Programming tachycardia zones to reduce avoidable defibrillator shocks

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Abstract

INTRODUCTION: Most of avoidable defibrillator therapies can be reduced by evidence-based programming, but defining tachycardia configurations across all device manufacturers is not straightforward. The aims were to determine if a uniform programming of tachycardia zones, independently of the manufacturer, result in a lower rate of avoidable shocks in primary-prevention heart failure (HF) patients and also if programming high-rate or delayed therapies can have some benefit. METHODS AND RESULTS: Prospective cohort with historical controls. HF patients with a primary-prevention indication for a defibrillator were randomized to receive one of two new programming configurations (high-rate or delayed therapies). A historical cohort of patients with conventional programming was analyzed for comparison. The primary endpoint was any therapy [shock or anti-tachycardia pacing (ATP)]. Secondary endpoints were appropriate shocks, appropriate ATP, appropriate therapies, inappropriate shocks, syncope and death. 89 patients were assigned for new programming group [high rate (n=47) or delayed therapy (n=42)]. They were compared with 94 historical patients with conventional programming. During a mean follow-up of 20±7 months, the new programming was associated with a reduction of any therapy (HR = 0.265, 95% CI 0.121-0.577, p=0.001), even after adjustment. Aproppriate ATP and any shock were also reduced. Syncope did not occur. Sudden, cardiovascular and all-cause deaths were not different between the groups. In the new programming group, neither high-rate nor delayed programming were better than the other. CONCLUSIONS: In our study, programming tachycardia zones homogeneously across all manufacturers was possible and resulted in a lower rate of therapies, shocks and appropriate ATP.

METHODS AND RESULTS:

Prospective cohort with historical controls. HF patients with a primary-prevention indication for a defibrillator were randomized to receive one of two new programming configurations (high-rate or delayed therapies). A historical cohort of patients with conventional programming was analyzed for comparison. The primary endpoint was any therapy [shock or anti-tachycardia pacing (ATP)] delivered. Secondary endpoints were appropriate shocks, appropriate ATP, appropriate therapies, inappropriate shocks, syncope and death. 89 patients were assigned for new programming group [high rate (n=47) or delayed therapy (n=42)]. They were compared with 94 historical patients with conventional programming. During a mean follow-up of 20±7 months, the new programming was associated with a reduction of any therapy (HR = 0.265, 95% CI 0.121-0.577, p=0.001), even after adjustment. Aproppriate ATP and any shock were also reduced. Syncope did not occur. Sudden, cardiovascular and all-cause deaths were not different between the groups. In the new programming group, neither high-rate nor delayed programming were better than the other.

CONCLUSIONS: In our study, programming tachycardia zones homogeneously across all manufacturers was possible and resulted in a lower rate of therapies, shocks and appropriate ATP.

Keywords: defibrillator; primary prevention; programming; shocks; anti-tachycardia pacing; avoidable shocks.

Abbreviations:

ACEI: Angiotensin-converting-enzyme inhibitors

ARB: Angiotensin II receptor blockers

ARNI: Angiotensin receptor-neprilysin Inhibitors

AF: Atrial fibrillation

ATP: Anti-tachycardia pacing

CI: Confidence Interval

CRT: Cardiac ressyncronization therapy

CV: cardiovascular

-D: defibrillator

ECG: electrocardiogram

h: hour

HR: hazard ratio

ICD: implantable cardioverter-defibrillator

LVEF: Left ventricle ejection fraction

SCD: Sudden cardiac death

SVT: Supra-ventricular tachycardia

VF: Ventricular Fibrillation

VT: Ventricular tachycardia

TEXT

INTRODUCTION

The use of implantable cardioverter-defibrillators (ICD) is a well stablished therapy[1]. It reduces the risk of sudden cardiac death (SCD) and all-cause mortality in patients with symptomatic heart failure (HF) and left ventricular ejection fraction (LVEF) of [?]35%, despite optimal medical therapy. Recent registries also corroborate the ICD benefit in contemporary HF patients[2]. However, increasing awareness of the frequency and the adverse outcomes associated with avoidable ICD therapies also emerged. Several studies [3-9] suggested that increasing detection duration and/or detection heart rate resulted in a reduction of inappropriate and unnecessary therapies and all-cause mortality when compared with conventional programming. Based on these studies and on a meta-analysis including all of them[10], generic device programming guidelines were issued in a 2015 Consensus Statement[11], intending to be applied to devices from all manufacturers. Nevertheless, the cited studies were specific to each manufacturer and extrapolating their data to a uniform programming to be used in clinical practice is not straightforward. In addition, concerns about failure of modern ICDs to treat VF have been raised and complex and unanticipated interactions between manufacturer-specific features and generic programming were adressed[12].

