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Long Detection Programming in Single-Chamber Defibrillators Reduces Unnecessary Therapies and Mortality

The ADVANCE III Trial

Maurizio Gasparini, MD,[a] Maurizio G. Lunati, MD,[b] Alessandro Proclemer, MD,[c] Angel Arenal, MD,[d] Axel Kloppe, MD,[e] Josè B. Martínez Ferrer, MD,[f] Ahmad S. Hersi, MD,[g] Marcin Gulaj, MD,[h] Maurits C.E. Wijffels, MD,[i] Elisabetta Santi, MS,[j] Laura Manotta, MS,[k] Niraj Varma, MD, PhD[l]

ABSTRACT

OBJECTIVES This study sought to evaluate the effects of programming a long detection in single-chamber (VVI) implantable cardioverter-defibrillators (ICDs) in the multicenter prospective ADVANCE III (Avoid DeliVering TherApies for Non-sustained Arrhythmias in ICD PatiEnts III) trial.

BACKGROUND Programming strategies may reduce unnecessary ICD shocks and their adverse effects but to date have been described only for dual-chamber ICDs.

METHODS A total of 545 subjects (85% male; atrial fibrillation 25%, left ventricular ejection fraction 31%, ischemic etiology 68%, secondary prevention indications 32%) receiving a VVI ICD were randomized to long detection (30 of 40 intervals) or standard programming (18 of 24 intervals) based on device type, atrial fibrillation history, and indication. In both arms, antitachycardia pacing (ATP) therapy during charging was programmed for episodes with cycle length 320 to 200 ms and shock only for cycle length <200 ms. Wavelet and stability functions enabled. Therapies delivered were compared using a negative binomial regression model.

RESULTS A total of 267 patients were randomized to long detection and 278 to the control group. Median follow-up was 12 months. One hundred twelve therapies (shocks and ATP) occurred in the long detection arm versus 257 in the control arm, for a 48% reduction with 30 of 40 intervals (95% confidence interval [CI]: 0.36 to 0.76; p = 0.002). In the long detection arm, overall shocks were reduced by 40% compared to the control arm (48 vs. 24; 95% CI: 0.38 to 0.94; p = 0.026) and appropriate shocks by 51% (34 vs. 74; 95% CI: 0.26 to 0.94; p = 0.033). Syncopal events did not differ between arms, but survival improved in the long detection arm.

CONCLUSIONS Among patients implanted with a VVI ICD, programming with the long detection interval significantly reduced appropriate therapies, shocks, and all-cause mortality. (Avoid DeliVering TherApies for Non-sustained Arrhythmias in ICD PatiEnts III [ADVANCEIII]; NCT00617175) (J Am Coll Cardiol EP 2017;3:1275–82) © 2017 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

From the [a]Humanitas Research Hospital IRRCCS, Rozzano Milan, Italy; [b]Azienda Ospedaliera Niguarda Ca' Granda, Milan, Italy; [c]Azienda Ospedaliero Universitaria Santa Maria della Misericordia, Udine, Italy; [d]Hospital Gregorio Maranon, Madrid, Spain; [e]Medizinische Klinik II, Kardiologie und Angiologie, Berufsgenossenschaftliches Universitätsklinikum Bergmannsheil, Ruhr-Universität-Bochum, Bochum, Germany; [f]Hospital de Txagorritxu C/ José Achotegui, Vitoria, Spain; [g]King Saud University, Riyadh, Saudi Arabia; [h]MSWiA Hospital, Bialystok, Poland; [i]St. Antonius Ziekenhuis Hospital, Nieuwegein, the Netherlands; [j]Medtronic, Rome, Italy; [k]Medtronic, Milan, Italy; and the [l]Cleveland Clinic Cardiovascular Medicine, Cleveland, Ohio. The ADVANCE III Study was supported financially by Medtronic, Inc. Medtronic participated in the design, conduct, and management of the study and had no role in the collection of data. Medtronic participated in the review and approval of the manuscript and had no role in the interpretation of data. Dr. Lunati has received research grants and honoraria from Medtronic, Inc. Dr. Varma has received research grants, consultant fees, and advisory board fees from Medtronic, Inc. Dr. Kloppe has received study grants and reimbursements for lecture fees. E. Santi and L. Manotta are employees of Medtronic, Inc. All other authors have reported that they have no relationships relevant to this paper to disclose.

