Reducing ICD Shocks for Ventricular Arrhythmias

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KEYWORDS

- Ventricular arrhythmia
- Implantable-cardioverter defibrillator • ICD shocks
- Defibrillation

Implantable cardioverter-defibrillators (ICDs) reduce mortality among high-risk patients with indication for primary or secondary prevention of sudden cardiac death.[1–3] Defibrillator shock therapy comes at a cost, however. Defibrillator shocks are acutely painful[4,5] and chronically detrimental to quality of life, due to diminished mental and physical well-being.[6–9] Both appropriate and inappropriate shocks are associated with subsequent mortality,[10–13] although causality has yet to be proved. Capacitor charging in anticipation of shock delivery results in considerable battery drain, decreased ICD longevity, and earlier ICD replacement. For all these reasons, reducing ICD shocks for ventricular arrhythmias is an important goal.

Current strategies aimed at reducing appropriate ICD shocks include device optimization, medical therapy, and catheter ablation. Device optimization may include programming changes to increase utilization of antitachycardia pacing (ATP), to increase the number of intervals to detect (NID) ventricular arrhythmia (VA), and to reconfirm VA immediately before shock delivery.

Device optimization may also include implantation of a left ventricular pacing lead for purposes of cardiac resynchronization therapy (CRT) and biventricular ATP in selected patients. Medical therapy may include β-blockers and amiodarone or class III antiarrhythmic drugs, whereas for drug-refractory patients, catheter ablation may achieve remission from ICD shocks.

ANTITACHYCARDIA PACING TO REDUCE ICD SHOCKS

ATP refers to the delivery of ventricular paced beats at coupling intervals slightly shorter than the ventricular tachycardia (VT) cycle length, with intent to penetrate an excitable gap in the VT circuit. Antidromic collision with the "head" of the VT wavefront and orthodromic block at the refractory "tail" of the VT may terminate tachycardia.

In slow VT, the excitable gap is typically large, so ATP more easily terminates the tachycardia. In fast VT, the excitable gap is shorter and ATP termination may be less reliable. Historically, this theoretic concern and fear of rate acceleration lead to underutilization of ATP for fast VT.

Prior to the Pacing Fast Ventricular Tachycardia Reduces Shock Therapies (PainFREE Rx) trials,[14,15] evidence for ATP safety was limited and mostly retrospective. For example, the Bilitch ICD Registry compared 1553 patients with shock-only ICDs to 550 patients with ATP-capable ICDs. After 24 months, survival was 89% in the shock-only group but improved to 94% in the ATP-capable group,[16] indicating potential survival benefit. Other early studies demonstrated that ATP successfully terminates 78% to 94% of slow VT (variably defined as <188 to 200 bpm), with only 2% to 4% risk of VT acceleration.[17–21]

The PainFREE Rx trials extended confidence in ATP as initial therapy to fast VT (defined as 188

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to 250 bpm). Published in 2001, the PainFREE Rx I trial enrolled 220 patients with coronary artery disease and a secondary prevention indication for ICD implantation. Coronary artery disease was chosen as a prerequisite to increase the likelihood of macroreentrant VT in the study population, and a secondary prevention indication was necessary for ICD implantation because that was the standard of care at the time, pre–Multicenter Automatic Defibrillator Implantation Trial II (MADIT II). All patients received an ICD programmed to deliver ATP (2 bursts and 8 pulses; 88% of the VT cycle length minus 10 ms between bursts) as initial therapy after detection of fast VT, defined as 12 of 16 R-R intervals at 240 to 320 ms. During a mean follow-up period of 6.0 $\pm$ 3.6 months, 1100 episodes of VA occurred, of which 624 (57%) were slow VT, 446 (40%) were fast VT, and 30 (3%) were ventricular fibrillation (VF). Eighty-five percent of fast VT episodes were successfully treated by the first ATP attempt (77% when adjusted for multiple episodes per patient). ATP accelerated VT rarely (4%), and there were no episodes where shock therapy was not successful after failed ATP. The median duration of fast VT episodes was 6 seconds when ATP was successful, and 21 seconds when shock therapy was required, such that syncope was rare (2%). Limitations of the trial included its nonrandomized/no-comparator design, focus on coronary artery disease, and permissive 12 of 16 NID that may have deemed ATP successful in episodes that would otherwise have been nonsustained. Moreover, the study was limited to a single manufacturer's ICDs (Medtronic).