The authors intent to determine if a uniform programming of tachycardia zones, independently of the manufacturer, result in a lower rate of avoidable shocks without compromising efficacy in patients with a primary prevention indication for a defibrillator. The authors also aimed to find if programming high-rate or delayed therapies can have some benefit over the other.

METHODS

Study design

The study was a single center, randomized clinical trial of two defibrillator tachycardia programming strategies and included a historical cohort of patients of the same institution, programmed at physician consideration.

Study population

Eligible patients were >18 years of age and had a primary prevention indication for a defibrillator [ICD or cardiac resynchronization therapy (CRT) with a defibrillator (CRT-D)] without a specific indication for individualized programming.

Prospective group included all consecutive patients that had presential scheduled consult between July and December 2017 and also those who implanted a defibrillator from July 2017 to July 2019.

The historical patients were all consecutive patients that had presential schedule consult between July and December 2014 and also those who implanted a defibrillator from July 2014 and July 2016. To avoid selection bias, being part of the randomized group was not an exclusion criterion for being included in the historical group. Otherwise, "good patients" (patients with a more favorable clinical profile and no previous therapies) would be excluded from the control group.

Data collection

Demographic data, cardiovascular risk factors, cause of HF (ischemic and non-ischemic), transthoracic echocardiograms (LVEF) and medications were recorded at the time of enrollment. Clinical summaries, device-stored electrograms, interval plots and episode logs were accessed during the follow-up on a regular basis (remote monitoring quarterly and schedule visits yearly). Data collection in historical patients were based on registries in schedule visits during the follow-up period retrieved from the national patient registry and from medical records or discharge letters, validated by reviewing patients' files. The same characteristics were analyzed.

Programming

Patients enrolled in the prospective group were randomized to one of the two programming configurations: high-rate detection or delayed detection (in a 1:1 consecutive fashion). Tachyarrhythmia detection and therapy settings were chosen to allow a uniform programming across all manufacturers. The paramount difference between the 2 configurations are a longer detection (from 12/18 to 30/40) and a lower threshold rate in the zone 2 (from 200 to 188 bpm). Details are displaced in figure 1. Programming of the VT/VF detection and therapy parameters in the historical group was not specified. It has been left at the discretion of the physician, variable from patient to patient and details were unavailable. SVT discriminators were used in all patients (in both groups), according to manufacturer's recommendation. Bradycardia pacing settings were programmed at the discretion of the physician.

2.5 Endpoints

Endpoints were assessed from the time of randomization (in the new programming group) through the end of the study (January 2020). Patients were censured if programming zones were changed. In the historical group, endpoints were assessed during an equivalent period of time, until January 2017.

The primary endpoint was any therapy [shock or anti-tachycardia pacing (ATP)] delivered by the defibrillator. Secondary endpoints were appropriate shocks, appropriate ATP, appropriate therapies, inappropriate shocks, syncope, sudden death, cardiovascular death and all-cause death.

ATP and shocks were reviewed by at least two qualified physicians of the study personnel. Syncope was defined as a transient loss of consciousness due to cerebral hypoperfusion, characterized by a rapid onset, short duration, and spontaneous complete recover. Sudden death was considered when an unexpected death occurred in a short period with no discernible cause.

2.6 Ethics

The study protocol was approved by the Ethical Committee of Centro Hospitalar de Setubal (record 43/17). The study is in compliance with the Helsinki Declaration. All subjects enrolled in the prospective portion of the study provided written, informed consent.

