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REVIEW

Programming implantable cardioverter-defibrillators in primary prevention: Higher or later



Programmation des défibrillateurs implantables en prévention primaire : plus haut ou plus tard

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KEYWORDS

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Summary Defibrillator shocks, appropriate or not, are associated with significant morbidity, as they decrease quality of life, can be involved in depression and anxiety, and are known to be proarrhythmic. Most recent data have even shown an association between shocks and overall mortality. As opposed to other defibrillator-related complications, the rate of inappropriate and unnecessary shocks can (and should) be decreased with adequate programming. This review focuses on the different programming strategies and tips available to reduce the rate of shocks in primary prevention patients with left ventricular dysfunction implanted with a defibrillator, as well as some of the manufacturers' device specificities.

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MOTS CLÉS

Défibrillateur ;

Résumé Les chocs délivrés par les défibrillateurs automatiques implantables sont associés à une baisse de la qualité de vie des patients implantés (dépression, anxiété), et peuvent avoir un effet pro-arythmogène. Les études les plus récentes ont même montré un lien entre les

Abbreviations: AF, Atrial fibrillation; ATP, Antitachycardia pacing; bpm, Beats per minute; ICD, Implantable cardioverter-defibrillator; LVEF, Left ventricular ejection fraction; SVT, Supraventricular tachycardia; VF, Ventricular fibrillation; VT, Ventricular tachycardia.

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Choc ; Prévention

chocs électriques internes et la mortalité totale. Contrairement aux autres complications, la fréquence de ces chocs peut (et doit) être diminuée grâce à une programmation adaptée. Cette revue de la littérature se focalise plus particulièrement sur les stratégies disponibles pour réduire la fréquence des chocs chez les patients implantés en prévention primaire pour une dysfonction systolique ventriculaire gauche, ainsi que sur les spécificités des appareils des différents constructeurs.

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Background

Implantable cardioverter-defibrillators (ICDs) significantly reduce all-cause mortality in the primary prevention of sudden cardiac death in patients at increased risk, especially those with a reduced left ventricular ejection fraction (LVEF). The Multicenter Automatic Defibrillator Implantation Trial II (MADIT-II) first established a strong mortality benefit for the ICD in patients with a LVEF $\leq 30\%$ and a previous myocardial infarction [1]. The reduction in total mortality was 31% in patients implanted with a prophylactic ICD compared with patients randomized to optimal medical therapy. This effect was durable, with a 34% reduction at 8 years by multivariable analyses; six patients had to be implanted to prevent one death [2]. The Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) confirmed these results in patients with a LVEF $\leq 35\%$ and ischaemic or non-ischaemic cardiomyopathy [3], finally leading to Class I recommendations in the current guidelines [4].

For the past 10 years, as the number of prophylactic ICD implantations has drastically increased, so have all the related complications: acute implant-related complications in up to 5% of patients (especially pocket haematoma, haemothorax, pneumothorax, cardiac tamponade); an almost 1% rate of 30-day mortality; lead dislodgement; pocket infection and lead-related endocarditis; lead and device failures; and inappropriate or unnecessary shocks [5].

The rate of inappropriate shocks during the first year of ICD implantation is reported to be 6–10%, affecting 11.5–17.4% of patients in major trials [6,7]. Such shocks are usually classified as supraventricular tachycardia (SVT)-related or oversensing-related inappropriate discharges. The former are the most frequent, due to the absence or failure of device discrimination algorithms, leading to the misdiagnosis of the supraventricular origin of arrhythmia as ventricular, whereas the latter can be ICD-related (QRS, T-wave or P-wave oversensing, inappropriate programming), lead-related (isolation defect, fracture, dislodgement) or environmental (electromagnetic interference, myopotentials).

The prevalence of unnecessary shocks is more difficult to quantify, as one cannot predict what would have happened if a shock had not been delivered to a ventricular arrhythmia. These are mainly represented by shocks to non-sustained ventricular tachycardias (VTs), which represent the majority of detected VTs. They may also be ICD-related, as antitachycardia pacing (ATP) can induce or accelerate ventricular arrhythmias and cause unnecessary shocks. Finally, the question of whether sustained asymptomatic VT should be treated remains controversial.

It is now well established that shocks, appropriate or not, are associated with significant morbidity, as they decrease quality of life, can be involved in depression and anxiety, and are known to be proarrhythmic [8–11]. Most recent data have even shown an association between shocks and overall mortality [6,7]. These data are easily explained: patients with more severe cardiomyopathy and a poorer prognosis usually present with a higher ventricular arrhythmia burden and thus may experience more appropriate shocks; most inappropriate shocks are related to atrial fibrillation (AF), which is one of the main factors associated with a poor outcome in patients with heart failure. Shocks were actually thought to reflect a more advanced cardiac disease. The results of the recent MADIT trial to reduce inappropriate therapy (MADIT-RIT) demonstrated that changing the ICD programming to reduce the rate of ICD shocks might lead to a reduction in overall mortality of up to 55% [12]. Even if the underlying mechanisms still remain unclear, the deleterious effects of shocks themselves, which can cause myocardial damage, may explain these findings. Shocks can be associated with an increased adrenergic response, inflammation and oxidative stress, which eventually may lead to an alteration of the patient's haemodynamics [13–15].

