109		
SGLT2-inhibitors	0.341 (0.107-1.088)	0.069	0.358 (0.086-1.492)	0.158

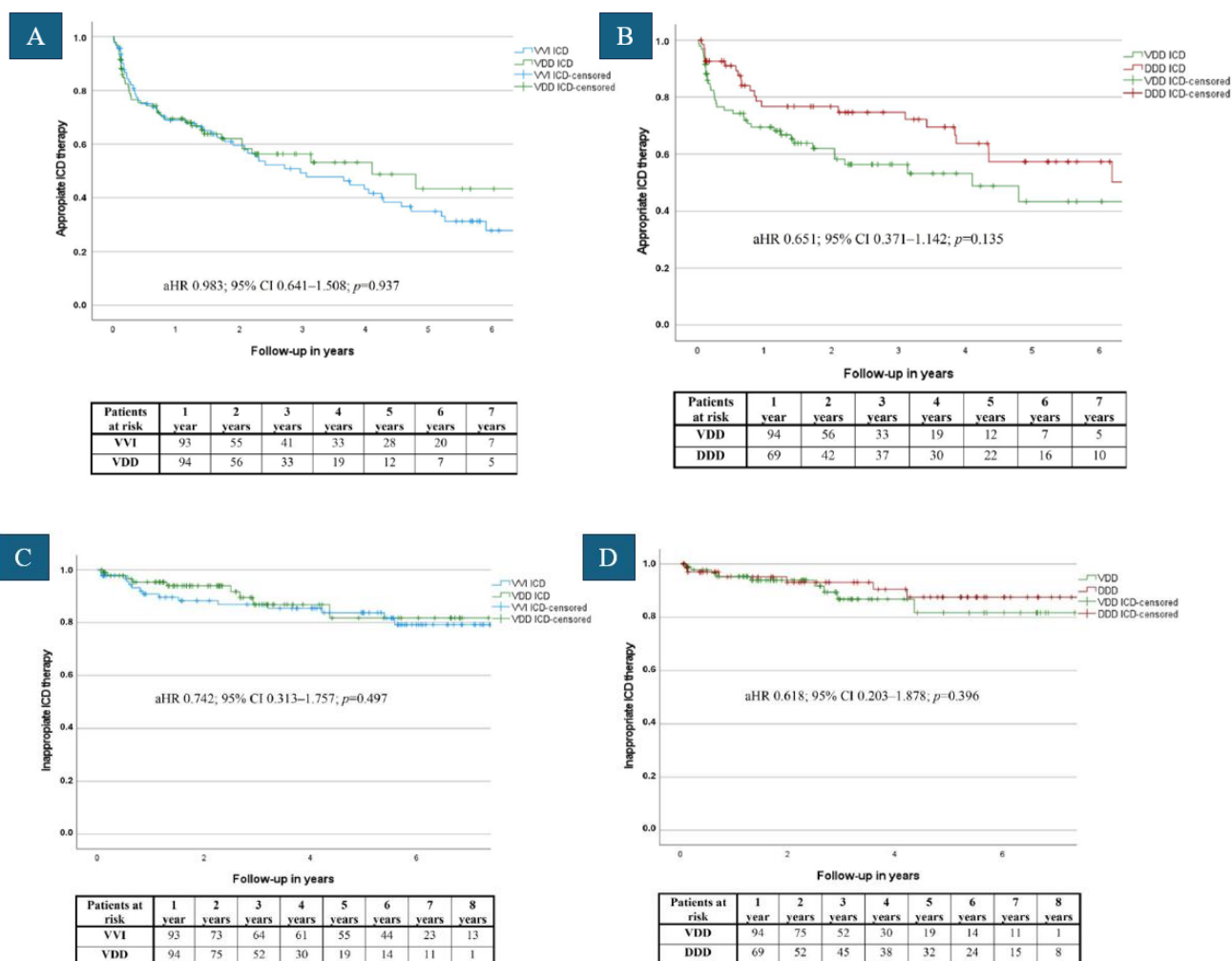
Supplementary Table 22. Multivariate analysis of all-cause mortality – single-chamber vs. dual-chamber