2.7 Statistics analysis

SPSS version 23 software (SPSS Inc., Chicago, Illinois) was used for statistical analysis. Data is expressed as means +- standard deviation for continuous variables and as frequencies and percentages for categorical variables. Baseline characteristics and outcomes were compared using the chi-square test for categorical variables and the T-student test for continuous variables. Cox regression analysis was used to calculate the hazard ratio (HR) and 95% confidence intervals (CI) of events. Kaplan–Meier survival function and the log-rank test were used to compare the survival distributions. A value of $p<0.05$ was considered statistically significant.

RESULTS

3.1 Study population

Between July and December 2017, 57 consecutive patients that attended in-clinic checkup were enrolled and 32 patients that underwent first implantation of ICD or CRT-D for primary prevention were also randomized at the time of the procedure. In a similar way, the historical cohort included 64 patients that attended in-clinic checkup and 30 consecutives patients who implanted a defibrillator (figure 2). Of note, 15 patients of the prospective group were included in the historical group.

The mean age of overall population was 67 +- 10 years and 82% were male. Characteristics of the two studied groups are shown in table 1. Patients in the new programming group were more frequently under spironolactone (49% vs 35%, p=0.016). No other characteristics differ between groups. Median follow-up was 20 +- 7 months. No patients were lost to follow-up.

3.2 Endpoints

3.2.1 Primary endpoint

The primary endpoint (any therapy delivered by the ICD) occurred in 30 patients: 10 patients in the new programming group (16%) and 30 patients in the conventional programming group (32%) (p=0.010). Subjects who experienced the primary endpoint did not differ from those who remained event-free, regarding basal characteristics, cardiovascular risk factors, NYHA class and medications. The new programming was significantly associated with a reduction in any therapy delivered by the defibrillator (HR=0.265, 95% CI 0.121-0.577, p=0.001) (table 2). Adjusted model for age, gender, ischemic HF, AF and standard HF medication (ACEI/ARB/ARNi, beta-blockers and aldosterone antagonists) showed similar results (HR 0.266 95% CI 0.120-0.591, p=0.001). Kaplan-Meier survival curve demonstrated that long-term survival free from therapies is better in patients with reduced therapy programming (logrank, $p<0.001$) (figure 2).

3.2.2 Secondary endpoints

3.2.2.1 Appropriate shocks

Appropriate shocks occurred in 18 patients: 6 patients in the reduced therapies group (7%) and 12 patients (13%) in the conventional therapy group (p=0.171). The new programming was not significantly associated with a reduction in appropriate shocks (HR 0.425, 95% CI 0.137-1.319, p=0.139) (table 2).

3.2.2.2 Appropriate ATP

Appropriate ATPs occurred in 20 patients: 5 patients in the reduced therapies group (6%) and 15 patients (16%) in the conventional group (p=0.025). Appropriate ATPs were reduced by the new programming (HR 0.276, 95% CI 0.093-0.817, p=0.020) (table 2). Adjusted model for age, gender, ischemic HF, AF and standard HF medication (ACEI/ARB/ARNi, beta-blockers and aldosterone antagonists) showed similar

results (HR 0.276 95% CI 0.092-0.828, p=0.022). No other variable was independently associated with appropriate ATP.

3.2.2.3 Appropriate therapies

Appropriate therapies occurred in 30 patients: 7 patients in the reduced therapies group (8%) and 23 patients (25%) in the conventional group (p=0.002). The risk of appropriate therapies was also reduced by the new programming (HR 0.232, 95% CI 0.089-0.600, p= 0.001) (table 2). After adjustment for age, gender, ischemic HF, AF and standard HF medication, new programming remained independently associated with appropriate therapies (HR 0.250 95% CI 0.099-0.360, p=0.003).

3.2.2.4 Inappropriate shocks

Inappropriate shocks occurred in 12 patients: 4 patients in the reduced therapies group (4%) and 8 patients (9%) in the conventional group (p=0.273). The risk of inappropriate shocks was not significantly reduced by the new programming, although a trend was identified (HR 0.155, 95% CI 0.019-1.242, p= 0.079) (table 2).