As opposed to other defibrillator-related complications, the rate of inappropriate and unnecessary shocks can be decreased with adequate programming. This review focuses on the different programming strategies available to reduce the rate of shocks in primary prevention patients with reduced LVEF, implanted with an ICD.

Supraventricular tachycardia discrimination

Discrimination is used to define the ability of the algorithms for differentiating non-ventricular-detected events from true ventricular tachyarrhythmias. The early generations of ICDs had only rate detection. Once the ventricular rate was detected above a preprogrammed rate during a minimal pre-specified duration, therapies were automatically delivered. The sensitivity (percentage of clinical ventricular arrhythmias accurately diagnosed as ventricular episodes) was high, but the specificity (percentage of accurately diagnosed ventricular arrhythmias among all ventricular episodes) was rather low, with a high-rate of inappropriate therapies. Algorithms were then progressively implemented in the software to improve specificity, while remaining safe (high sensitivity); they should be used routinely, but in patients with permanent complete atrioventricular block in which rapid ventricular rates can only have a ventricular origin.

Single-chamber algorithms

Three criteria are mainly used: the sudden onset criterion is able to discriminate sinus tachycardia from VT, as the former usually displays a gradual rate increase; the stability criterion can discriminate AF from VT, as the former usually displays irregular RR intervals; the morphology criterion is used to discriminate supraventricular from ventricular arrhythmia by comparing the similarity of the ventricular electrogram during tachycardia with a reference electrogram template acquired during a rhythm in which the supraventricular origin is certain.

These three main algorithms can usually be used in combination to improve discrimination accuracy. In a tiered-therapy cardioverter-defibrillator study, a programmed stability of 40ms (interval maximum variation between detected interval and any of the three previous intervals) decreased detection of AF by 95–99%, with a sensitivity for true VT episodes of 100% [16]. In the same study, a programmed sudden onset ratio of 87% (detected interval divided by the mean of the four preceding intervals) rejected 98% of sinus tachycardia episodes, while 0.5% of true VT episodes were misdiagnosed. A strategy of programming both stability and onset criteria has proven effective in decreasing the rate of inappropriate therapies by > 50% [17]. Some manufacturers have since implemented morphology algorithms (Table 1).

Dual-chamber algorithms

Addition of an atrial lead allows analysis of the atrioventricular relationship during arrhythmia. Each manufacturer uses its own approach, but the main principles are similar:

- if the ventricular electrograms are more frequent than the atrial electrograms ($V > A$), which is actually the case in >90% of VTs, the ventricular origin is certain;
- if the number of detected ventricular electrograms equals those from the atrium ($V = A$), the supraventricular origin is more probable, although VT with a 1:1 retrograde conduction cannot be ruled out;
- if the atrial electrograms are more frequent ($A > V$), the supraventricular origin is also more probable, although dual-tachycardia should also not be ruled out (VT in a patient with AF, for instance).

Single-chamber algorithms and PR association analyses are then implemented to achieve a final diagnosis (Figs. 1–5).

Single or dual-chamber?

If the Detect Supraventricular Tachycardia (DETECT SVT) study showed better specificity in dual-chamber patients, the rate of inappropriate therapies was significantly higher than in single-chamber patients [18]; this might be related to the prerequisite of reliable atrial sensing for accurate performance of dual-chamber algorithms. Atrial undersensing, especially frequent when AF occurs, atrial undercounting due to atrial blanking periods, and atrial oversensing

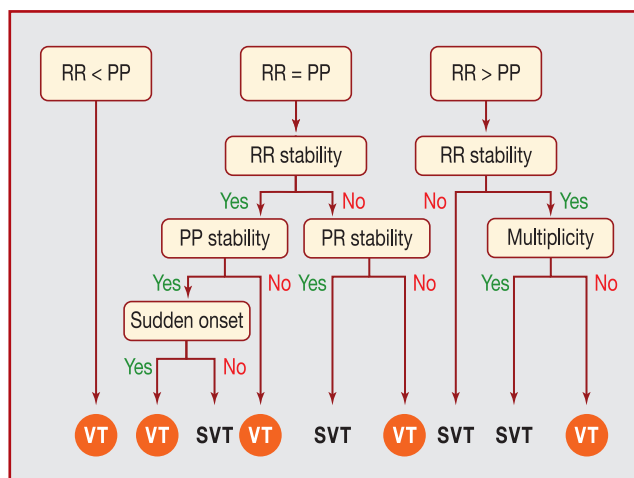


Figure 1. Biotronik SMART detection algorithm for dual-chamber implantable cardioverter-defibrillators. Atrial (PP intervals) and ventricular (RR intervals) cycle lengths are first compared; the rhythm is then checked for stability (RR, PP and PR intervals) in the RR = PP diagnostic branch, and for multiplicity (N:1 atrioventricular association) in the RR > PP branch. The RR < PP branch is diagnostic for ventricular tachycardia (VT). SVT: supraventricular tachycardia.