ABBREVIATIONS AND ACRONYMS

ATP = antitachycardia pacing

CI = confidence interval

CRT = cardiac resynchronization therapy

DDD = dual chamber

ICD = implantable cardioverter-defibrillator

IRR = incidence rate ratio

VF = ventricular fibrillation

VT = ventricular tachycardia

VVI = single chamber

The implantable cardioverter-defibrillator (ICD) improves survival in high-risk patients. At the same time, there is increasing awareness that unnecessary ICD therapies may have adverse clinical effects. Strategies to reduce these effects have included optimization of programming, particularly delay to delivered therapy. Positive results from large trials have earned this approach strong recommendations (1-6). However, the majority of the results described to date are related to dual-chamber (DDD) ICDs, likely because these systems have sophisticated discriminatory algorithms, often considered essential to reduce the risk for inappropriate shocks (i.e., therapy delivered for nonventricular tachyarrhythmias) in comparison to single-chamber (VVI) ICDs. This remains controversial but important to resolve because implantation of DDD ICDs in patients without pacing indications is associated with increased complications (7) and may be contested by insurance carriers. Recent programming guidelines remain ambiguous, advocating the use of discriminators (Class I, Level of Evidence: IB-R) to reduce inappropriate therapies but simultaneously stating that it is reasonable to select a VVI ICD if the sole reason for DDD ICD implant is only for supraventricular tachycardia discrimination (Class IIa, Level of Evidence: B-NR). There is a strong recommendation to use antitachycardia pacing (ATP) (Class Ia) unless ATP is known to be proarrhythmic or ineffective, although this determination may require dual-chamber electrograms. These contradictions exist because of the dearth of data for VVI ICDs, which, although included in trials testing ICD efficacy, have been excluded from most trials testing optimal programming strategies.

The ADVANCE III (Avoid DeliVering TherApies for Non-sustained Arrhythmias in ICD PatiEnts III) trial demonstrated that extending the duration of monitoring delay before initiation of therapy reduced ICD therapies by 37% compared to conventional programming. This study aimed to elucidate the efficacy of this programming strategy among patients receiving a VVI ICD (4).

METHODS

The ADVANCE III trial was a prospective superiority trial that tested the effect of long detection intervals in reducing unnecessary ICD therapies. The protocol and primary manuscript have been published previously (4,8). In brief, 1,902 patients implanted with commercially available VVI, DDD, and cardiac resynchronization therapy (CRT) ICDs (Medtronic, Inc., Mounds View, Minnesota) for primary or secondary prevention of sudden cardiac death between 2008 and 2010 were enrolled in 94 international centers and randomized to intervention with long detection settings or to standard interval programming (control). Randomization was stratified strategically to balance baseline characteristics, such as ICD indication (primary vs. secondary), type of device (VVI, DDD, or CRT), and atrial fibrillation, to avoid bias due to these potential confounders. Patients were followed every 3 months for 1 year. The ethics review committee at each center approved the protocol, and all patients provided written informed consent.

DEVICE PROGRAMMING. All ICDs were programmed with a ventricular fibrillation (VF) zone to detect arrhythmias with cycle length ≤320 ms, with a single attempt at ATP during the capacitor charge for fast arrhythmias with cycle length up to 200 ms but shock only for cycle length <200 ms. VVI discriminators enabled were wavelet (match threshold 70%) and stability (50 ms). In the intervention arm, detection was prolonged to 30 of 40 intervals to permit delay in therapy (if needed). In the standard interval detection group, detection was programmed to 18 of 24 intervals as used in the PainFREE II (Pacing Fast VT REduces Shock ThErapies) trial (9). A ventricular tachycardia (VT) therapy zone was allowed only in cases of documented VT with cycle length >320 ms, with specific programming individualized by the implanting physician.

STUDY OBJECTIVES. In this analysis of patients receiving a VVI ICD, we applied the test measures used in the main trial, that is, whether intervention with long detection intervals would reduce ICD therapies for treatment of episodes with a fast cycle length ≤320 ms with ATP and shocks (combined or

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individually), rates of appropriate and inappropriate therapies, hospitalizations, and incidences of arrhythmic syncope and death.