3.2.2.5 Appropriate or inappropriate shocks

Appropriate or inappropriate shocks occurred in 27 patients: 9 patients in the reduced therapies group (10%) and 18 patients (19%) in the conventional group (p=0.085). New programming reduced the risk of shocks (HR 0.223, 95% CI 0.076-0.660, p=0.007) (table 2). It remained independently associated after adjustment (OR 0.197 95% CI 0.065-0.597, p=0.004). There was a trend for the use of ACEI/ARB/ARNi as a protective factor for shocks (OR 0.947 95% CI 0.897-1.001, p=0.053).

3.2.2.6 Syncope

No patient had syncopal events during the follow-up.

3.2.2.7 Sudden death

Sudden death occurred in 2 patients: one patient in each group. Both of them had remote monitoring but the device did not transmit the arrythmic events before collapse (they were not near the transmitter). In both of them autopsy and postmortem device interrogation were not performed. Thus an arrhytmic event was a possibility but not the definite cause of death. Of note, the patient who died suddenly in the new programming group had a Boston Scientific CRT-D and he was randomized for the high-rate arm which corresponds to the actual recommended manufacturer-specific programming configurations[14].

3.2.2.8 Cardiovacular death and all-cause death

Cardiovascular death occurred in 12 patients: 5 patients in the new programming group (6%) and 7 patients (7%) in the conventional programming group (p=0.617). New programming was not significantly associated with death (HR 0.637, 95% CI 0.186-2.176, p= 0.472) (table 2).

Death from all-cause occurred in 34 patients: : 18 patients in the new programming group (20%) and 16 patients (17%) in the conventional programming group (p=0.578). New programming was not significantly associated with death (HR 1.045, 95% CI 0.516-2.113, p= 0.904) (table 2). Age (HR 1.063, 95% CI 1.016-1.111, p= 0.008 for each year) and diabetes (HR 3.139, 95% CI 1.497-6.580, p=0.002) were both independently associated with death.

3.3 High rate versus delayed therapy

Basal characteristics of the two randomized groups did not differ between the groups (supplementary table 1). Patients in the high-rate programming group had more frequently obstructive sleep apnea (19% versus 5%, p=0.040) and less frequently history of stroke or TIA (6% versus 21%, p=0.038). No other characteristics differ between the groups.

Regarding primary endpoint, no programming strategy was better than the other (HR 0.901, 95% CI 0.311-2.614, p=0.849 for delayed detection programming). Also, for secondary endpoints no differences were found.

DISCUSSION

The concept of optimal ICD programming has evolved in recent years from quick detection and treatment of VT/VF to a more permissive strategy, in order to reduce avoidable shocks[11]. Demonstration of an increased defibrillation threshold when VF was prolonged[14], concerns about undersensing and underdetection of VF and its use in secondary prevention patients with a higher risk of arrhythmic events were responsible for the idea of programming of short interval for detection and treatment of rapid tachycardia.

Nowadays, concepts have changed and the adverse effects of avoidable therapies were emphasized. As such, an evidence-based programming is recommended[11]. However, manufacturer-specific translations of recommendations into clinical practice is not straightforward and obtaining a universal (or almost universal) programming to apply in clinical practice is not easy. However, for clinicians who deal with defibrillator programming on a daily basis, it would be more practical to have only one programming that could be used across all manufacturers.

We have shown in the present study, that it was possible to program defibrillators from all the five manufacturers with one of two tachycardia configurations, based on high-rate or delayed detection. Both strategies were effective and safe. As expected, due to the reduced number of patients assigned in each arm no conclusion about the benefit of one programming over the other could be obtained. Despite this fact, when comparing the new programming group with a historical group of patients treated in the same institution, some conclusions were drawn. When comparing our interventional group (new programming) with our historical group (conventional programming), the primary outcome (all therapies) was significantly reduced by the new programming strategy. By analyzing secondary outcomes, the reduction in the number of appropriate ATP mostly accounted for these results. However, all shocks (appropriate and inappropriate together) were also reduced. There was a trend for a benefit regarding inappropriate shocks (HR 0.155, p=0.079), while appropriate shocks were not minimized.