(often due to far-field R-wave sensing), may all impair dual-chamber discrimination and lead to inappropriate therapies. Moreover, it has been demonstrated that dual-chamber ICD implantations are associated with a 50% increase in perioperative adverse events and a two-fold increase in the perioperative mortality rate compared with single-chamber ICD implantations [19]. It is now accepted that dual-chamber ICDs should not be implanted in order to improve discrimination, but should be implanted in patients without permanent AF and needing to be paced.

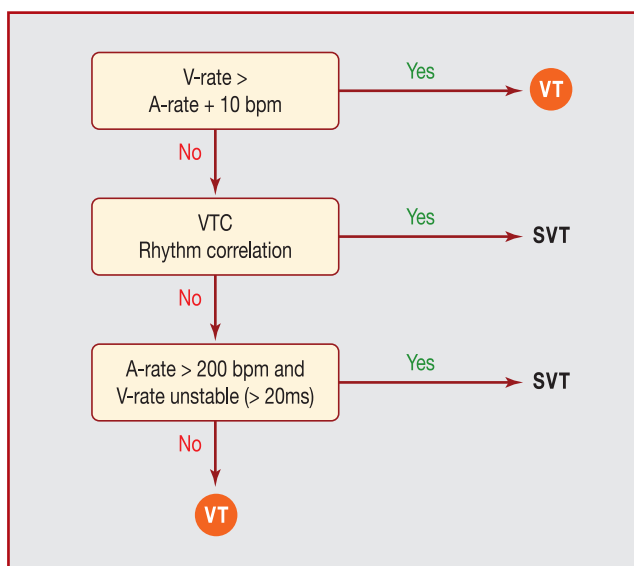


Figure 2. Boston Scientific Rhythm ID detection algorithm for dual-chamber implantable cardioverter-defibrillators. Diagnosis of ventricular tachycardia (VT) requires either a higher ventricular rate (V rate) than atrial rate (A rate) or a non-correlated morphology associated with stable RR intervals. SVT: supraventricular tachycardia; VTC: vector timing and correlation.

Table 1 Main discrimination algorithms specific to the latest generation of single-chamber implantable cardioverter-defibrillators.					
	Biotronik ^a	Boston Scientific ^b	Medtronic ^c	St. Jude Medical ^d	Sorin Group ^e
Sudden onset	Fulfilled if the average of the last four DIs is X% shorter than the average of the previous DI (eight DI sliding window) Nominal: X = 20%	Available with onset/stability only Fulfilled if the average of the four consecutive DIs following sudden onset is X% shorter than the average of the four consecutive DIs preceding the two intervals before sudden onset Nominal: X = 9%	Fulfilled if the average of four DIs is < X% of the average of the four previous DIs Nominal: X = 81%	Fulfilled if the average of the last four DIs is > X% (adaptive) or < Y ms (fixed) shorter than one of the averages of four consecutive DIs within the last eight DIs Nominal: X = 18%; Y = 100 ms	Fulfilled if a DI is > X% shorter than the average of the four previous DIs Nominal: X = 19%
Stability	Fulfilled if the difference between a DI and each of the three previous DIs is < X ms Nominal: X = 24 ms	Available with onset/stability, and with rhythm ID for redetection only Fulfilled if a DI varies by > X ms from the average variation of the five previous intervals Nominal: X = 30 ms (rhythm ID) or 20 ms (onset/stability)	Fulfilled if the fourth DI is within X ms of the three preceding DIs Nominal: X = 40 ms	Fulfilled if the difference between the second longest and the second shortest interval during a window of X consecutive DIs is < Y ms Nominal: Y = 80 ms; X = eight	Fulfilled if a majority (> X%) of DIs within the last Y intervals vary by < Z ms Nominal: X = 75%; Y = eight; Z = 65 ms
Morphology	None	Available with rhythm ID for initial detection only Vector timing and correlation: SVT is indicated if three of the last 10 complexes are similar (> X%) to template; VT is indicated if eight of the 10 last complexes are not correlated Nominal: X = 94%	Wavelet: detection is suspended if three of the last eight complexes are similar (> X%) to template; detection is fulfilled if six of the last eight complexes differ (< X%) from template Nominal: X = 70%	Far-field morphology discrimination: SVT is indicated if Y out of Z DIs are similar (> X%) to template Nominal: X = 90%; Y = three out of Z (= 10 DIs)	None
Others	None	None	None	None	Long cycle occurrence: therapy is inhibited for 24 cycles if a DI is longer than the average of the four previous DIs by > X ms Nominal: X = 170 ms

DI: detected interval within a VT therapy zone; SVT: supraventricular tachycardia; VT, ventricular tachycardia; X, Y and Z: programmable values.

^a Berlin, Germany.
^b Natick, MA, USA.
^c Minneapolis, MN, USA.
^d St. Paul, MN, USA.
^e Milan, Italy.