All episodes of sustained VT/VF and monitored VT with stored electrograms were reviewed by at least 2 members of a blind episode review committee to assess appropriateness of device classification and therapy efficacy. Appropriate therapy was defined as therapy delivered for monomorphic or polymorphic VT and for VF. All ICD therapies delivered for supraventricular episodes or nonarrhythmic events (e.g., noise, oversensing) were classified as inappropriate therapies. A second independent adverse event committee reviewed and classified all syncopal events and deaths.

STATISTICAL ANALYSIS. Methods for sample size calculation, randomization process, and data collection have been previously described (4). Categorical variables are reported as counts and percentage, and continuous data are reported as mean ± SD. Comparisons of baseline characteristics were performed using the Student's *t*-test and chi-square test for continuous and categorical data, respectively. Rates of delivered therapies are expressed per 100 patient-years and compared between groups by incidence rate ratio (IRR) and 95% confidence interval (CI). IRR <1 indicates a lower incidence of therapies in the long detection group. Survival is represented by Kaplan-Meier curves and were compared between study arms using the log-rank test. Hazard ratio and relative 95% CI are reported and were computed using the Cox proportional hazards survival model. A random effect was included to take into account intercenter heterogeneity. All tests were 2-sided, and a 2-tailed p value of 0.05 was considered statistically significant. Stata version 12.1 (Stata Corporation, College Station, Texas) was used for computation.

RESULTS

A total of 545 patients received a VVI ICD in ADVANCE III (28.7% of the overall population) and were equally distributed in the study arms. The patients had similar baseline characteristics, except for a slight difference in the incidence of prior revascularization (Table 1). A previous history of sustained VT was documented in 62 patients in the control arm and 48 patients in the long detection arm therefore a VT zone was programmed according to the physician's discretion. During median follow-up of 12 months (25th to 75th percentiles: 11 to 13 months), session records remained virtually complete in both groups, with 258 of 278 patients (92.8%) and 251 of 267 patients (94.0%) with available save to disks in the long detection arm and in the control arm, respectively. Hospitalizations, syncopal events, and deaths are reported for the complete cohort of patients implanted with a VVI ICD,

TABLE 1 Baseline Characteristics

Single Chamber	Control Arm (n = 278, 51%)	Long Detection Arm (n = 267, 49%)
Patient demographics		
Age, yrs	62 (12)	62 (13)
Male	238 (86)	228 (85)
Medical history		
Secondary prevention	90 (32)	85 (32)
VF/ventricular flutter	35 (13)	27 (10)
Sustained VT history	62 (22)	48 (18)
Permanent atrial fibrillation	37 (13)	41 (15)
NYHA functional class III or IV	63 (23)	6 (23)
Angina	37 (14)	27 (10)
Coronary artery disease	181 (65)	190 (71)
Previous revascularization*	113 (41)	134 (50)
QRS, ms	109 (27)	105 (24)
LBBB	30 (11)	36 (13)
Hypercholesterolemia	149 (54)	145 (55)
Diabetes	83 (30)	77 (29)
Chronic kidney disease	33 (12)	29 (11)
Baseline echocardiographic measures		
Moderate/severe mitral regurgitation	32 (20)	26 (16)
LVEF, %	31 (11)	31 (10)
LVDD, mm	62 (10)	61 (9)
Baseline medical therapy		
ACE inhibitor/ARB	219 (79)	212 (79)
Antiarrhythmic drug	43 (15)	38 (14)
Beta-blocker	232 (83)	227 (85)
Diuretic	205 (73)	181 (68)
Antiplatelet	157 (56)	175 (66)
Anticoagulant	96 (35)	78 (29)
Cardiac glycoside	44 (16)	35 (13)
Hypolipidemic	168 (60)	163 (61)
Nitrate	47 (17)	37 (14)
Other cardiac medications	36 (13)	15 (6)

Values are n (%). *p < 0.05.

