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Review Article

Optimal programming management of ventricular tachycardia storm in ICD patients

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Abstract

Ventricular tachycardia storm (VTS) is defined as a life-threatening syndrome of three or more separate episodes of ventricular tachycardia (VT) leading to implantable cardioverter defibrillator (ICD) therapy within 24 hours. Patients with VTS have poor outcomes and require immediate medical attention. ICD shocks have been shown to be associated with increased mortality in several studies. Optimal programming in minimization of ICD shocks may decrease mortality. Large controlled trials showed that long detection time and high heart rate detection threshold reduced ICD shock burden without an increase in syncope or death. As a fundamental therapy of ICD, antitachycardia pacing (ATP) can terminate most slow VT with a low risk of acceleration. For fast VT, burst pacing is more effective and less likely to result in acceleration than ramp pacing. One algorithm of optimal programming management during a VTS is presented in the review.

Keywords: implantable cardioverter defibrillator, optimal programming, ventricular tachycardia storm

Introduction

Implantable cardioverter defibrillator (ICD) has revolutionized the preventive treatment of patients at risk for sudden cardiac death and has been widely used for these high-risk individuals [1-3]. However, ICD does not target the pathological substrate responsible for ventricular arrhythmias. Consequently, a certain percentage of ICD recipients experience multiple episodes of ventricular tachycardia (VT) and/or ventricular fibrillation (VF) in a syndrome called "electrical storm" (ES). ES is a devastating event and associated with an adverse prognosis and reduced quality of life [4]. The review focuses on VT storm (VTS) and optimal programming strategies for VTS in ICD patients.

Although there is still no consensus on formal definition of VTS, it is generally accepted that three or more separate episodes of VT leading to ICD therapies [antitachycardia pacing (ATP) or shock] over a 24 hour period constitute VTS^[4-6]. The end of a VTS is defined as termination of ES without VT recurrence in two weeks^[7]. No study to date has examined the threshold burden of ventricular arrhythmias which would result in an adverse outcome. Whether ventricular arrhythmias should rely on ICD therapies and how to define the time interval of separate episodes of VT are still unsettled. The definition of VTS remains empiric and is subject to amendment pending the results of large outcome studies^[6].

Occurrence of VTS and its implication

In patients who have ICDs for secondary prevention of sudden cardiac death, 10%–20% will experience a

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VTS within two years of ICD implant^[8]. In contrast, the incidence is lower for primary prevention patients at 4% over an average of 20.6 months^[6]. Possible triggering factors are acute heart failure, acute myocardial ischemia, electrolyte disturbance, acute infection, and abnormal sympathetic activity. However, there are still other undetermined causes which were reported to account for 64% of VTS events^[9].

A meta-analysis showed that ICD for secondary prevention, monomorphic VT as triggering arrhythmia, lower ejection fraction and class I anti-arrhythmic drugs were associated with ES, which could be used to define high risk populations for $\mathrm{ES}^{^{[10]}}$. Advanced age and male gender in ES patients had a trend towards increased prevalence, but with no statistical significance. One study observed that the combination of left ventricular ejection fraction < 25% and QRS duration > 120 ms was a powerful predictor of the occurrence of $\mathrm{ES}^{^{[11]}}$.

Many studies have consistently found that VTS is associated with higher mortality in both secondary and primary prophylaxis patients. A recent meta-analysis enrolling 5,912 cases showed that ES was a strong mortality risk factor, which accounted for a 3.2-fold increased risk of death and was associated with a 3.4-fold increased risk for the composite endpoint of death, heart transplantation, and hospitalization for heart failure^[10]. However, whether VTS directly contributes to increased mortality or is merely a marker of progression of the underlying disease remains elusive^[5-6]. In fact, it has also been shown that repeated ICD shocks delivered for treatment of refractory VT might contribute to the progression of heart failure and cardiac injury, which in turn increases mortality^[12].

The occurrence of VTS seriously impairs the quality of life and psychological status of the patients^[4-6]. As a clinical emergency, physicians should intervene early to prevent the recurrence of ventricular arrhythmias.

The comprehensive management of VTS includes seeking and eliminating the triggering factors using sedation, anti-arrhythmic drugs, ICD programming, catheter ablation and/or cardiac sympathetic denervation. Optimization of programming to prevent unnecessary shocks is paramount to these patients.

Optimal programming strategies of VTS in ICD patients

The detection and treatment of ventricular arrhythmias by an ICD involves a series of sequential steps, each of which provides an opportunity to prevent unnecessary shocks (*Fig. 1*). These steps include heart rate detection, number of intervals to detect (NID), tachycardia detection, supraventricular tachycardia (SVT)-VT discrimination, VT confirmation, ATP, reconfirmation, and shock. During a VTS, optimal programming to minimize unnecessary shocks is discussed in detail based on the recent trials (*Table 1*).