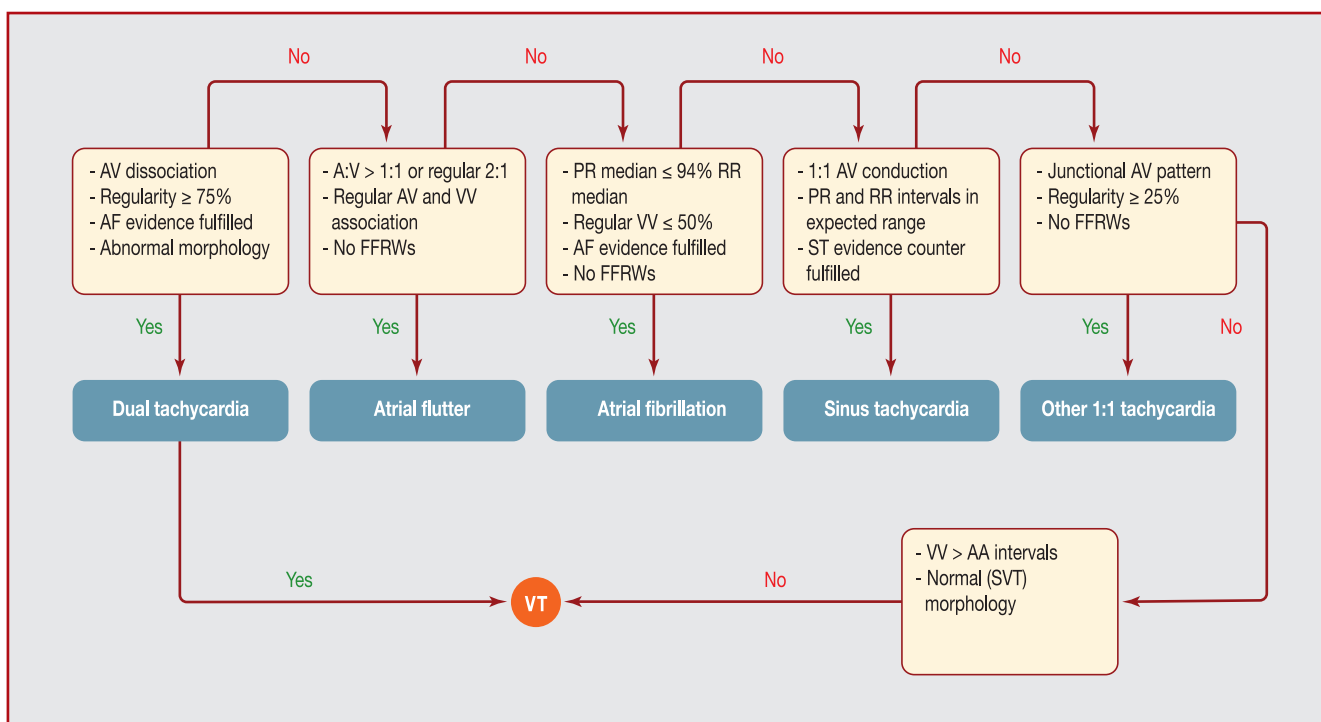


Figure 3. Medtronic enhanced PR Logic/Wavelet detection algorithm for dual-chamber implantable cardioverter-defibrillators. Tachyarrhythmias are classified according to prespecified patterns, according to atrioventricular (AV) relationship, morphology and regularity. A far-field R-wave (FFRW) algorithm is also used to discriminate ventriculoatrial crosstalk oversensing. A: atrial; AF: atrial fibrillation; ST: sinus tachycardia; SVT: supraventricular tachycardia; V: ventricular; VT: ventricular tachycardia.

Specificities of biventricular devices

Discrimination during cardiac resynchronization therapy usually uses the same dual-chamber algorithms, but in patients with chronic AF. As patients with biventricular devices are supposed to be paced permanently, a morphology algorithm may appear less relevant, as a template of

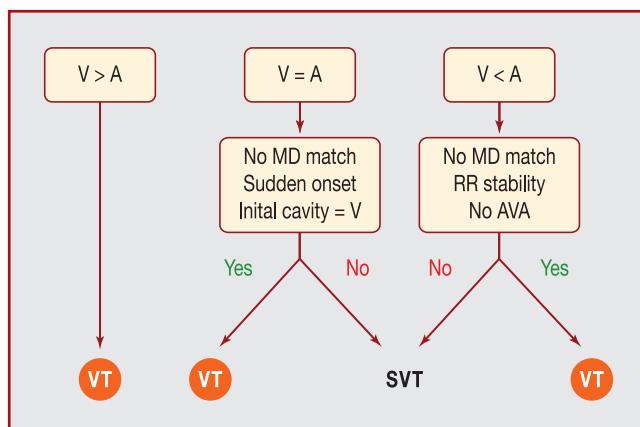


Figure 4. St. Jude Medical Discrimination algorithm for dual-chamber implantable cardioverter-defibrillators. Three decision branches according to atrioventricular relationship are initially used; discrimination is then performed using programmable single-chamber algorithms (morphology, sudden onset and stability). Initial cavity (chamber onset, atrial [A] or ventricular [V]) helps to discriminate 1:1 atrial tachycardia in the A=V branch. AVA: atrial ventricular association; MD match: morphology similar to template; SVT: supraventricular tachycardia; VT: ventricular tachycardia.

the spontaneous QRS might not be obtained. In Boston Scientific devices, for instance, a stability/onset algorithm is favoured over morphology.

