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RESEARCH ARTICLE

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.
Aims: 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: 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.
Results: 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 in 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 highrate 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 cardiovertor-defibrillator
LVEF: Left ventricle ejection fraction
SCD: Sudden cardiac death
SVT: Supra-ventricular tachycardia
VF: Ventricular Fibrillation
VT: Ventricular tachycardia

1. INTRODUCTION

Implantable cardioverter-defibrillators (ICD) have a high success rate in terminating ventricular tachycardia (VT) or ventricular fibrillation (VF) rapidly. Along with the results of clinical trials showing improvement in survival, the use of implantable cardioverter-defibrillators (ICD) is a well stablished therapy in European guidelines[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 (primary prevention). Recent registries also corroborate with ICD benefit in contemporary HF patients [2, 3].

Conventional ICD therapies include anti-tachycardia pacing (ATP) and internal shocks (usually with 36 Joules). ATP refers to the use of pacing stimulation techniques for termination of tachyarrhythmias and offer the potential for painless termination of certain types of arrhythmias, particularly slow monomorphic VT involving a reentry circuit. However, in a few cases, it can accelerate or degenerate a monomorphic tachycardia into polymorphic VT or FV. Indeed ATP is generally programmed as a first attempt to terminate a slow VT (generally monomorphic) or while charging an internal shock in faster VT or VF. Shocks have a higher efficacy in terminating VT or VF but are very painful.

Programming tachycardia zones in patients with ICD is not straightforward since there are many particularities and different algorithms according to different manufacturers. Generally, patients in secondary prevention are programmed according to their previous tachycardias, but is expected that patients in primary prevention (who did not experience any VT or VF) are programmed in a similar way. The main objective is to treat VT/VF while avoiding unnecessary shocks.

In recent years, increasing awareness of the frequency and the adverse outcomes associated with avoidable ICD therapies also emerged. Several studies, including four randomized trials (MADIT-RIT, EMPIRIC, ADVANCE III and PROVIDE)[4-8] and 2 prospective studies (PREPARE and RELEVANT)[9-10] suggested that increasing detection duration and/or detection heart rate resulted in a reduction of inappropriate therapies and all-cause mortality when compared with conventional programming. Based on these studies and on a meta-analysis including all of them[11], generic device programming guidelines were issued in a 2015 Consensus Statement[12], 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[13].

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.

2. METHODS

2.1 Study design

The study was a prospective, single center, randomized clinical trial of two defibrillator tachycardia programming strategies and included a retrospective cohort of patients of the

same institution, programmed at physician consideration.

2.2 Study population

Eligible patients for the prospective cohort were >18 years of age and had a defibrillator [ICD or cardiac resynchronization therapy (CRT) with a defibrillator (CRT-D)] implanted for primary prevention of SCD after 2013. Patients with a specific indication for individualized programming were excluded. For the retrospective nonrandomized programming cohort, the same eligibility criteria were applied. To avoid selection bias, being part of the randomized group was not an exclusion criterion for being included in the retrospective group. Otherwise, "good" patients with no previous therapies would be excluded from the control group.

2.3 Study procedures

In the prospective cohort, all subjects who met eligibility requirements were randomized to receive an ICD programming intended to reduce therapies, as follows: a high-rate detection group and a delayed detection group (table 1). Subjects were randomized in schedule presential checkup or at the time of device implantation. In the same center, a retrospective cohort of patients programmed at physician consideration was identified, providing they met eligibility.

2.4 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 control 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 patients´ characteristics were analyzed.

2.5 Programming

Patients enrolled in the study group were randomized to one of the two programming configurations: high-rate detection or delayed detection. Tachyarrhythmia detection and therapy settings were chosen to allow a uniform programming across all manufacturers. Details are displaced in table 1. The time taken to detect 30 intervals using fixed 8 of 10 interval detection plus adding a time delay was approximated according to recommendations[12]. Programming of the VT/VF detection and therapy parameters in the control cohort was not specified and was at the discretion of the physician and variable from patient to patient. 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.

Table 1: Programming settings in the new programming group

		"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.

2.6 Endpoints

Endpoints were assessed from the time of randomization (in the new programming group) through the end of the study or if programming zones were exchanged. In the control group, endpoints were assessed during an equivalent

period of time prior to the beginning of randomization.

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.