Prolongation of arrhythmia detection time

The use of prolonged arrhythmia detection time is one programming strategy that has been widely evaluated [13-16]. The prospective, multicentre, non-randomized 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 compared a long VT/VF detection vs. standard ICD programming (NID 30/40 vs. 12/16) and showed that longer detection time reduced overall ICD therapy burden and heart failure hospitalizations without any increase of syncope or death in primary prevention of non-ischemic heart failure patients [13]. The PROVIDE (Programming Implantable Cardioverter Defibrillators in Patients with Primary Prevention Indication to Prolong Time to First

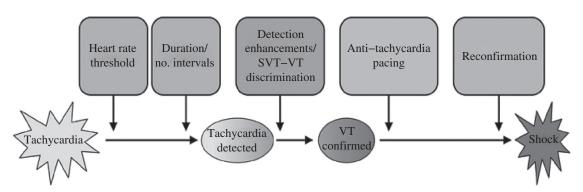


Fig. 1 Overview of detection and treatment of ventricular tachyarrhythmias by implantable cardioverter defibrillator (ICD). The detection and treatment of ventricular tachyarrhythmias by an ICD involves a sequence of events which provide opportunities for optimal programming. SVT: supraventricular tachycardia; VT: ventricular tachycardia.

Table 1. Clinical trials of shock reduction programming

			Follow-up			Secondary		
Study	Year	Cases	time	Design	CAD (%)	prevention (%)	Detection group	Control group
PainFREE Rx II ^[22]	2004	634	11 months	RCT	85	52	FVT: 188–250 bpm; NID 18/24; ATP; Shock	FVT: shock
PREPARE ^[20]	2008	1391	1 year	OBS	64	0	VF: 250 bpm; NID 30/40 FVT: 182 bpm; NID 30/40; ATP × 1 VT: 167 bpm; NID 32; monitor only	Physician tailored
RELEVANT ^[13]	2009	324	14 months	OBS	0	0	VF: 182–500 bpm; NID 30/40 FVT: 182–250 bpm; NID 30/40 ATP × 1 VT: 167–182 bpm; NID 32	VF: NID 12/16 VT: NID 16
MADIT-RIT ⁽¹⁵⁾	2012	1500	1.4 years	RCT	53	0	High-rate therapy group: VF: 200 bpm; 2.5s; ATP × 1 VT: 170 bpm; monitor only Delayed group: VF: 250 bpm; 2.5s; ATP × 1 FVT: 200 bpm; 12s; ATP × 1 VT: 170 bpm; 60s; ATP × 1	VF: 200 bpm; 1s; ATP × 1 VT: 170 bpm; 2.5s; ATP × 1
ADVANCE III ^[16]	2013	1902	12 months	RCT	60	25	VF: 188 bpm; NID 30/40; ATP × 1 VT: 150 bpm; NID 32; monitor only	VF: 188 bpm; NID 18/24; ATP × 1 VT: 150 bpm; NID 32; monitor only
PROVIDE ^[14]	2014	1670	530 days	RCT	62	0	VF: 250 bpm; NID 12 VT2: 214 bpm; NID 18; ATP \times 1 VT1: 181 bpm; NID 25; ATP \times 2	VF: 214 bpm; NID 12 VT2: 181 bpm; NID 12; ATP × 2 VT1: 150 bpm; NID 12; monitor only
PainFree SST ⁽¹⁸⁾	2014	1308	10.6 months	OBS	43	34	VF: 188 bpm (or faster if VT enable Primary prevention: NID 30/40; Secondary prevention: NID randomized to 18/24 vs. 30/40 SVT Limit: 230 bpm SST algorithms: ON	ed)

OBS: observational, nonrandomized study; RCT: randomized clinical trial; NID: number of intervals to detect; VT: ventricular tachycardia; VF: ventricular fibrillation; FVT: fast ventricular tachycardia; SVT: supraventricular tachycardia; ATP: antitachycardia pacing; CAD: coronary artery disease.