Risk factor	unadjusted HR (95% CI)	p-value	adjusted HR (95% CI)	p-value
Discrimination algorithm	0.930 (0.598-1.448)	0.749	0.714 (0.426-1.197)	0.201
Age at implantation	1.034 (1.019-1.050)	<0.001	1.027 (1.009-1.045)	0.003
Male	2.315 (1.373-3.903)	0.002	2.290 (1.326-3.956)	0.003
Secondary prophylaxis	0.677 (0.473-0.970)	0.034	0.826 (0.541-1.262)	0.376
Ischemic etiology	1.723 (1.218-2.438)	0.002	1.339 (0.923-1.942)	0.124
Previously diagnosed atrial fibrillation/atrial flutter	1.151 (0.807-1.641)	0.438		
Hypertension	1.833 (1.149-2.926)	0.011	1.432 (0.864-2.372)	0.164
Diabetes mellitus	1.654 (1.164-2.350)	0.005	1.223 (0.820-1.824)	0.323
Stroke/TIA	1.817 (1.023-3.229)	0.042	1.356 (0.714-2.575)	0.353
Bradypacing indication	1.006 (0.636-1.593)	0.979		
LVEF	0.966 (0.951-0.982)	<0.001	0.969 (0.951-0.986)	<0.001
Heart rate	1.001 (0.991-1.011)	0.822		
Creatinine	1.004 (1.001-1.006)	0.004	1.000 (0.993-1.007)	0.985
eGFR	0.986 (0.977-0.994)	<0.001	1.000 (0.989-1.011)	0.975
Hemoglobin	0.982 (0.972-0.991)	<0.001	0.982 (0.972-0.992)	<0.001
Antiplatelets	1.339 (0.952-1.883)	0.093	0.987 (0.604-1.613)	0.959
Anticoagulation	1.196 (0.850-1.682)	0.304		
Beta-blocker	0.439 (0.214-0.900)	0.025	0.250 (0.120-0.525)	<0.001
RAAS	1.656 (0.810-3.387)	0.167		
Diuretics	2.468 (1.576-3.867)	<0.001	1.209 (0.697-2.098)	0.500
MRA	1.765 (1.156-2.695)	0.008	0.796 (0.460-1.375)	0.413
Digitalis	1.447 (0.759-2.756)	0.262		
CCB	0.380 (0.155-0.929)	0.034	0.192 (0.047-0.785)	0.022
Amiodaron	1.438 (0.999-2.072)	0.051	1.239 (0.834-1.842)	0.288
Statins	1.498 (1.029-2.181)	0.035	1.110 (0.703-1.754)	0.654
SGLT2-inhibitors	1.159 (0.580-2.316)	0.676		

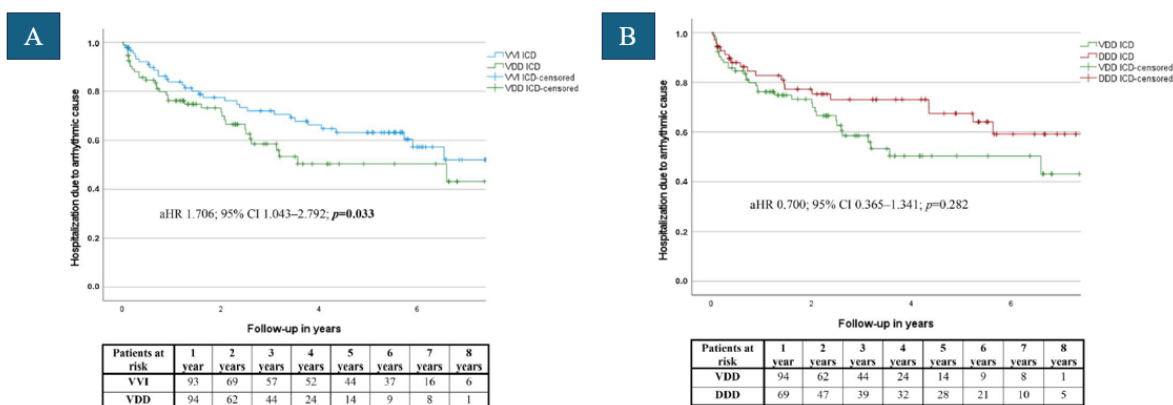
Supplementary Figure 1. Ventricular sensing in VVI vs. VDD vs. DDD ICDs at 6th month



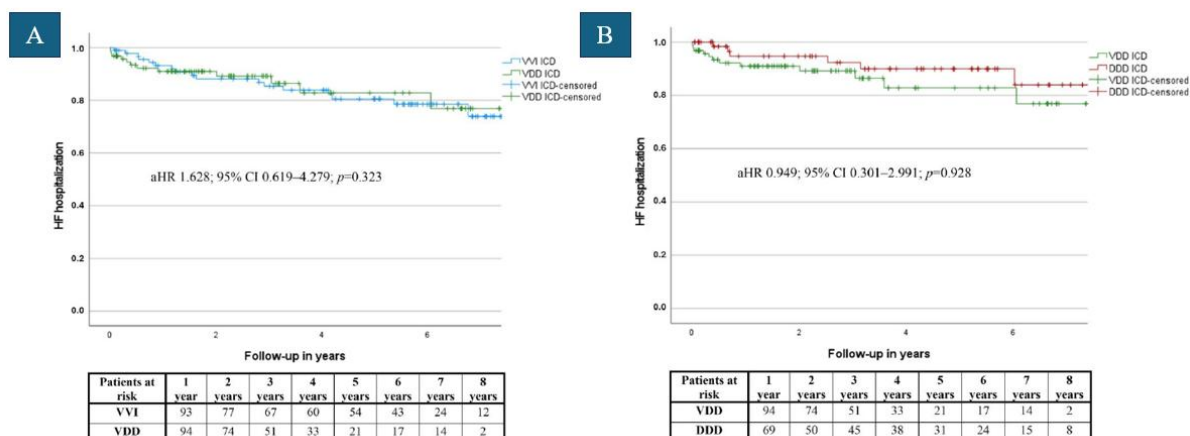
Supplementary Figure 2. (A) Time to first appropriate therapy – VVI vs. VDD **(B)** Time to first appropriate therapy – VDD vs. DDD **(C)** Time to first inappropriate therapy – VVI vs. VDD **(D)** Time to first inappropriate therapy – VDD vs. DDD