2.7 Ethics

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

2.8 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. Univariate and multivariate logistic regression analysis was used to calculate the odds ratio (OR) 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.

3 RESULTS

3.1 STUDY POPULATION

Between January and June 2017, 57 patients that had scheduled in-clinic checkup were enrolled. Starting from 2017 and until 2019, 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 had scheduled checkup between January and June 2014 and 30 who implanted a defibrillator afterwards and until the end of 2016 (figure 1).

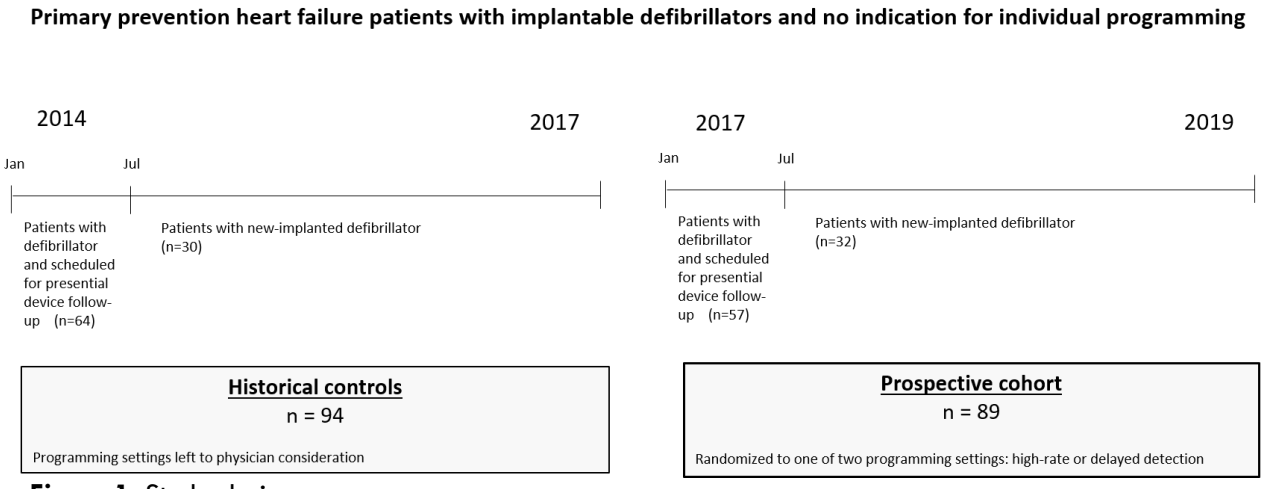


Figure 1: Study design

The mean age of overall population was 67 ± 10 years and 82% were male. Basal characteristics of the two studied groups are shown in table 2. Patients in the new programming group were more frequently under spironolactone (49% vs 35%, p=0.016). No other characteristics differ between the groups. Median follow-up was 20 ± 7 months. No patients were lost to follow-up.

Table 2: Baseline characteristics of the studied groups

	Therapy reduced programming (n=89)	Conventional Programming (n=94)	p-value
Demographic Data			
Age (years), mean ± SD	66 ± 9	67 ± 10	0.243
Male gender, n (%)	68 (76)	80 (85)	0.135
Heart failure condition			
Ischemic heart failure, n (%)	47 (53)	61 (65)	0.071
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			
Hypertension, n (%)	62 (70)	64 (68)	0.818
Diabetes mellitus, n (%)	36 (40)	42 (45)	0.563
Smoking[1], n (%)	30 (34)	36 (38)	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			
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			
Implantable cardioverter-defibrillator, n (%)	47 (53)	54 (57)	0.528