Shock) study reported that in a large cohort of patients, a combination of programmed parameters including higher detection rate, longer detection intervals, empiric ATP, and optimized SVT discriminators were associated with a significant reduction of ICD shock therapy with reduction in all-cause mortality and without increasing arrhythmic syncope^[14]. The MADIT-RIT (Multicenter Automatic Defibrillator Implantation Trial-Reduce Inappropriate Therapy) study was a large randomized controlled trial and included 1,500 patients^[15]. In this study, patients were randomly assigned to the delayed (with a 60-second delay at 170 to 199 bpm, a 12-second delay at 200 to 249 bpm, and a 2.5-second delay at

≥ 250 bpm) and the conventional groups. The results showed that programming with a prolonged delay was associated with reductions in inappropriate therapy and all-cause mortality. The recent ADVANCE III (Avoid Delivering Therapies for Non-sustained Arrhythmias in ICD Patients III) trial has demonstrated that the use of a long detection interval (30 out of 40 intervals), combined with ATP during charging, significantly reduces the rate of appropriate therapies (ATP and shocks) and inappropriate shocks in comparison with the standard detection interval (18 out of 24) in single, dual and triple chamber ICDs, regardless of indication [16]. The ADVANCE III trial confirmed and

reinforced the results of MADIT-RIT in a larger and broader primary prevention ICD population. A meta-analysis including the above four trials concluded that the use of long detection time could significantly decrease the burden of inappropriate shock therapy (RR 0.50) and all-cause mortality (RR 0.77) without significant increase in the risk of syncope^[17].

The PainFree SST trial was designed to evaluate the inappropriate shock free rate at one-year post implant in primary and secondary prevention patients with single, dual and triple chamber ICDs by SmartShock Technology (SST)^[18]. The primary results showed that over 98% of the patients were free of inappropriately shocked episodes during their first year after implantation and no difference was detected between primary (1.6% with inappropriate shocks) and secondary (2.3%)prevention patients. A cohort of secondary prevention patients were randomized in a 1:1 fashion to either a standard interval (NID = 18/24) or prolonged interval (NID = 30/40) detection of VT/VF ≥ 188 bpm (VF zone). In this large randomized trial involving high-risk secondary prevention patients, longer detection intervals did not increase the risk of syncope, ensuring the safety of this programming strategy. Prolonged interval detection programming did not impact the rates of inappropriate shocks, which were low using advanced discrimination algorithms in both groups at one year.

In conclusion, the increase of detection time could prevent both inappropriate shocks (shocks for rhythms other than VT or VF) and unnecessary shocks (shocks for self-terminating episodes) in patients with VTS. However, we should closely evaluate the status of cardiac function to determine if each individual could tolerate possible risk resulted from the delayed therapy of malignant ventricular arrhythmias. Additionally, VT may recur immediately after successful ATP, which

may lead to misclassification of unsuccessful ATP, and subsequent unnecessary shocks may be delivered^[5]. In some ICDs, we can decrease the number of intervals for declaring an end of episode to obtain an early definition of return to sinus rhythm.

Increasing heart rate detection threshold

According to the heart rate, programmable zones are strictly defined. ICDs usually provide three zones, VT, fast VT (FVT), and VF. The description of arrhythmia characteristics in ICD patients with primary and secondary prevention indications could guide the settings of programmable zones^[19]. A shorter VT cycle length (CL, 303 ± 54 ms vs. 366 ± 71 ms) and a longer SVT CL (363 \pm 70 ms vs. 323 \pm 75 ms) are found in patients with primary preventive ICDs compared with those with secondary prevention indications (Fig. 2). These data indicate that ICD patients of primary prevention have faster VT and smaller overlap of SVT and VT; as a result, these patients may benefit from higher rate detection zones. On the contrary, patients with a secondary prevention indication will benefit from slower detection zones and SVT-VT discrimination algorithms because of the greater overlap between SVT and VT. Several trials have investigated the strategy combined with longer detection time in primary prevention patients.

In the PREPARE (Primary Prevention Parameters Evaluation) study, detection rate was set to 182 bpm (FVT) and VF 250 bpm^[20]. In the MADIT-RIT trial, detection rate for ventricular arrhythmias was set to 200 bpm with a 2.5-second delay in the high-rate therapy group^[15]. Similarly, the PROVIDE study defined VT, FVT and VF zones as 181 bpm, 214 bpm, and 250 bpm, respectively^[14]. Consistently, these high

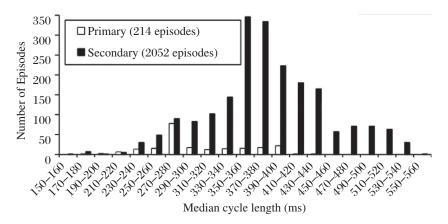


Fig. 2 Rates of ventricular arrhythmias detected in 978 patients in whom an ICD was implanted for primary and secondary prevention. Patients with primary preventive ICDs have a shorter cycle length of ventricular tachycardia compared with secondary preventive patients and may benefit from higher detection zones. (Cited from: Wilkoff BL, et al. J Cardiovasc Electrophysiol. 2004;15(9):1002–1009^[19] with permission)