"Appropriate" ATPs were reduced in the new programming group. This is expectable since ATPs were exclusively delivered in the FV zone (figure 1) while charging and it is also consistent with previous studies[4-10]. Despite the fact that ATP can be effective and avoids shocks[15], it can also be responsible for acceleration and degeneration to polymorphic VT or VF. According to previous studies, ATP programming can cause acceleration of VT or degeneration to VF in 1.2% to 21% of patients[15-16], being responsible for shock delivery and even incessant electrical storm. The potential adverse effects of using ATP only during charge, such as syncope, did not occur. Avoidable" ATPs were almost eradicated in the new programming group, suggesting that many episodes of nonsustained VT that would have terminated spontaneously were treated prematurely in the conventional programming group.

Inappropriate shocks affected 4% of patients in the new programming group, a proportion similar to other studies[3-9], comparing to 9% in the conventional programming group. There was a trend for a reduction in inappropriate shocks with the new programming (HR 0.155, p=0.079), which would be expected considering previous studies[3-9]. The absence of statistical significance is probably related to the reduced number of events.

The total number of shocks was significantly reduced, but not the number of appropriate shocks, which occurred in 5.6% of all patients. The rate was independent of the programming, probably because they are unavoidable, since these patients are at a high risk of SCD. The same occurred in other studies, in which a minority of patients received appropriate ICD shocks (3-6%) and no significant difference in the risk of appropriate shocks was observed with new programming[3-9].

On the other hand, some reports raised the question of ineffectiveness of ICD when specific tachycardia configurations are used. Differences in sensing and detection methods among manufacturers may limit the applicability of generic programming recommendations. An update of the previous expert consensus

statement was released in 2019[13], including manufacturer-specific translations into clinical practice. Despite these recent concerns and the fact that many patients were programmed with tachycardia configuration different from those used in randomized trials, potential adverse effects did not occur. The risks of applying these tachycardia settings, such as syncope and arrhythmic death, were minimal. No syncopal episodes were detected but two sudden deaths occurred, one of them in the new programming group. In both patients it was not possible to have access to the EGM and autopsy was not performed, so an arrhythmic cause for death was possible but not certain. The patient belonging to the new programming group was randomized to the high rate arm so his tachycardia configuration was in accordance with MADIT-RIT, which efficacy and safety have been previously demonstrated. Togerson et al reported that in most patients in whom failure of ICDs to treat VF occurred, ICD programming deviated from values validated in manufacturer-specific clinical trials, although complying with the more generic recommendations of the Consensus Statement[12]. This is not what happened in our case since the patient had a programming in accordance with a previous randomized trial[4-5]. In the patient who died suddenly in the conventional programming group, it was not possible to access tachycardia settings.

The number of deaths was high in our study (18%), comparing with previous ones. Our population was older and had a higher incidence of hypertension, diabetes and AF, which can explain this result. However, the majority of patients died from non-cardiovascular causes. Probably related to this fact, we found no benefits in mortality with new programming. Others had found otherwise[10] and hypothesized that the significant reduction in appropriate and inappropriate ATP and shocks may have contributed to the observed mortality reduction. In fact, these studies change our concepts about tachycardia programming by demonstrating a benefit in mortality rates with ICD programming. In the present study, such an observation could not be done. Nevertheless, the benefit of the reduction of all therapies is *per si* enough to advice for such programming. Although not translating into a survival benefit in our study, inappropriate shocks are painful and associated with increased anxiety and depression[17], so every effort should be made to reduce them.

Finally, the role of medical therapy in reducing the risk of SCD is well established. Thus, recent studies highlighting the benefit of defibrillators are influenced by the increasing use of these drugs comparing to studies performed some years ago[18]. In the present study, patients were receiving adequate medical therapy: 96% were taking ACEI/ARB/ARNI; 90% beta-blockers, 46% mineralocorticoid receptor antagonists (MRA). These proportions are comparable to controlled trials and better than recent registries[19]. Only the proportion of patients under MRA was higher in the new programming group (55% versus 37%, p=0.016). Although MRA reduce the risk of SCD[20], this difference is unlikely to influence our results in what concerns device therapies.

The present study highlights the benefits of having a structured protocol to program all patients with a defibrillator implanted for primary prevention. Our principal finding is that it was possible to program tachycardia settings across all device manufacturers, while the reduction of all defibrillator therapies without safety concerns was achieved.