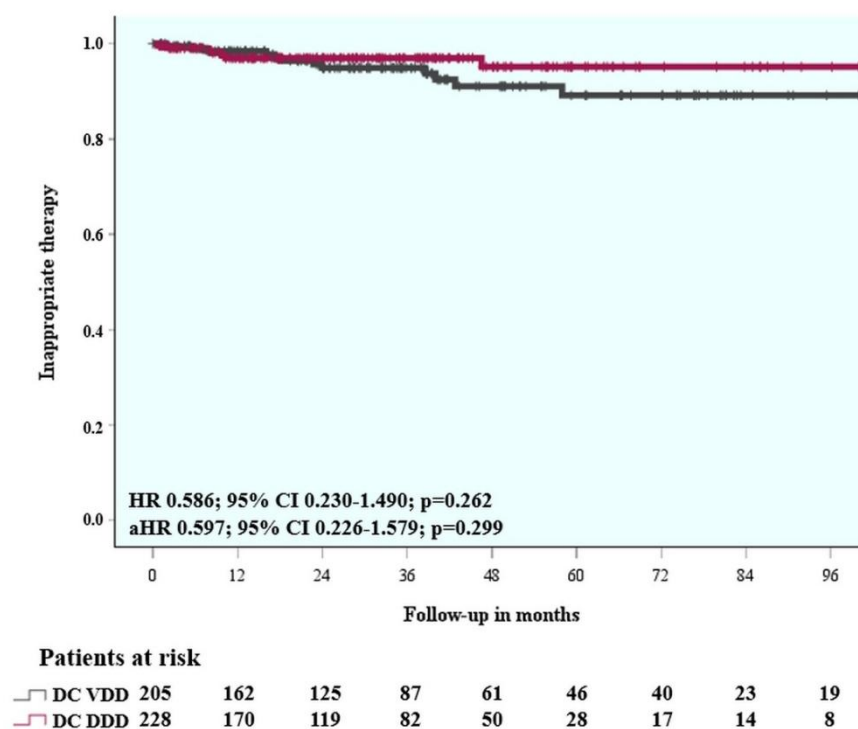
Supplementary Figure 3. (A) Time to first hospitalization due to arrhythmic cause – VVI vs. VDD **(B)** Time to first hospitalization due to arrhythmic cause – VDD vs. DDD



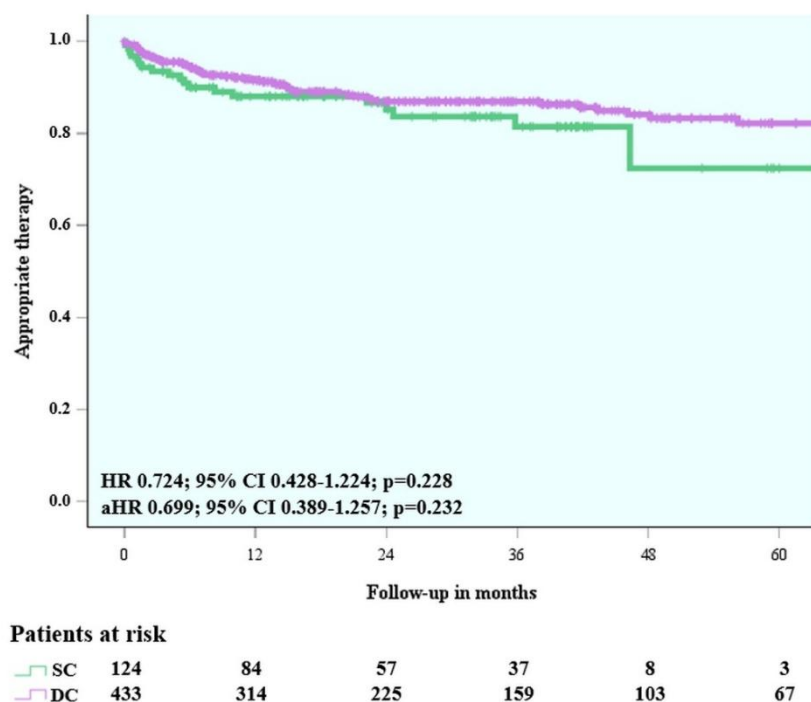
**Supplementary Figure 4. (A) Time to first heart failure (HF) hospitalization – VVI vs. VDD
(B) Time to first HF hospitalization – VDD vs. DDD**



Supplementary Figure 5. Time to first inappropriate therapy – dual-chamber discriminator VDD vs. dual-chamber discriminator DDD



Supplementary Figure 6. Time to first appropriate therapy – single-chamber vs. dual-chamber



Supplementary Figure 7. All-cause mortality – single-chamber vs. dual-chamber