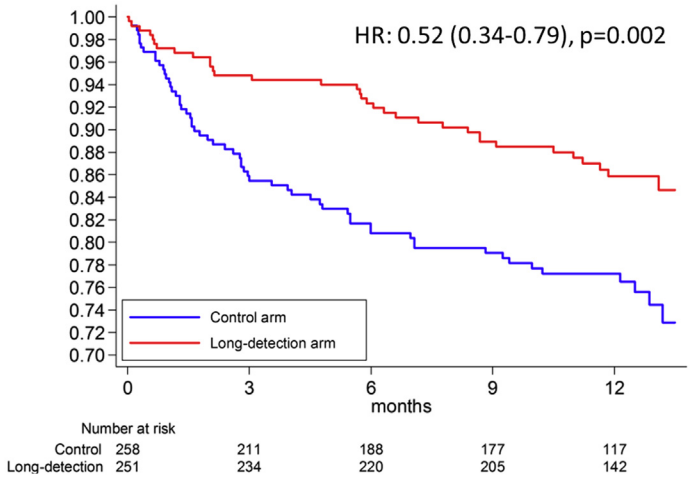
ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; LBBB = left bundle branch block; LVDD = left ventricular diastolic diameter; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; VF = ventricular fibrillation; VT = ventricular tachycardia.

TABLE 2 Results of Delivered ICD Therapies According to Intention-to-Treat Analysis

		No. of Therapies (# of Treated Patients)	Rate per 100 Patient-Years	IRR (95% CI)	p Value
Overall	Standard interval	257 (60)	106 (93-120)	1.00	0.002
	Long detection	112 (34)	45 (38-55)	0.52 (0.36-0.76)	
ATP	Standard interval	140 (57)	58 (49-68)	1.00	<0.001
	Long detection	53 (31)	22 (16-28)	0.49 (0.33-0.72)	
Shock	Standard interval	117 (42)	48 (40-58)	1.00	0.026
	Long detection	59 (26)	24 (18-31)	0.60 (0.38-0.94)	

ATP = antitachycardia pacing; CI = confidence interval; IRR = incidence rate ratio.

FIGURE 1 Therapy-Free Survival Estimate



Kaplan-Meier plot of appropriate and inappropriate implantable cardioverter-defibrillator therapy (antitachycardia pacing and shocks). HR = hazard ratio.

whereas the subgroup of patients with at least 1 save to disk available was used for the analysis of delivered therapies.

OVERALL THERAPIES DELIVERED. Programming long detection intervals dramatically reduced therapies overall and ATPs and shocks individually (Table 2, Figure 1).

Overall, 112 therapies were delivered in 34 patients in the long detection arm versus 257 therapies in 60 patients in the control arm, for a 48% reduction with intervention (IRR: 0.52; 95% CI: 0.36 to 0.76; p = 0.002). The number of shocks delivered was 40% less in the long detection group (24 per 100 patient-years; 95% CI: 18 to 31) versus the control arm (48 per 100 patient-years; 95% CI: 40 to 58) (IRR: 0.60; 95% CI: 0.38 to 0.94; p = 0.026). ATP delivery rates of 22 per 100 patient-years (95% CI: 16 to 28) in the long detection arm contrasted with 58 per 100 patient-years (95% CI: 49 to 68) in the control arm (IRR: 0.49; 95% CI: 0.33 to 0.72; p < 0.001).

TABLE 3 Results of Appropriate ICD Therapies According to Intention-to-Treat Analysis

		No. of Therapies (# of Treated Patients)	Rate per 100 Patient-Years	IRR (95% CI)	p Value
Overall	Standard interval	179 (48)	74 (63-85)	1.00	0.001
	Long detection	73 (23)	30 (23-38)	0.45 (0.28-0.71)	
ATP	Standard interval	105 (45)	43 (35-52)	1.00	0.001
	Long detection	39 (21)	16 (11-22)	0.43 (0.27-0.71)	
Shock	Standard interval	74 (30)	30 (24-38)	1.00	0.033
	Long detection	34 (15)	14 (10-19)	0.49 (0.26-0.94)	

Abbreviations as in Table 2.