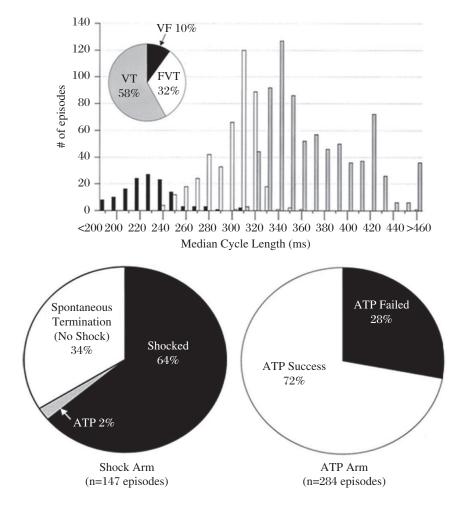


Fig. 3 Results of the PainFree Rx II (Pacing Fast Ventricular Tachycardia Reduces Shock Therapies) trial. The upper graph shows distribution of ventricular arrhythmias by detection zone and median cycle length. The pie charts show percentages of terminating therapy for FVT episodes in each arm. ATP could terminate FVT in 72% of episodes. FVT: fast ventricular tachycardia; ATP: antitachycardia pacing. (Cited from: Wathen MS, et al. Circulation. 2004;110(17):2591–2596^[22] with permission)

heart rate detection groups had significant reductions in ICD shocks without an increase in syncope or death. In Mayo Clinic, the recommended detection rate of primary prevention patients is set to 200 bpm with a 5-to 9-second delay for ICD therapies^[5].

Increasing the efficacy of ATP

ATP is rapid pacing at a CL shorter than VT that terminates reentrant VT by penetrating the circuit and blocking the reentry. ATP can reduce unnecessary shocks, improve quality of life, and lengthen pulse generator life. Previous studies have demonstrated that ATP terminated 85%–90% of slow VT (< 188–200 bpm) with a low risk of acceleration $(1\%-5\%)^{[21]}$. In PainFREE Rx II (Pacing Fast Ventricular Tachycardia Reduces Shock Therapies) trial, patients were randomized to ATP followed by shock or shock alone for the treatment of FVT (188–250 bpm)^[22]. The results showed that a single 8-pulse burst of ATP was successful in

terminating FVT in 72% of episodes and resulted in a significant reduction in shocks with improved quality of life and low rates of VT acceleration and syncope (*Fig. 3*). However, recent studies showed that efficacy of ATP with longer NID was not as high as previously reported. In ADVANCE III trial, ATP efficacy for FVT (CL 240–320 ms) was 54% [generalized estimating equation (GEE) adjusted]. One latest report showed that a new automatic ATP algorithm (an initial ATP train based on heart rate history, subsequent trains based on post-ATP interval and shocks applied at timer expiry) improved ATP efficacy for FVT to 59% (GEE adjusted)^[23].

ATP mode selection

ATP was usually classified as burst if all paced beats were delivered at the same CL, and ramp if the beat-to-beat pacing CL was shortened within each pacing train. Burst and ramp pacing sequences have similar efficacy

Condition	Arrhythmia	Programming
Primary prevention	VF: ≥ 200 bpm	Longer detection time or 30 of 40 NID. Use 1–2 sequences of burst.
	FVT: 170–199 bpm	Monitor only.
Secondary prevention	VF: ≥ 200 bpm	30 of 40 NID. Use 1–2 sequences of burst.
	FVT: 170-199 bpm	Use multiple sequences of ATP.
	VT: < 170 bpm	Monitor only.

Table 2. Suggested ICD programming for specific ICD indications

ICD: Implantable cardioverter defibrillator; NID: number of intervals to detect; VT: ventricular tachycardia; VF: ventricular fibrillation; FVT: fast ventricular tachycardia.

in slow VTs^[21]. For FVT with CL < 300 ms, burst is more effective and less likely to result in acceleration than ramp. One study has investigated the efficacy of four ATP modes, including burst, ramp, scan (if the

pacing CL was shortened between each pacing train), and ramp/scan (if the pacing CL was shortened both between and within each pacing train). As a result, when the VT rate was > 200 bpm, ATP was less successful,

Finding out and eliminating the possible reversible factors. Sedation; anti–arrhythmic drug use.

Preparing advanced cardiac life support.