LIMITATIONS

It was not a pure prospective study since it was performed a comparison with historical controls in which the tachycardia settings were unknown and not standard. However, since patients from the historical control group were included after 2014, the ICD programming was probably in line with the programming guidelines published in 2015[11]. It's entirely possible that a proportion of the patients in this group already received some form of contemporary programming, so the difference between the conventional and novel program in groups could be underestimated. If the historical group had been earlier, the benefit would probably have been higher.

Also, in order to avoid selection bias that might result from the exclusion of the so called "good patients" (namely those without previous therapies), some of our study patients were also included in the early historical control group. However, even with the inclusion of these patients, who had defibrillators for a longer time and were free from previous episodes of ICD therapies, we had found significant differences in

the studied endpoints.

It was not possible to determine the total number of ventricular events for each group in order to understand if the number of ICD therapies has been reduced due to less arrhythmic events or because of the new programming configurations. This information was not available in the conventional programming group.

Finally, due to the small number of randomized patients the analyses of the relationship between device programming and endpoints in the high rate and delayed detection groups had limited power.

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LEGENDS OF FIGURES

Figure 1 – Programming settings in the new programming group

Figure 2 – Study design and enrolment

Figure 3 –Kaplan-Meier survival curve for the primary endpoint (any therapy)

Tables

Table 1 - Baseline demographic and clinical characteristics according to treatment group

	New programming (n=89)	Conventional Programming (n=94)	p-value
Demographic Data	Demographic Data	Demographic Data	Demographic Data
Age (years), mean ± SD	66 ± 9	67 ± 10	0.243
Male gender, n (%)	68 (76)	80 (85)	0.135
Heart failure condition	Heart failure condition	Heart failure condition	Heart failure condition
Ischemic heart failure, n (%)	49 (55)	61 (65)	0.101
LV ejection fraction (%), mean ± SD	27 ± 6	28 ± 7	0.537
NHYA class I-II, n (%)	70 (78)	67 (71)	0.250
Risk factors and history	Risk factors and history	Risk factors and history	Risk factors and history
Hypertension, n (%)	62 (70)	64 (68)	0.818

	New programming (n=89)	Conventional Programming (n=94)	p-value
Diabetes mellitus, n (%)	36 (40)	42 (45)	0.563
Smoking[1], n (%)	30 (34)	34 (36)	0.398
Dyslipidemia, n (%)	55 (62)	66 (70)	0.669
Lung disease[2], n (%)	12 (14)	10 (11)	0.554
Obstructive Sleep Apnea, n (%)	11 (12)	12 (13)	0.934
Stroke/transient ischemic attack, n (%)	12 (14)	20 (21)	0.165
Atrial fibrillation (AF)	34 (38)	43 (46)	0.302
Medication	Medication	Medication	Medication
ACEI/ARB/ARNI, n (%)	85 (96)	90 (96)	0.937
Beta-blocker, n (%)	81 (91)	83 (88)	0.548
Aldosterone antagosnists, n (%)	49 (55)	35 (37)	0.016
Diuretic, n (%)	66 (74)	63 (67)	0.290
Digoxin, n (%)	8 (9)	10 (11)	0.708
Anti-arrhytmic drugs[3], n (%)	9 (10)	15 (16)	0.242
Oral anticoagulation, n (%)	43 (48)	49 (52)	0.606
Type of device	Type of device	Type of device	Type of device
Implantable cardioverter-defibrillator, n (%)	47 (53)	54 (57)	0.528

[1] Includes current and past smoking.[2] Includes chronic obstructive pulmonary disease (COPD) and asthma
[3] Includes amiodarone and sotalol.