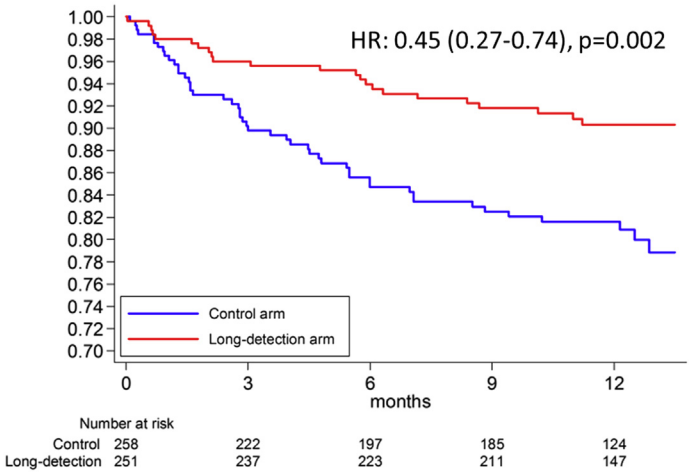
APPROPRIATE THERAPIES. Appropriate therapies (both ATP and shocks) were markedly reduced in the long detection arm (30 per 100 patient-years; 95% CI: 23 to 38) compared to the standard programming group (74 per 100 patient-years; 95% CI: 63 to 85), representing a 55% reduction (IRR: 0.45; 95% CI: 0.28 to 0.71; p = 0.001) (Table 3, Figure 2). Notably, fewer patients in the long detection arm (15 of 251 [5.9%]) experienced an appropriate shock in comparison with the control arm (30 of 258 [11.6%]), leading to fewer shocks to treat ventricular arrhythmias in the long detection arm (14 per 100 patient-years; 95% CI: 10 to 19) versus the control arm (30 per 100 patient-years; 95% CI: 24 to 38) (IRR: 0.49; 95% CI: 0.26 to 0.94; p = 0.033). In addition, appropriate ATP therapies also were reduced (16 per 100 patient-years; 95% CI: 11to 22 in the long detection arm vs. 43 per 100 patient-years; 95% CI: 35 to 52) (IRR: 0.43; 95% CI: 0.27 to 0.71; p = 0.001).

INAPPROPRIATE THERAPIES. Inappropriate therapies occurred infrequently in the study population overall (6.1%). Fewer inappropriate interventions were reported in the long detection arm (39 therapies in 14 patients in the long detection arm vs. 78 in 17 patients in the control arm). However, given the paucity of these types of events, it was not possible to demonstrate any statistically significant difference between the interventions (IRR: 0.57; 95% CI: 0.24 to 1.36; p = 0.207). Twenty-five inappropriate shocks were delivered in 12 patients in the long detection arm versus 43 in 15 patients in the control group (IRR: 0.78; 95% CI: 0.37 to 1.67; p = 0.522). A similar trend was observed with inappropriate ATP therapies (14 ATPs in 13 patients programmed with the long detection interval vs. 35 ATPs in 17 patients with the standard setting; IRR: 0.72; 95% CI: 0.37 to 1.42; p = 0.342).

HOSPITALIZATIONS, SYNCOPAL EVENTS, AND DEATHS. Kaplan-Meier estimates of time to first all-cause and cardiovascular hospitalization are shown in Figure 3. Patients in the long detection arm had a 27% probability of being hospitalized for any cause at 1 year compared to 36% in the control group (p = 0.04). This result was mainly driven by cardiovascular-related hospitalizations (20% vs. 28% risk; p = 0.04). Syncopal episodes related to arrhythmic episodes occurred rarely and were reported for only 2 patients (2 events) in the long

detection arm versus 6 patients (7 events) in the control arm (IRR: 0.26; 95% CI: 0.04 to 1.75; p = 0.165). Programming long detection had a significant survival advantage. Eight patients (3.0%) in the long detection arm died versus 20 (7.2%) in the control arm during 12-month follow-up. Intervention was associated with a 59% reduction in mortality (hazard ratio: 0.41; 95% CI: 0.17 to 0.99; p = 0.047). Kaplan-Meier estimates of survival in the 2 arms is shown in **Figure 4**. Considering that mortality did not show any difference when calculating on the overall population of patients enrolled in the ADVANCE III trial (i.e., single-, dual-, and triple-chamber ICDs), we also analyzed separately the DDD+CRTD cohort to refute an increased risk of death in that subgroup. No increased mortality was found in DDD+CRTD patients in the long detection group (Online Figure 1).