ICD programming:

- Prolong or disable safety features.
- Prolong duration or NID, especially for primary prevention ICDs.
- Increase heart rate detection threshold, especially for primary prevention ICDs.
- Use burst or scan for FVT.
- Use 1–2 sequences of ATP for FVT.

Use 1-3 sequences of ATP in primary prevention ICDs.

Use multiple sequences of ATP for slow VT.

Use multiple sequences of ATP in secondary prevention ICDs.

- Adjust RS1 or add burst+ or ramp+.
- Change to biventricular or left-ventricular pacing in biventricular ICDs
- Increase the lower pacing rate, especially for long–pause dependent ventricular arrhythmias.
- Turn off ICD.



IABP.

Catheter ablation.

Long-term anti-arrhythmic drug use.

Fig. 4 A flowchart of optimal programming strategies during a ventricular tachycardia storm. NID: number of intervals to detect; VT: ventricular tachycardia; FVT: fast ventricular tachycardia; ATP: antitachycardia pacing; IABP: intra-aortic balloon pump.

however, burst and scan exhibited greater efficacy (81.2% and 87.1% respectively) compared with ramp $(57.1\%)^{^{[24]}}$.

Multi-site ATP

Several studies have reported greater success with biventricular ATP. One retrospective and observational study showed that in heart failure patients with biventricular (BiV) ICD, ATP efficacy of left ventricular (LV) and BiV pacing was higher than right ventricular (RV) ATP BiV-ATP and LV-ATP were safer than RV-ATP for slow VT (150–188 bpm). The ADVANCE CRT-D trial was a randomized and controlled multicenter trial aimed at comparing the efficacy and safety of BiV- versus RV-ATP in heart failure patients treated with cardiac resynchronization therapy-defibrillator left. The results showed that BiV-ATP seemed to be more effective and safer in ischemic patients than RV-ATP.

Multi-sequence ATP

The majority of FVTs were successfully treated by one or two ATP attempts. Only a small minority of patients were responsive to > 3 ATPs. Programming a high number of ATP attempts in the FVT zone is both safe and efficient and could prevent shocks in ICD recipients [27]. One latest study demonstrated that a second burst pacing increased the effectiveness of ATP (GEE-adjusted, 65% vs. 75%) for FVT (CL 250–320 ms) and therefore, reduced the need for high-energy shocks [28].

Adjusting R-S1 interval (%RR)

Generally, burst CL should be 85%–90% of the VT CL for FVTs and 70%–80% for slow VTs^[21]. When an unsuccessful ATP occurred, analysis of the return CL is helpful to optimize ICD programming^[5]. The CL of the drive train could be shortened or an extrastimulus added at the end of the drive train (for example, "burst +" mode) in order to penetrate the circuit. If the CL of VT is unaffected, increasing the number of paced beats could facilitate penetrating the circuit by peeling away refractoriness.

Anti-arrhythmic drug therapy

Intensive therapy of the anti-arrhythmic drugs, especially β -blockers and amiodarone, could help decrease the VT rate and increase the ATP efficacy^[29].

Increasing the lower pacing rate temporally

In some patients, overdrive pacing by increasing the lower pacing rate of the ICD may avoid the long pause after a ventricular ectopic beat, shorten the QT interval and suppress recurrent VT/VF, particularly if dual chamber pacing is available [5,30].

Overall, during a VT storm, ICD programming should focus on minimizing shocks. *Table 2* shows the suggested optimal programming for shock reduction based on ICD indications. Importantly, safety features that a shock is applied after a programmable time window independently from ATP should be prolonged or disabled^[5]. Additionally, ICD therapies are often turned off in hospitalized patients. Catheter ablation might be the only option when a VTS is refractory to programming and drug therapies. A flowchart of optimal programming management during a VTS is exhibited in *Fig. 4*.

Conclusion

VTS, a life-threatening emergency, is associated with poor prognosis in ICD patients and requires immediate medical attention. Optimal programming aiming at reducing inappropriate or unnecessary shocks may provide up to a 30% relative decrease in mortality with no apparent increase in the risk of syncope ^[31]. During a VTS, ICD programming focuses on minimizing the frequency of shocks. Long detection time and high heart rate detection threshold are key methods, especially for primary prevention patients. ATP therapy should be intensified in many ways including ATP mode, number of sequences, and pacing sites. However, the comprehensive management of VTS including optimal pharmacological therapy, sedation, trigger or substrate ablation and denervation is comparably essential.

The optimal programming strategies from the present clinical trials are mostly aimed at ICD patients for primary prevention of sudden cardiac death. Future studies are needed to clarify the roles of different programming strategies on secondary prevention patients.

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