The PainFREE Rx II trial resolved many of these issues, with a randomized design comparing ATP (1 burst and 8 pulses; 88% of VT cycle length) with shock for initial therapy of fast VT, defined as 18 of 24 R-R intervals at 240 to 320 ms. Inclusion criteria were broader, excluding only patients believed unlikely to have monomorphic VT susceptible to ATP (eg, hypertrophic cardiomyopathy, long QT syndrome, and Brugada syndrome). A total of 634 patients were enrolled, with 313 patients randomized to the ATP arm and 321 to the shock arm. During a mean follow-up period of 11 $\pm$ 3 months, 1342 episodes of VA occurred, of which 777 (58%) were slow VT, 431 (32%) were fast VT, and 134 (10%) were VF. Eighty-one percent of fast VT episodes were successfully treated by ATP (72% when adjusted for multiple episodes per patient). When compared with the shock arm, programming ATP as initial therapy resulted in a relative shock reduction of 70%. On a per-patient basis, 80% of patients benefited from ATP. No significant differences were observed in acceleration (2% ATP arm and 1% shock arm), median episode duration (10 seconds in ATP arm and 9.7 seconds in shock arm), syncope (2 episodes in ATP arm and 1 episode in shock arm), or sudden death (1 in ATP arm and 2 in shock arm). Taken together, PainFREE Rx II provided clear evidence that ATP is highly effective in treating fast VT.

The findings of PainFREE Rx II were subsequently confirmed in the Comparison of Empiric to Physician-Tailored Programming of Implantable Cardioverter-Defibrillators (EMPIRIC) trial,[22] which randomized 900 ICD patients to standardized (n = 445) or physician-tailored (n = 455) programming. Standardized programming was similar to the ATP arm of PainFREE Rx II, with ATP (1 burst and 8 pulses; 88% of VT cycle length) provided as initial therapy for fast VT, defined as 18 of 24 R-R intervals at 240 to 300 ms. In addition, burst then ramp ATP was enabled for slow VT, and Medtronic's proprietary supraventricular tachycardia discrimination algorithm was turned on. Although the EMPIRIC trial was not designed to compare specific programming options, the increased utilization of ATP on the standardized arm, when coupled with the high efficacy (92%) of ATP for VT, resulted in a significant reduction in shocked episodes of VT (13%) in the standardized arm compared with the physician-tailored arm (21%). This was accomplished with no significant differences in incidence of VT acceleration or syncope. Thus, it seems reasonable to program ATP as initial therapy for both slow and fast VT in all patients regardless of clinical presentation. For example, modeling of outcomes anticipated if EMPIRIC programming had been utilized in the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) has suggested that the number of shocked VA episodes could have been reduced by 59% and the percentage of patients receiving shocks for VA could have been reduced from 31% to 26%.[23]

Increased utilization of ATP not only may reduce pain but also may reduce mortality. After pooling data from 2135 patients in 4 pivotal trials incorporating ATP to reduce shocks (PainFREE Rx,[14] Pain-Free Rx II,[15] EMPIRIC,[22] and Primary Prevention Parameters Evaluation [PREPARE][24]), predictors of mortality (n = 138; 6.5%) were identified.[13] Whereas ATP-terminated fast VT did not increase mortality, shocked fast VT increased risk by 32%. Survival rates were highest among patients with no VA (93.8%) or treated with ATP only (94.7%), and lowest for shocked patients (88.4%) over 10.8 $\pm$ 3.3 months' follow-up. Although this analysis could not exclude the possibility that ATP-refractory (and necessarily shocked) VT may be a marker for higher-mortality risk patients, the