FIGURE 2 Appropriate Therapy-Free Survival Estimate



Kaplan-Meier plot of appropriate implantable cardioverter-defibrillator therapy (antitachycardia pacing and shocks). HR = hazard ratio.

DISCUSSION

Our principal findings are that, in a large population of patients treated with a VVI ICD, programming long detection intervals (30 of 40) with the capability to deliver ATP during capacitor charge significantly reduced unnecessary therapies, shocks, overall and cardiovascular hospitalizations, and all-cause mortality. Overall, there was a 48% reduction in all therapies (ATP and shock). Hence, the programming strategy tested in VVI ICDs was strongly and consistently effective across a range of tested metrics.

Consensus exists that unnecessary ICD therapies (appropriate or inappropriate) should be avoided, as evidence mounts for their adverse effects, including impaired quality of life, increased health care utilization, and an association with increased mortality. Shocks (appropriate or inappropriate) may cause cell injury, negative inotropy, and hemodynamic compromise, and they may be proarrhythmic.

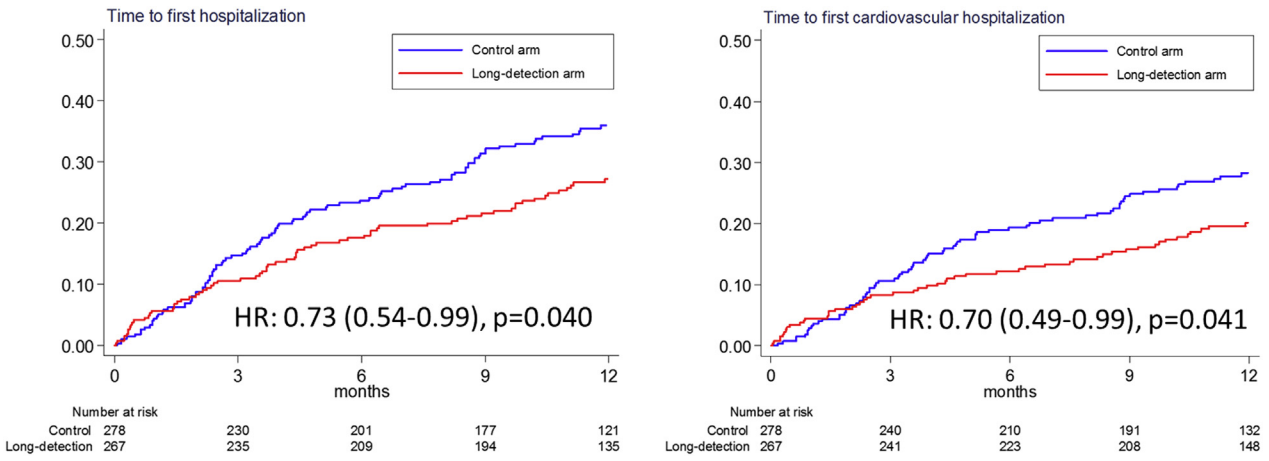
Enabling discrimination algorithms with DDD ICDs to precisely identify supraventricular tachycardias and withhold therapy is a widely exercised option, although it does not reduce appropriate therapy for ventricular arrhythmias that may have self-terminated with time. Optimizing ICD programming is an alternative method to reduce unnecessary ICD therapies. Studies to date have prolonged time to arrhythmia detection and therapy to allow self-termination of nonsustained events and have shown reductions in appropriate and inappropriate therapies (1-5,9). Notably, these trials predominantly tested DDD ICDs, that is, they superimposed delayed therapies on embedded discrimination algorithms and largely excluded VVI ICDs. In this regard, our results are important, revealing that prolonged detection was highly effective on the single-chamber ICD platform despite the limited discriminators of these devices.

The application of programming delayed therapies to VVI ICDs has significant practical implications. In the United States, data from the National Cardiovascular Data Registry indicate that >60% of ICDs implanted for primary prevention are DDD ICDs, and 60% of patients receiving them have no pacing indication (7). DDD ICDs are associated with greater acute procedural and follow-up complications (7,10) and higher costs to health care systems (11). Any advantage of conventionally programmed DDD ICDs in reducing overall shock therapies simply because they have sophisticated discriminatory algorithms appears to be marginal, if any, and should not form the basis for their use.