Subcutaneous defibrillator

Cameron Health (Boston Scientific) has developed a specific discrimination algorithm for the S-ICD System, which uses, in a so-called “conditional zone”, three criteria for analysis of morphology:

- comparison of the QRS morphology with a memorized template (static morphology);
- comparison of the QRS morphology with the morphology of the previous complex (dynamic morphology);
- change in QRS width.

Three far-field sensing vectors are available for the analysis of morphology. A sensitivity for appropriate detection of ventricular tachyarrhythmias of 100% and a specificity for supraventricular arrhythmias of 98% were shown in the START study, in which S-ICD discrimination was even better than some conventional transvenous systems [20]. A standard shock zone is also programmable with rate-only detection.

Discrimination algorithms have become mandatory to reduce the rate of inappropriate detection of supraventricular arrhythmias and their subsequent treatment. The algorithms are rather diverse because of proprietary patents from the different manufacturers. A precise understanding of these algorithms is useful to appropriately reprogramme the device after a therapy is delivered.

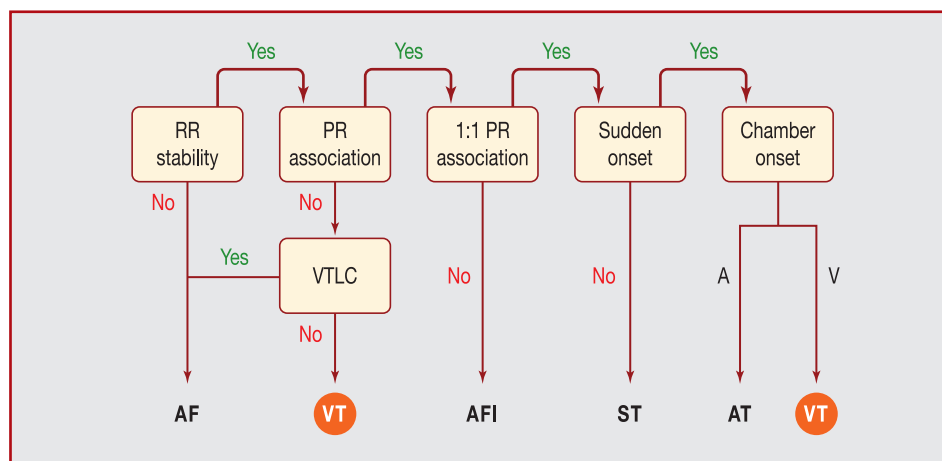


Figure 5. Sorin Group PARAD+ detection algorithm for dual-chamber implantable cardioverter-defibrillators. Discrimination is based on analysis of stability, PR association (N:1 atrioventricular association), long cycle occurrence (VTLC), sudden onset and chamber onset (atrial [A] or ventricular [V]), in this specific order. AF: atrial fibrillation; AFI: atrial flutter; AT: atrial tachycardia; ST: sinus tachycardia; VT: ventricular tachycardia.

Oversensing discrimination

Device-related oversensing

Around 10% of inappropriate therapies result from noise/artefact and oversensing [21]. Specific algorithms have been developed to avoid signal-related oversensing, and T-wave oversensing has become rare (2%), although it might still occur in specific situations (electrolyte abnormalities, drugs) or patients (low ventricular electrogram amplitude, hypertrophic cardiomyopathy, short/long QT and Brugada syndromes), usually causing ventricular double counting. All latest generation ICDs allow automatic adjustment of the sensitivity threshold on the detected R-wave amplitude, with smooth decay with time, usually preventing T-wave detection. Some manufacturers, such as Medtronic, Boston Scientific and St. Jude Medical, rely on algorithms to improve signal processing (frequency analysis with band-pass filters) and thus noise-to-signal ratio [22,23]. Biotronik and St. Jude Medical enable the adjustment of detection algorithms (threshold start value and decay delay), but these must be used with caution as they might compromise sensing of ventricular tachyarrhythmias.

Lead-related oversensing

Inappropriate shocks on oversensing are mainly related to lead fracture (up to 1.1% per year) [21]. Kleemann et al. reported a 40% rate of ICD lead dysfunction at 8 years [24]. These failures are often lead material and design specific, such as in the Medtronic Fidelis and St. Jude Medical Riata leads. Some algorithms have been developed based on signal processing, with analysis of both near-field and far-field electrograms (noise usually manifests on near-field signals), avoiding 83.7% of inappropriate shocks in a computer model study [23]. Coupled with variation in lead impedance measurements, the Medtronic algorithm, for instance, automatically prolongs detection duration and alerts the patient; this allowed a drastic reduction

in the rate of inappropriate shocks in patients implanted specifically with Sprint Fidelis leads [25], but may also be useful with non-Medtronic leads [26]. Detection of ventricular oversensing/noise events then withholds therapy delivery, without compromising sensitivity to ventricular arrhythmias. Combined with home monitoring, this allows rapid and adequate management of ICD lead defects in these patients (device deactivation and surgical revision) [27,28].