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

3.2 Endpoints

3.2.1 Primary endpoint

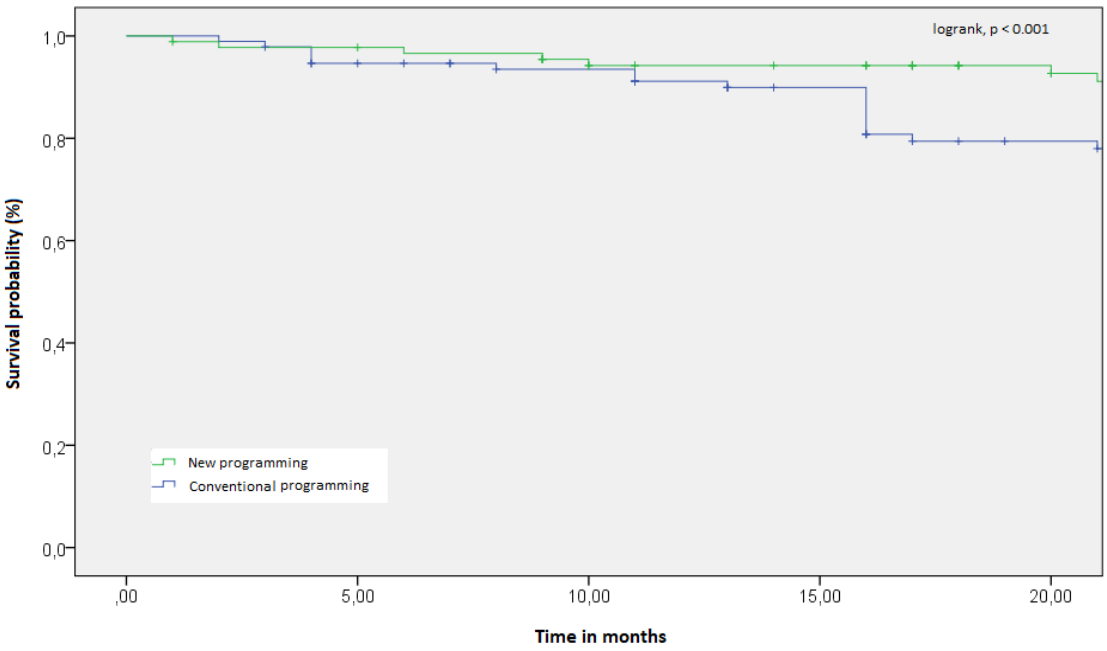
The primary endpoint (any therapy delivered by the ICD) occurred in 30 patients: 10 patients in the new programming group (16%) comparing with 30 patients in the conventional programming group (32%) (p=0.010). Subjects who experienced the primary endpoint did not differ from those who remained event-free, 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 (Hazard Ratio (HR) = 0.265, 95% confidence interval (CI) 0.121-0.577, p=0.001) (table 3). 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). If cardiovascular risk factors, comorbilities and use of other medication were considered, the results remained almost unchanged. Kaplan-Meier

survival curve demonstrated that long-term survival free from therapies is better in patients with NEW programming (logrank, p<0.001) (figure 2).

Table 3: Univariate logistic regression analysis for each of the secondary endpoints

	Hazard ratio (HR)	Confidence interval (CI)	p-value
Primary endpoint			
Any therapy	0.265	0.121-0.577	0.001
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

Figure 2: Kaplan-Meier survival curve for the primary endpoint (any therapy)



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). Device programming was not significantly associated with a reduction in appropriate shocks (HR 0.425, 95% CI 0.137-1.319, p=0.139) (table 3).

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 3). 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 3). 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 3).

3.2.2.4 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 3). 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).

3.2.2.5 Syncope

No patient had syncopal events during the follow-up.

3.2.2.5 Sudden death

Sudden death occurred in 2 patients: one patient in each group. In both of them autopsy was not requested. 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]. Is was not possible to know the programming settings of the patient who died suddenly in the conventional programming group.

3.2.2.6 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). Device programming was not significantly associated with death (HR 0.637, 95% CI 0.186-2.176, p= 0.472) (table 3).

Death from all-caused occurred in 34 patients: : 18 patients in the new programming group (20%) and 16 patients (17%) in the conventional programming group (p=0.578). Device programming was not significantly associated with death (HR 1.045, 95% CI 0.516-2.113, p= 0.904) (table 3). 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.

4.1 High rate versus delayed therapy

Basal characteristics of the two randomized groups are shown in table 4. 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.