Our results have particular gravity because the "standard" intervals (18 of 24) we applied in our control arm are longer than nominal ICD settings ("conventional" in MADIT-RIT [Multicenter Automatic Defibrillator Implantation Trial-Reduce Inappropriate Therapy]), indicating that even further prolongation of time to delivered therapy extends the advantages of this programming strategy.

ICD THERAPIES. Our results are remarkable for showing that among patients receiving a VVI ICD, programming long detection not only reduced all appropriate therapies (ATP and shock) by more than

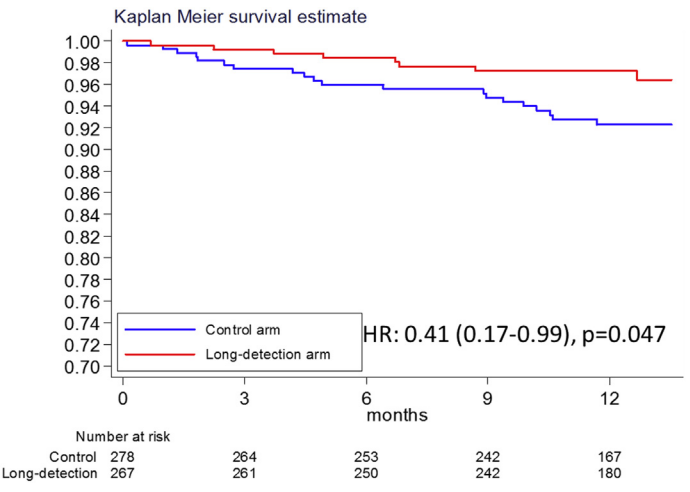
FIGURE 3 Time to First Hospitalization



Kaplan-Meier estimates of first occurrence of all-causes **(left)** and cardiovascular hospitalization **(right).** HR = hazard ratio.

50% but also ATP therapies (27 of 43 [63%]) and shocks (16 of 30 [53%]) when considered individually. These results differ from the overall results from ADVANCE III (including VVI, DDD, and CRT devices) and MADIT-RIT (testing DDD and CRT ICDs), which both found a significant reduction of overall appropriate therapies without a reduction in the number of appropriate shocks. The same results were also found in the DECREASE (Reduction of inappropriate ICD therapies in patients with primary prevention of sudden cardiac death) study (12). Here, during follow-up, 30 of 258 patients (11.6%) programmed to standard settings received appropriate shocks compared to 15 of 251 (5.9%) in the long detection group. This finding suggests that the population of patients receiving a VVI ICD in this trial represents patients with a specific arrhythmic profile characterized by the frequent occurrence of short ventricular arrhythmias lasting >18 beats but prone to self-termination within 29 beats, and that therapy for these events is unnecessary. This assumption is supported by the historical cohort of the PainFREE II study (9), which enrolled patients mainly with a history of coronary artery disease and with no indication for CRT, similar to our study population.

FIGURE 4 Survival



Kaplan-Meier estimates of survival. HR = hazard ratio.

Device-based mechanisms to distinguish supraventricular tachycardia from VT are limited on VVI ICDs (e.g., onset, stability, morphology) but share T-wave recognition, noise oversensing, and prediction of lead failure (13). Atrial lead-based discrimination algorithms are widely used to improve the specificity of ICD therapies. However, whether this practice reduces inappropriate shocks compared to VVI ICDs remains unclear, with some studies showing superiority and others neutrality. This balance indicates that benefits, if any, are likely to be slight. Programming may be more effective. In the MADIT-RIT trial, conventional programming (time to therapy <3.5 s for heart rates ≥170 beats/min) resulted in a high rate of inappropriate antitachycardia therapies, which was attributed to frequent atrial tachyarrhythmias occurring in the range from 170 to 199 beats/min despite the use of atrial lead-based device discriminators in this

range (5). However, these were significantly reduced in Test Arm B of the trial, in which time to therapy was extended (but to <5 s). This suggests greater efficacy of prolonged detection over dual-chamber discriminators, and that many supraventricular tachycardias in ICD populations are short self-terminating events. The control arm (18 of 24) of our current study instituted an even greater delay (>5 s in PainFREE II), likely accounting for the low incidence of inappropriate therapies observed. Further extension of detection intervals to 30 of 40 was associated with trends to further reduction in overall inappropriate therapy rates and in ATPs and shocks individually, but these did not reach statistical significance given the paucity of overall events. Thus, we showed that consistent use of the limited discriminator algorithms available in VVI ICDs combined with a prolonged detection programming strategy yields a low rate of inappropriate therapies (11).