Other detection algorithms

Redetection

Occurring after therapy delivery, redetection determines whether an episode has terminated. Typically, three to eight intervals classified as sinus are required to terminate the treatment sequence. It is important to point out that during redetection, the discrimination algorithm uses fewer algorithms (or sometimes none) than are necessary during initial detection, depending on the manufacturer, to avoid delaying the next therapy. As stated by Koneru et al., reducing the number of redetection intervals might be interesting in some patients with incessant VT episodes associated with temporary efficacy of ATP, permitting repetition of the first sequence without moving towards more aggressive therapies [29]. Conversely, redetection duration may be increased if VT termination by ATP is systematically preceded by a transient acceleration.

Reconfirmation

These algorithms ensure whether an arrhythmia has self-terminated after capacitor charging. After charge completion, a window of a few detected beats allows shock abortion whenever detected intervals are longer than the maximum-programmed interval in the therapy zone. Inappropriate shocks may still be delivered if the

therapy zone (including the monitoring zone in some devices) is programmed to a long cycle length when a sinus tachycardia follows ventricular arrhythmia spontaneous resumption. A new shock algorithm from Medtronic addresses this concern by aborting therapy whenever re-detected intervals are ≥ 60 ms longer than the detected VT intervals.

Timers

These algorithms (called Sustained Rate Duration, High-Rate Time Out, SVT Time Out or Sustained VT) induce therapy delivery whenever an event (supraventricular or ventricular) lasts longer than a programmable duration value. There is a consensus that these algorithms should be turned to OFF to avoid inappropriate therapies for sustained SVT events.

Antitachycardia pacing

This mode of therapy consists of an overdrive pacing that employs ventricular stimulation at intervals that are shorter than the tachycardia cycle length. ATP offers several advantages: it has been proven to be a painless but effective therapy, reducing the necessity of shock delivery and hospitalization, improving patient quality of life, and increasing battery longevity.

Slow ventricular tachycardia

Below 180 bpm, ATP has been proven efficient in treating VT episodes [30], but therapies for low ventricular rates should not be initially programmed in primary prevention patients. Conversely, adding a monitoring zone for slow VT may be interesting to document symptomatic events.

Fast ventricular tachycardia

Above 180 bpm, ATP has been proven to efficiently treat most monomorphic VT episodes. Grimm et al. reported 86% of episodes terminated with ATP (mean VT rate: 204 bpm) [31]. In the PROVE trial, ATP (two bursts, eight stimuli, 88% of tachycardia cycle length) terminated 92% of VT episodes [32]. The PITAGORA (Project for the Investigation and Treatment of ventricular Arrhythmias: a General Observational Registry on Antitachycardia pacing efficacy) ICD trial randomly compared two ATP strategies for fast VT episodes > 187 bpm (one sequence of 88% coupling interval, eight-pulse burst versus one sequence of 91% coupling interval, eight-pulse ramp) and demonstrated a 75% efficacy for burst versus 54% for ramp [33]. A 15-pulse ATP strategy did not show any superiority over an eight-pulse strategy [34]. More recently, Martins et al. showed that one or two sequences of ATP terminated $> 98\%$ of fast VT episodes (average of 1.1 ATP sequences), but programming up to 10 attempts (five bursts then five ramps) remained safe, while avoiding shocks in 12.4% of patients [35].

If ATP programming is selected, there is enough evidence to suggest that at least two sequences of ATP should be programmed, with eight stimuli bursts at 88% of the tachycardia cycle length.

Ventricular fibrillation zone

In the ventricular fibrillation (VF) zone, ATP should be programmed before or during charging, when available, as it has proven safe and efficient. Schoels et al. reported efficacies for monomorphic and polymorphic VT episodes of 77% and 44%, respectively [36].

Shocks

Although the subject remains controversial, current data do not support the systematic testing of the defibrillation threshold or safety margin [37]. Therefore, until further data are available, programming maximum energy shocks routinely can be recommended. Beyond better efficacy, they have not been proven to be more painful than lower energy shocks and the slightly longer capacitor charging time may allow arrhythmias (appropriately or inappropriately detected) to self terminate.

Zone programming

In primary prevention patients, two programming options may appear relevant: single zone programming with a VF zone (discrimination OFF) and a monitoring-only zone below; dual-zone programming with a VT zone (discrimination ON) with ATP followed by shocks, and a VF zone above.

The latter strategy may not necessarily be more efficient than programming for a single (VF) zone. Duncan et al., in a retrospective study, compared patients programmed for a single VF zone (mean > 193 bpm) with patients programmed for two-zones (mean VT zone > 171 bpm, mean VF zone > 205 bpm) [38]. The two-zone group actually received more appropriate shocks than the group with a single VF zone (22% and 12%, respectively). As efficient as it can be, ATP is only useful if a true SVT event is not misdiagnosed as VT. Moreover, ATP programming may not always prevent symptoms, as it may only delay the occurrence of an efficient therapy; it may also accelerate non-sustained VT and provoke unnecessary ICD shock. In the study by Grimm et al., this was the case in up to 14% of VT episodes and 48% of patients [31]. More recently, Schukro et al. showed that 8.5% of patients presented with accelerated ventricular tachyarrhythmias within a mean follow-up of > 5 years, mainly caused by appropriate ATP, and that this was associated with a higher mortality rate [39].