Table 2 – Univariate logistic regression analysis for each of the secondary endpoints

	Hazard ratio (HR)	Confidence interval (CI)	p-value
Primary endpoint	Primary endpoint	Primary endpoint	Primary endpoint
Any therapy	0.265	0.121-0.577	0.001
Secondary endpoints	Secondary endpoints	Secondary endpoints	Secondary endpoints
Appropriate therapies	0.232	0.089-0.600	0.003
Appropriate shocks	0.425	0.137-1.319	0.139
Appropriate ATP	0.276	0.093-0.817	0.020
Inappropriate shocks	0.155	0.019-1.242	0.079
Any shock	0.223	0.076-0.660	0.007
Sudden death	1.137	0.071-18.175	0.928
Cardiovascular death	0.637	0.186-2.176	0.472
All-cause death	1.045	0.516-2.113	0.904

Supplementary table 1 - Baseline demographic and clinical characteristics of the randomized

new programming group

		High rate therapy (n=47)	Delayed therapy (n=42)	p-value
Demographic Data	Demographic Data	Demographic Data	Demographic Data	Demographic Data
Age (years), mean ± SD	67 ± 9	67 ± 9	65 ± 9	0.589
Male gender, n (%)	37 (79)	37 (79)	32 (76)	0.775
Heart failure condition	Heart failure condition	Heart failure condition	Heart failure condition	Heart failure condition
Ischemic heart failure, n (%)	23(49)	23(49)	24 (57)	0.439
LV ejection fraction (%), mean ± SD	27 ± 7	27 ± 7	28 ± 6	0.152
NHYA class I-II, n (%)	38 (81)	38 (81)	32 (76)	0.250
Risk factors and history	Risk factors and history	Risk factors and history	Risk factors and history	Risk factors and history
Hypertension, n (%)	30 (64)	30 (64)	32 (76)	0.205
Diabetes mellitus, n (%)	16 (34)	16 (34)	20 (48)	0.193
Smoking[1], n (%)	17 (36)	17 (36)	13 (31)	0.326
Dyslipidemia, n (%)	29 (62)	29 (62)	26 (62)	0.984
Lung disease[2], n (%)	6 (13)	6 (13)	10 (11)	0.554
Obstructive Sleep Apnea, n (%)	9 (19)	9 (19)	2 (5)	0.040
Stroke/transient ischemic attack, n (%)	3 (6)	3 (6)	9 (21)	0.038
Atrial fibrillation (AF)	16 (34)	16 (34)	18 (43)	0.393
Medication	Medication	Medication	Medication	Medication
ACEI/ARB/ARNI, n (%)	45 (96)	45 (96)	40 (95)	0.908
Beta-blocker, n (%)	42 (89)	42 (89)	39 (93)	0.565
Aldosterone antagosnists, n (%)	28 (60)	28 (60)	21 (50)	0.365
Diuretic, n (%)	33 (70)	33 (70)	33 (79)	0.369
Digoxin, n (%)	4 (9)	4 (9)	4 (10)	0.868
Anti-arrhytmic drugs[3], n (%)	6 (13)	6 (13)	3 (7)	0.380

		High rate therapy (n=47)	Delayed therapy (n=42)	p-value
Oral anticoagulation, n (%)	23 (49)	23 (49)	20 (48)	0.901
Type of device Implantable cardioverter-defibrillator, n (%)	Type of device 26 (55)	Type of device 26 (55)	Type of device 21 (50)	Type of device 0.616

[1] Includes current and past smoking[2] Includes chronic obstructive pulmonary disease (COPD) and asthma.
[3] Includes amiodarone and sotalol

		"High-rate" therapy	"Delayed" therapy
Zone 1	Heart rate (1)	≥150 bpm (400ms)	≥150 bpm (400ms)
	Time/intervals for detection	12 sec / 32 intervals	12 sec / 32 intervals
	Therapy	Monitor only	Monitor only
Zone 2	Heart rate (1)	≥200 bpm (300ms)	> 188 bpm (320ms) (3)
	Time/intervals for detection	2.5 sec / 12 (or 12/18) intervals	10 sec / 30 (or 30/40) intervals
	Therapy	Shock + quick convert ATP (2)	Shock + quick convert ATP (2)

(1) For devices using cycle length instead of heart rate the value is under parenthesis. (2) Anti-Tachycardia Pacing (ATP) during charge. (3) 190 bpm in case of Boston Scientific® devices; 187 bpm in case of Abbott® devices. Cycle length < 320ms (188 bpm) for Biotronik devices.