OUTCOMES. A prevalent concern that extension of detection intervals will increase syncopal events due to delay in therapy for hemodynamically compromising ventricular arrhythmia was not supported by our study. Syncope occurred infrequently in both study arms. However, intervention reduced all-cause and cardiovascular hospitalizations by almost one-third.

An important finding was the 59% reduction in all-cause mortality among patients randomized to the long detection group in our subset of patients from ADVANCE III treated with a VVI ICD. These data support the notion that reducing ICD therapies improves survival, as reported by the MADIT-RIT Investigators (5). MADIT-RIT restricted enrollment to patients receiving only DDD and CRT ICDs, but the survival benefit of 44% to 55% reported aligns well with our observations. VVI devices were included in the PROVIDE (Programming Implantable Cardioverter-Defibrillators in Patients with Primary Prevention Indication to Prolong Time to First Shock) trial (14), whose results are in line with those of MADIT-RIT. The mechanism(s) underlying this effect is uncertain. MADIT-RIT and PROVIDE proposed a reduction in inappropriate shocks and/or reduction in ATP (5,15). However, we noted no significant difference in the rates of inappropriate therapies, which were infrequent in any case. In contrast, we demonstrated a large reduction in appropriate ICD therapies (both shocks and ATP). The association of appropriate shocks with mortality may be considered the pivotal observation initiating the promotion of strategies to minimize the number of therapies delivered (16). Our data support the hypothesis that treatment of arrhythmias that may otherwise self-terminate may cause long-term patient harm and erode the survival benefit of the ICD. The mortality reduction found in this subgroup of patients implanted with a VVI ICD may raise concern that the reduction might be counterbalanced by an increased risk of death in the remaining ADVANCE III population (DDD ICD and CRT), given the overall neutral results found in the trial. However, no sizable difference in deaths was found in the DDD ICD+CRT cohort.

STUDY LIMITATIONS. Reasons for VVI ICD treatment allocation are not available in this post hoc analysis, although the patient groups compared (18 of 24 vs. 30 of 40) were well matched for demographics (**Table 1**). This may have influenced our results because we did not observe any mortality benefit in DDD+CRT ICDs considered separately (Online Figure 1). Compared to the overall study cohort, the ADVANCE III VVI subgroup had a higher incidence of coronary artery disease, shorter QRS durations, and fewer patients with left bundle branch block (Online Table 1). Thus, it is possible that this sicker group of patients benefited more from a programming long detection strategy. We included patients with atrial fibrillation or with secondary prevention (groups excluded in other large trials testing programming), so our results are applicable to the broader patient population treated with ICD therapy. The degree of benefit of programming varied between DDD ICDs and CRTDs in MADIT-RIT (17), and here in ADVANCE III we report the strongest effect of long detection in VVI ICDs. We tested devices from only 1 manufacturer (Medtronic, Inc.), and application of our findings to other algorithms and devices is uncertain.

CONCLUSIONS

In this large ancillary analysis of the ADVANCE III trial, we show that an optimized programming combining a long detection setting with ATP during capacitor charge significantly reduced ICD therapies, reduced hospitalizations, and improved clinical outcome with a survival benefit in patients implanted with a VVI ICD.

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ADDRESS FOR CORRESPONDENCE: Dr. Maurizio Gasparini, Electrophysiology and Pacing Unit, Humanitas Research Hospital, IRRCCS, Via Manzoni 56, 20089 Rozzano (MI), Italy. E-mail: maurizio.gasparini@humanitas.it.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Programming a long detection is associated with a lower risk of therapies, shocks, hospitalization, and death among patients implanted with a single-chamber ICD.

TRANSLATIONAL OUTLOOK: Additional randomized trials enrolling a larger cohort of patients receiving a single-chamber ICD and with longer follow-up are warranted to clarify the relationship between long detection programming and death in this compromised population.

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APPENDIX For a supplemental figure and table, please see the online version of this article.