The same concerns can be applied to inappropriate therapies. In MADIT-II, the incidence of inappropriate shocks was 11.5% [6]. Similarly, in the Pacing Fast VT Reduces Shock Therapies (PainFREE Rx II) trial, 15% of primary prevention patients had inappropriate therapies, despite the systematic use of ATP for fast VT episodes (> 188 bpm) [40]. In the Detect Supraventricular Tachycardia Study, inappropriate therapies remained very frequent and 31% of SVT episodes were inappropriately detected [18]. In a "real-life" prospective study of 1544 patients (mean follow-up 41 months) at least one inappropriate shock occurred in 13% of ICD recipients [41]. Devices were programmed with a monitoring zone of 150–188 bpm, a VT zone with two bursts

of ATP of 188–210 bpm and a shock-only zone above. Inappropriate shocks were related to SVT or sinus tachycardia episodes in 76% of cases (11.5% of patients). In the study by Duncan et al., inappropriate shocks were also more frequent in the two-zone programming group (10% vs 2%) [38]. There was no SVT-related inappropriate shock in the single VF zone group.

Detection duration

Programming long detection intervals is effective in reducing both appropriate and inappropriate therapies. The EMPIRIC (Comparison of Empiric to Physician-Tailored Programming of Implantable Cardioverter-Defibrillators) trial has already shown that standardized programming with longer intervals (18 of 24) in the VT zone is associated with a significant reduction in shocks of any cause [42]. The Primary Prevention Parameters Evaluation (PREPARE) study compared a long-delay strategy (30 of 40 detection intervals for fast VT > 182 bpm, 30 of 40 for VF zone > 250 bpm) with a standard programming cohort [43]. After 12 months of follow-up, the rate of appropriate shocks in the long-delay group was 8.5% (43% reduction) and the rate of inappropriate shocks was 3.6% (a 52% reduction). The RELEVANT (Role of long dEtection window programming in patients with LEft Ventricular dysfunction, Non-ischemic eTiology in primary prevention treated with a biventricular ICD) study used 30 of 40 detection intervals in non-ischaemic patients, with an 84% reduction in inappropriate shocks [44]. Interestingly, > 90% of VT episodes detected after 12 intervals spontaneously resumed before reaching 30 intervals. Most VT episodes are non-sustained, and if ATP is very efficient, it is also probably useless for the majority of episodes and may lead to a significant amount of unnecessary shocks. Indeed, an 88% reduction in appropriate therapies was observed in the long-delay group. There was also a trend towards reduction in appropriate shocks in the long-delay group, although this was not significant. The usefulness of a strategy of programming a 30 of 40 intervals detection window was recently confirmed in the randomized ADVANCE III trial [45].

The MADIT-RIT trial randomized 1500 primary prevention patients into three groups:

- a standard ICD programming group (170–199 bpm VT zone with a 2.5 s delay, ≥ 200 bpm VF zone with a 1.0 s delay);
- a high-rate cut-off programming group (170–199 bpm monitoring zone, ≥ 200 bpm VF zone with a 2.5 s delay);
- a prolonged-delay programming group (170–199 bpm VT1 zone with a 60 s delay, 200–249 bpm VT2 zone with a 12 s delay, ≥ 250 bpm VF zone with a 2.5 s delay) [12].

After a mean follow-up of 1.4 years, the reduction in occurrence of first inappropriate therapy in the long-delay group compared with in the standard programming group was 76%. The reduction in all-cause mortality was 44%.

When treating in the VT zone is decided upon, it is safe to say that detection duration should exceed 30 of 40 intervals in Medtronic devices before ATP, and eventually shocks, are delivered. Appropriate detection timings with the (very) different classification and binning algorithms of other major manufacturers still wait to be assessed, but detection should

be programmed in order to exceed 10 s between tachycardia onset and therapy delivery [46,47]. However, despite a drastic improvement in discrimination algorithms, SVT episodes may still be inappropriately detected and then treated if sustained. Thus, in the RELEVANT study, around 90% of inappropriate episodes were related to SVT, both in the group programmed with longer detection intervals and in the control group.

Detection rate

In the SCD-HeFT trial, a single VF zone at 188 bpm was programmed (18 of 24 beats), leading to a high incidence of shocks for VT episodes that may have been asymptomatic and non-sustained [7]. Some of these appropriate shocks may then have been unnecessary therapies for appropriately detected episodes. Indeed, the PainFREE Rx II trial found that approximately 34% of the fast VT episodes terminated spontaneously during capacitor charging [40]. Inappropriate shocks are also very frequent with a low rate single zone (up to 17.4% in SCD-HeFT), as SVT episodes are not discriminated.

In a recent study, we showed that high-rate cut-off programming (single VF zone > 220 bpm) appeared to be safe and effective in maintaining a low rate of inappropriate shocks (6.6% of patients at 40 months) [48]. SVT-related inappropriate shocks were only present in 2.7% of the patients after a mean follow-up of 3.5 years. Most inappropriate shocks were related to oversensing (58%). The maximum ventricular rate during SVT should rarely exceed 220 bpm, as confirmed by the results of the Altitude Reduces Study, which showed a majority of inappropriate shocks for an event rate < 200 bpm and a majority of appropriate shocks for an event rate ≥ 200 bpm [49]. The authors concluded that increasing rate detection to ≥ 200 bpm resulted in a four-fold reduction in overall shock risk of both appropriate and inappropriate therapies and was not associated with excess mortality.