Table 4: Baseline characteristics of the randomized new programming group

	High rate therapy (n=47)	Delayed therapy (n=42)	p-value
Demographic Data			
Age (years), mean ± SD	67 ± 9	65 ± 9	0.589
Male gender, n (%)	37 (79)	32 (76)	0.775
Heart failure condition			
Ischemic heart failure, n (%)	23(49)	24 (57)	0.439
LV ejection fraction (%), mean ± SD	27 ± 7	28 ± 6	0.152
NHYA class I-II, n (%)	38 (81)	32 (76)	0.250
Risk factors and history			
Hypertension, n (%)	30 (64)	32 (76)	0.205
Diabetes mellitus, n (%)	16 (34)	20 (48)	0.193
Smoking[1], n (%)	17 (36)	13 (31)	0.326
Dyslipidemia, n (%)	29 (62)	26 (62)	0.984
Lung disease[2], n (%)	6 (13)	10 (11)	0.554
Obstructive Sleep Apnea, n (%)	9 (19)	2 (5)	0.040
Stroke/transient ischemic attack, n (%)	3 (6)	9 (21)	0.038
Atrial fibrillation (AF)	16 (34)	18 (43)	0.393
Medication			
ACEI/ARB/ARNI, n (%)	45 (96)	40 (95)	0.908
Beta-blocker, n (%)	42 (89)	39 (93)	0.565
Aldosterone antagosnists, n (%)	28 (60)	21 (50)	0.365
Diuretic, n (%)	33 (70)	33 (79)	0.369
Digoxin, n (%)	4 (9)	4 (10)	0.868
Anti-arrhytmic drugs[3], n (%)	6 (13)	3 (7)	0.380
Oral anticoagulation, n (%)	23 (49)	20 (48)	0.901
Type of device			
Implantable cardioverter-defibrillator, n (%)	26 (55)	21 (50)	0.616

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

DISCUSSION

The concept of optimal ICD programming has evolved in recent years from a perception of a rapid detection and treatment of VT/VF to a more permissive strategy, in order to reduce avoidable shocks[12]. Numerous reasons have been postulated for this change, including initial doubt in ICD efficacy, concerns in undersensing and underdetection of VF and its use in secondary prevention patients with a higher risk of arrhythmic events. Also, demonstration of an increased defibrillation threshold when VF was prolonged[15] was responsible for the idea of programming for rapid tachycardia detection and treatment as soon as possible.

Nowadays, concepts have evolved and, on the contrary, the adverse effects of avoidable therapies were empathized. As such, an evidence-based programming is recommended[12]. 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. Some manufacturers use seconds to quantify the duration of an episode, while others use intervals, which is not the same since it depends on the heart rate of the tachycardia. Even the heart rate limit to define the tachycardia zones is not exactly the same between manufacturers. For clinicians who deal with defibrillator programming on a daily basis, it would be more practical to have only one programming that can be used across all manufacturers.

In the present study, 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 of the strategies were effective and safe. However, no conclusion about the benefit of one programming over the other could be done, due to the reduced number of patients assigned (related to the number of patients who implanted a defibrillator in our center). Despite this fact, the authors consider important conclusions can be drawn from this study.

When comparing our interventional group (new programming) with a recent but historical group of the same center (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 in this interventional group ATPs were exclusively delivered in the FV zone while charging and it is also consistent with previous studies[4-10]. Despite the fact that ATP can be effective and avoids shocks[16-17], 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[16-20], being responsible for shock delivery and even incessant electrical storm. Using ATP therapy exclusively during charge, as in new programming group, had no adverse effects, such as syncope. In fact, "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.

There was a trend for a reduction in inappropriate shocks with the new programming (HR 0.155, p=0.079). The absence of statistical significance is probably related to the reduced number of events since the total number of shocks was significantly reduced, but not the number of appropriate shocks. In fact, inappropriate shocks affected 4% of patients in the new programming group, a proportion similar to other studies[4-10].

Regarding appropriate shocks, they occurred in 5.6% of all patients, independently of 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[4-10].

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[14], 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 access 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 in the high rate arm so his tachycardia configuration was in accordance with MADIT-RIT (the same manufacturer and the same programming used in the clinical trial), thus its 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 they complied with more generic recommendations of the Consensus Statement[13]. This is not what happened in our case since the patient had a programming in accordance with a previous randomized trial[5-6].

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 such differences[11] 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 therapy reduced programming. In the present study, such deduction cannot 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 [21,22], 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 [2,3,23] comparing to studies performed some years ago [24-26]. 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[27]. 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[28], 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 reducing all defibrillator therapies, with no safely concerns.

LIMITATIONS

This was a single center study and included an historical control group, in which the tachycardia settings were not uniform across all patients. The number of randomized patients was low and analyses of the relationship between device programming and endpoints in the high rate and delayed detection groups have limited power.

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Conflicts of interest: none

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