The MADIT-RIT trial confirmed these results, with a 79% reduction in first inappropriate therapy occurrence and even a 55% reduction in all-cause mortality in the high-rate group (cut-off at 200 bpm), without difference in risk of syncope [12].

Programming a single-therapy zone without discrimination (VF zone) < 200 bpm should not be performed in primary prevention patients, as this strategy is related to a high-rate of both appropriate and inappropriate shocks.

Higher or later?

No direct comparison has been made between high-rate and long-delay strategies, as it was not prespecified in the MADIT-RIT study design [50]. Both strategies are succinctly compared in Table 2.

Overall, if these strategies can be used safely, as discussed previously, programming one single VF zone should be associated with a high-rate cut-off (≥ 200 bpm), while programming therapies in the VT zone should be associated with rather long detection duration (≥ 10 s) (Fig. 6).

Table 2 Pros and cons of long-delay versus high-rate implantable cardioverter-defibrillator programming strategies in primary prevention patients.

	Long-delay	High-rate
Pros	Sustained VT episodes < RCO are appropriately treated Efficient and painless ATP can be extensively used	SVT episodes < RCO cannot be inappropriately treated Asymptomatic VT episodes < RCO are not treated Monitoring episodes < RCO allow adequate reprogramming if necessary
Cons	Sustained SVT episodes < RCO may be inappropriately treated Asymptomatic VT episodes < RCO are treated ATP may cause unnecessary shocks	Symptomatic sustained VT episodes < RCO are not treated VT episodes \geq RCO are rapidly treated with shocks

ATP: antitachycardia pacing; RCO: rate cut-off for VF zone in the high-rate strategy; SVT: supraventricular tachycardia; VT: ventricular tachycardia.

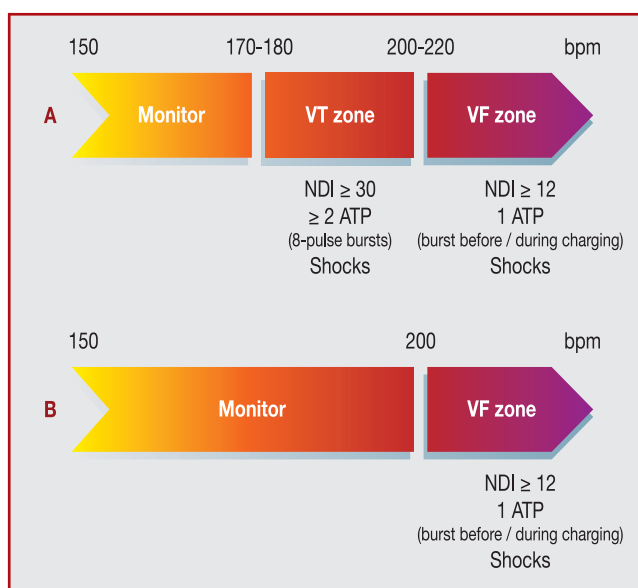


Figure 6. Examples of programming strategies in primary prevention patients. A. Long-delay programming requires up to three zones: a monitoring zone, a ventricular tachycardia (VT) zone with a number of detection intervals (NDI) of 30 or more below 200 beats per minute (bpm) (\geq 10s detection time), which might even be extended up to 60s as in MADIT-RIT, and a ventricular fibrillation (VF) zone. Antitachycardia pacing (ATP) should also be prioritized before shocks below 200 bpm. Over 200 bpm, programming an FVT zone with ATP up to 250 bpm is also possible. B. High-rate cut-off programming uses a monitoring zone below 200 bpm, and a shock zone above. ATP burst should be used before or during charging in the shock zone.

Conclusions

Careful programming of ICDs in primary prevention should remain a major concern for physicians after implantation (Table 3). Several studies have recently raised the importance of reducing both inappropriate and unnecessary therapies, and manufacturers have made several tools available in order to achieve this goal. The recent results from the MADIT-RIT trial, showing the effect of adequate

Table 3 Basic tips for programming implantable cardioverter-defibrillators in primary prevention patients.

Bradycardia pacing should be minimized in non-biventricular devices (VVI mode at 40 bpm, algorithms for reduction of ventricular pacing)

Dual-chamber is not superior to single-chamber discrimination; an atrial lead should be implanted only if pacing is needed

Discrimination algorithms should be used below 200 bpm, but in patients with complete atrioventricular block

Prolonged detection time should be used before delivering therapies below 200 bpm (typically > 10 s or 30 intervals)

ATP should precede shocks below 250 bpm; the slower the detection rate, the more ATP sequences should be used

Maximum energy shocks should be used

A monitoring zone should be used, but should not exceed 200 bpm

Redetection and reconfirmation should be used; discrimination timers should be turned off

Algorithms to negate oversensing (noise, T-wave, etc.) should be used

ATP: antitachycardia pacing; bpm: beats per minute.

programming in reducing overall mortality in these patients, have made this programming phase even more crucial.

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